As confidentially submitted to the Securities and Exchange Commission on September 8, 2017.
This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

DENALI THERAPEUTICS INC.
(Exact name of Registrant as specified in its charter)

Delaware	2836	46-3872213
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080
(650) 866-8548
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Ryan J. Watts, Ph.D.
President and Chief Executive Officer
Denali Therapeutics Inc.
151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080
(650) 866-8548
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Tony Jeffries Jennifer Knapp Wilson Sonsini Goodrich & Rosati, P.C. 650 Page Mill Road Palo Alto, California 94304 (650) 493-9300	Steve E. Krognes Chief Financial Officer and Treasurer Denali Therapeutics Inc. 151 Oyster Point Blvd., 2nd Floor South San Francisco, California 94080 (650) 866-8548	Alan F. Denenberg Stephen Salmon Davis Polk & Wardwell LLP 1600 El Camino Real Menlo Park, California 94025 (650) 752-2000

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price (1)(2)	Amount of Registration Fee (3)
Common Stock, $0.01 par value per share	$	$

(1) Includes offering price of any additional shares of common stock that the underwriters have the option to purchase.
(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
(3) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended, based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION. DATED ,

Shares

Common Stock

This is an initial public offering of shares of common stock by Denali Therapeutics Inc.

Prior to this offering, there has been no public market for our common stock. It is currently estimated that the initial public offering price will be between $ and $ per share.

We intend to apply to list our common stock on under the symbol "DNLI."

We are an "emerging growth company" as defined under the federal securities laws and, as such, have elected to comply with certain reduced reporting requirements for this prospectus and may elect to do so in future filings.

Investing in our common stock involves risks. See the section titled "Risk Factors" beginning on page 12 to read about factors you should consider before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities, or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts(1)	$	$
Proceeds to Denali Therapeutics Inc., before expenses	$	$

(1) See the section titled "Underwriting" for additional information regarding compensation payable to the underwriters.

To the extent that the underwriters sell more than shares of common stock, the underwriters have the option to purchase up to an additional shares from us at the initial public offering price less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on , .

Goldman Sachs & Co. LLC **Morgan Stanley** **J.P. Morgan**

Prospectus dated , .

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Prospectus

Through and including , 2017 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

We and the underwriters have not authorized anyone to provide you any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: we have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus and is qualified in its entirety by the more detailed information and financial statements included elsewhere in this prospectus. It does not contain all of the information that may be important to you and your investment decision. You should carefully read this entire prospectus, including the matters set forth under the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes. In this prospectus, unless context requires otherwise, references to "we," "us," "our," "Denali," or "the company" refer to Denali Therapeutics Inc.

Overview

We discover and develop therapeutics to defeat degeneration.

Neurodegeneration represents one of the most significant unmet medical needs of our time, with few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or ALS, and other neurodegenerative diseases. We believe the time is right to make a focused and ambitious effort to defeat neurodegeneration. Recent genetic insights are revealing the underlying biology of neurodegeneration and potential drug targets while enabling better patient selection, similar to how genetic insights have transformed the field of oncology. Identifying and selecting targets based on validated genetic drivers of neurodegeneration is a core principle of our strategy. The second core principle of our strategy is to develop medicines that effectively cross the blood-brain barrier, or BBB, and target the brain. We have engineered a proprietary BBB platform technology that we believe will allow therapeutically relevant concentrations of our product candidates in the brain. The third core principle of our strategy is to develop biomarkers that enable better patient selection and can demonstrate target and pathway engagement of our product candidates. By executing this strategy with a team of passionately dedicated scientists and drug developers, we believe we can succeed in a field that has shown limited progress over the past several decades.

Our Team

We have assembled a team with a deep set of scientific, clinical, business and leadership capabilities in biotechnology, and specifically in neurodegenerative diseases, who worked together at Genentech for many years prior to the founding of Denali. Our Co-Founder and Chief Executive Officer, Ryan J. Watts, Ph.D., is a world-leading drug developer and neuroscientist, with particular expertise in BBB therapeutic delivery. Dr. Watts most recently led the neuroscience research team at Genentech and has led multiple discovery teams, including programs in Alzheimer's disease, Parkinson's disease and ALS. Our Co-Founder and Chief Operating Officer, Alexander O. Schuth, M.D., MBA, held various operational and leadership roles at Genentech for nearly ten years, including leading the partnering groups for neuroscience as well as technology innovation and diagnostics. Dr. Schuth has led more than 35 partnering transactions and a clinical stage development program. Our Co-Founder and director, Marc Tessier-Lavigne, Ph.D., is a world-leading neuroscientist, was formerly Chief Scientific Officer at Genentech and serves as President of Stanford University. Carole Ho, M.D., our Chief Medical Officer, brings over a decade of clinical development experience, most recently as Vice President, Non-Oncology Early Clinical Development at Genentech. Dr. Ho has overseen or contributed to more than ten IND filings and three drug approvals. Our Chief Financial Officer, Steve E. Krognes, MBA, brings over two decades of operational and corporate finance experience, most recently serving six years as Chief Financial Officer and member of the Executive

Committee at Genentech. Mr. Krognes has led more than 40 strategic deals and led or contributed to several capital raising transactions.

Our leadership team is joined by about 120 employees, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, they bring expertise across relevant disciplines, including neuroscience, BBB biology, genetics, oncology, immunology, translational science, antibody engineering, chemistry and biomarker development.

To complement our internal capabilities, we have entered into arrangements with biopharmaceutical companies such as Genentech and F-star, patient-focused data companies such as 23andMe and Patients Like Me, numerous leading academic institutions such as Harvard University, Massachusetts General Hospital, Washington University in St. Louis, the University of California, San Diego and Vlaams Instituut voor Biotechnologie, and foundations such as the Michael J. Fox Foundation to gain access to new product candidates, enable and accelerate the development of our existing programs and deepen our scientific understanding of certain areas of biology. We believe that accessing external innovation is important to our success, and we plan to remain active in accessing external innovation through business development activities.

Our Strategy

Our strategy is guided by three overarching principles:

- **Genetic Pathway Potential**: We select our therapeutic targets and disease pathways based on degenogenes, which are genes that when mutated cause, or are major risk factors for, neurodegenerative diseases.
- **Engineering Brain Delivery**: We engineer our product candidates to cross the blood-brain barrier and act directly in the brain.
- **Biomarker-Driven Development**: We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates.

We believe that the application of these principles will significantly increase the probability of success and will accelerate the timing to bring effective therapeutics to patients with neurodegenerative diseases.

Degenogenes

Since 2007, the number of genetic associations discovered in neurodegenerative diseases has grown rapidly, with more than 100 genes associated with Alzheimer's disease, Parkinson's disease and ALS collectively. As the cost of genome sequencing has decreased, there has been an increase in the discovery of genetic mutations that have been linked to neurodegeneration (Figure A).

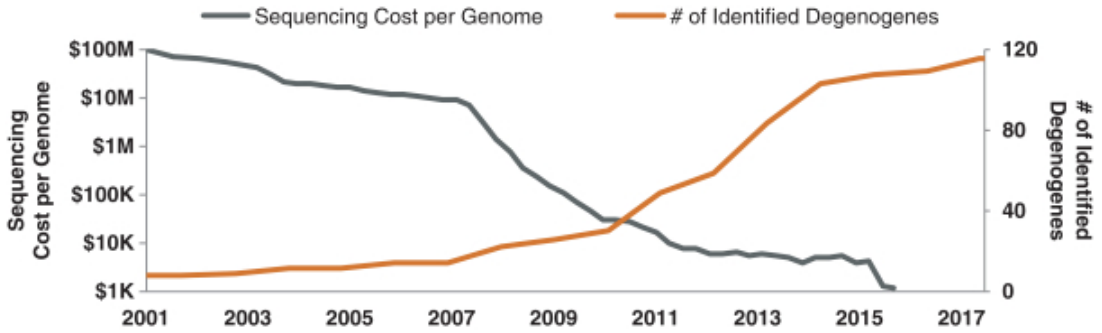


Figure A: This figure shows the increasing number of identified degenogenes linked to Alzheimer's disease, Parkinson's disease and ALS from 2001 to 2017 and the declining cost of genome sequencing from 2001 to October 2015 (the latest date for which we have data). There has been a dramatic reduction in the cost of DNA sequencing which has recently led to the discovery of numerous genetic mutations that have been linked to Alzheimer's disease, Parkinson's disease and ALS.

The degenogenes directly point to important disease pathways that are disrupted in neurodegeneration and are our scientific foundation for identifying and pursuing promising targets for drug development. We have chosen to initially focus on three such pathways:

- **Lysosomal Function**: Dysfunction of the lysosomal system is associated with several neurodegenerative diseases, including Parkinson's disease and neurodegeneration in the context of lysosomal storage diseases, or LSDs. Degenogenes linked to lysosomal function include LRRK2, aSyn and lysosomal enzymes, including IDS and GBA.
- **Glial Biology**: Degenogenes implicate immune dysfunction in the brains of patients with Alzheimer's disease and other neurodegenerative diseases. These genes include TREM2 and numerous other genes that are highly expressed in inflamed microglia, the resident immune cells of the brain. We believe the impact of immune modulation in neurodegeneration is a promising approach to treating disease. Specifically, RIPK1, a kinase downstream of the TNF receptor pathway, is overactive in inflamed microglia and several other cells in the brain.
- **Cellular Homeostasis**: Defects in protein, RNA or metabolic homeostasis lead to the death of neurons and dysfunction of the nervous system. This includes spreading of protein aggregates resulting in proteinopathy in Alzheimer's and Parkinson's diseases. The clearance of macromolecules in the brain is particularly susceptible to imbalances that result in aggregation and degeneration in nerve cells. Degenogenes linked to cellular homeostasis include APP, Tau and APOE.

BBB Platform Technology

Our proprietary BBB platform technology is designed to effectively transport antibodies (antibody transport vehicle, or ATV) and enzymes (enzyme transport vehicle, or ETV) across the BBB. This technology is designed to engage specific BBB transport receptors, which are ubiquitously expressed

in brain capillaries and facilitate transport of proteins into the brain (Figure B). In an animal model, an antibody engineered with our ATV technology has demonstrated over 20-fold greater brain penetration than a control antibody not enabled by this technology. This improvement in brain exposure may enable therapeutically relevant concentrations of our ATV antibody product candidates in the brain, making them potentially superior to traditional monoclonal antibody therapeutics.

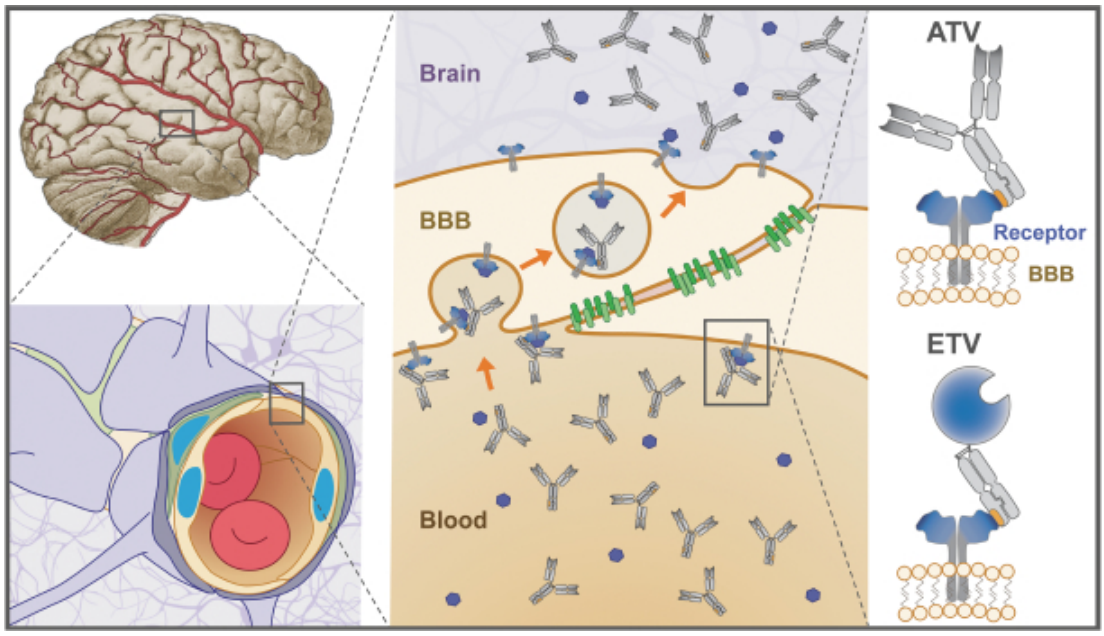


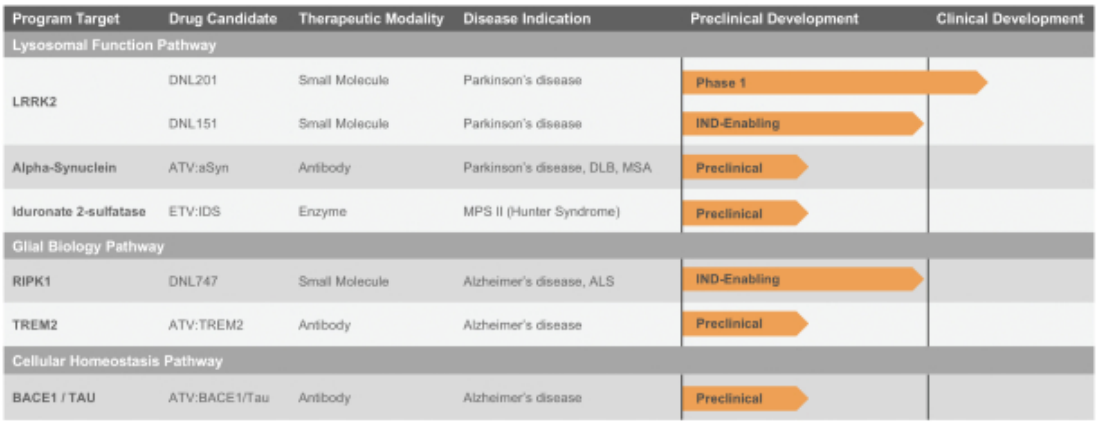
Figure B: Engineering brain delivery. Schematic of the ATV and ETV technologies, designed to cross the BBB through receptor-mediated transcytosis, leveraging endogenous receptors expressed on endothelial cells in the vasculature of the brain.

Biomarkers

As part of our strategy, we are using available reagents as well as developing proprietary reagents and assays to create biomarkers for each of our core programs. These biomarkers, which are relevant for both animal models and human trials, are critical for patient selection, measuring target engagement, supporting dose selection and enabling decisions on progression of product candidates to the next phase of development. We have identified target engagement biomarkers for all six of our core programs. Further, we are developing patient selection biomarkers for these programs.

Our Programs

We have a focused yet diversified portfolio that currently consists of six core and five seed programs. Our most advanced program targets LRRK2 for the treatment of Parkinson's disease and has a product candidate currently in Phase 1 development. Our next most advanced program targets RIPK1 for the treatment of Alzheimer's disease and ALS and currently has a product candidate in IND-enabling studies with an IND or CTA filing planned for early 2018. In addition, we have four core programs in preclinical development that use our proprietary BBB platform technology.



ATV: Antibody Transport Vehicle; **ETV**: Enzyme Transport Vehicle; **DLB**: Dementia with Lewy Bodies; **MSA**: Multiple System Atrophy; **MPS II**: Mucopolysaccharidosis Type II; **ALS**: Amyotrophic Lateral Sclerosis.

Our lead LRRK2 product candidates, DNL201 and DNL151, are potent, selective and brain penetrant small molecule inhibitors of LRRK2. LRRK2 regulates lysosomal genesis and function, which is impaired in Parkinson's disease and may be restored by LRRK2 inhibition. Mutations in the LRRK2 gene are the most frequent genetic cause of Parkinson's disease and a major driver of lysosomal dysfunction, which contributes to the formation of Lewy body protein aggregates and neurodegeneration. DNL201 is currently in a single and multiple ascending dose study in healthy volunteers. We expect data from this study to establish CSF exposure and target engagement by the first half of 2018. These data, if positive, will demonstrate our ability to safely deliver therapeutically relevant concentrations of DNL201 to the brain and achieve sufficient target engagement to drive therapeutic efficacy which will be evaluated in future patient trials. We plan to submit an IND or CTA for DNL151 in the fourth quarter of 2017.

Our lead RIPK1 product candidate, DNL747, is a potent, selective and brain penetrant small molecule inhibitor of RIPK1 for Alzheimer's disease and ALS. Microglia are the resident immune cells of the brain and play a significant role in neurodegeneration. RIPK1 activation in microglia results in production of a number of pro-inflammatory cytokines that can cause tissue damage. Pending the results from our IND-enabling preclinical studies, we plan to submit an IND or CTA for DNL747 in early 2018 and initiate a Phase 1 clinical trial in healthy volunteers in the first half of 2018.

Our four other core programs all leverage our proprietary BBB platform technology to deliver antibody-based or enzyme-based therapies to the brain. Our three antibody programs are against known targets including aSyn, TREM2 and a bi-specific therapeutic agent against both BACE1 and Tau. Our BACE1 and Tau program is an example of combination therapy, which we believe holds significant promise in developing effective therapies in neurodegenerative diseases. We believe each of these programs have characteristics that may allow for them to be best in class. Our fourth program is an enzyme replacement therapy for MPS II patients in which we deliver IDS to the brain. Neurodegeneration is a hallmark of MPS II patients that is not addressed by current enzyme replacement therapies which fail to reach the brain.

We have development and commercialization rights to all of our core programs, and we have a broad patent portfolio supporting our core programs.

Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should consider before investing in our company. These risks are described more fully in the section titled “Risk Factors” in this prospectus. These risks include, but are not limited to, the following:

- We are in the early stages of clinical drug development and have a very limited operating history and no products approved for commercial sale.
- We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.
- If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.
- We are heavily dependent on the successful development of our BBB platform technology and the product candidates currently in our core programs, which are in the early stages of preclinical and clinical development.
- We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products.
- We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- We have concentrated our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development.
- The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable.
- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours.
- If we are unable to obtain and maintain patent protection for any product candidates we develop and for our BBB platform technology, our competitors could develop and commercialize products and technology similar or identical to ours.
- We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop.
- Our rights to develop and commercialize our BBB platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

Corporate Information

We were incorporated in Delaware in 2013. Our principal executive offices are located at 151 Oyster Point Blvd., 2nd Floor, South San Francisco, California 94080. Our telephone number is (650) 866-8548. Our website address is www.denalitherapeutics.com. Information contained on the website is not incorporated by reference into this prospectus, and should not be considered to be part of this prospectus.

We use Denali Therapeutics®, the Denali Therapeutics logo, and other marks as trademarks in the United States and other countries. This prospectus contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. We will remain an emerging growth company until the earliest to occur of: the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; the issuance, in any three-year period, by us of more than $1.0 billion in non-convertible debt securities; and the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the SEC. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company may take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, upon completion of this offering we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

THE OFFERING	
Common stock offered by us	shares
Common stock to be outstanding after this offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full)
Underwriters' option to purchase additional shares of common stock from us	shares
Use of proceeds	We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the estimated initial public offering price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $ million. We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, through 2019 as follows: (1) to fund the costs of Phase 1 trials in healthy volunteers for each of DNL201 and DNL151 and a Phase 1b study in LRRK2 mutation-carrying Parkinson's disease patients, as well as preparation for a potential future Phase 2 clinical trial; (2) to fund the costs to advance our RIPK1 program through Phase 1 and early Phase 2 clinical development, substantially represented by the planned Phase 1 clinical trial in healthy volunteers for DNL747, a Phase 2a clinical trial in ALS patients and a Phase 2a clinical trial in Alzheimer's disease patients; (3) to optimize and broaden our ATV and ETV platform technologies and to advance our four core antibody and enzyme replacement programs through preclinical development and IND-enabling activities; (4) if we exercise our option to acquire all outstanding shares of F-star Gamma, to fund the initial exercise payments; and (5) the remainder to fund seed programs, general research and development activities, working capital and other general corporate activities. See the section titled "Use of Proceeds" for additional information.
Proposed trading symbol	"DNLI"

The number of shares of our common stock to be outstanding after this offering is based on the 288,674,403 shares of our common stock (including convertible preferred stock on an as-converted basis) outstanding as of June 30, 2017, and excludes the following:

- 23,816,215 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of June 30, 2017, at a weighted-average exercise price of $0.65 per share;
- 1,320,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after June 30, 2017, at a weighted-average exercise price of $2.40 per share;
- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
  - 1,461,675 shares of common stock reserved for future issuance under our 2015 Stock Incentive Plan, as amended, or our 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Equity Incentive Plan, or our 2017 Plan;
  - shares of common stock reserved for future issuance under our 2017 Plan, which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans;” and
  - shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans.”

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a -for- reverse stock split of our common stock and convertible preferred stock effected on ;
- no exercise of outstanding options;
- no exercise by the underwriters of their option to purchase up to an additional shares of our common stock from us;
- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 234,401,367 shares of our common stock, which will occur immediately prior to the closing of this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the effectiveness of our amended and restated bylaws, which will occur immediately prior to the closing of this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial data for the periods and as of the dates indicated. We have derived the consolidated statements of operations and comprehensive loss data for the years ended December 31, 2015 and 2016 from our audited consolidated financial statements included elsewhere in this prospectus. The consolidated statements of operations and comprehensive loss data for the six months ended June 30, 2016 and 2017 and the balance sheet data as of June 30, 2017 have been derived from our unaudited interim condensed consolidated financial statements included elsewhere in this prospectus and have been prepared in accordance with generally accepted accounting principles in the United States of America on the same basis as the annual audited consolidated financial statements and, in the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, necessary for the fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of results that may be expected in the future, and results for the six months ended June 30, 2017 are not necessarily indicative of the results to be expected for the full year ending December 31, 2017. You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing elsewhere in this prospectus and the information in the sections titled “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share amounts)			
Consolidated Statements of Operations and Comprehensive Loss Data:				
Operating expenses:				
Research and development	$ 11,571	$ 75,702	$ 31,153	$ 37,474
General and administrative	5,108	11,731	5,572	6,838
Total operating expenses	16,679	87,433	36,725	44,312
Loss from operations	(16,679)	(87,433)	(36,725)	(44,312)
Interest income (expense), net	(109)	781	38	858
Net loss	(16,788)	(86,652)	(36,687)	(43,454)
Other comprehensive income (loss)	—	(373)	16	(4)
Comprehensive loss	$ (16,788)	$ (87,025)	$ (36,671)	$ (43,458)
Net loss per share, basic and diluted (1)	$ (1.40)	$ (3.37)	$ (1.69)	$ (1.16)
Weighted-average number of shares outstanding, basic and diluted (1)	12,025,514	25,698,880	21,742,166	37,380,492
Pro forma net loss per share, basic and diluted (unaudited) (1)		$ (0.44)		$ (0.16)
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited) (1)		195,696,975		271,781,859

(1) See the consolidated statements of operations and Note 12 to our consolidated financial statements, and the condensed consolidated statements of operations and Note 8 to our unaudited condensed consolidated financial statements, for further details on the calculation of net

loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts and unaudited pro forma information.

	As of June 30, 2017		
	Actual	Pro Forma (1)	Pro Forma As Adjusted (2)
		(in thousands) (unaudited)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents and marketable securities	$ 212,839	$ 212,839	$
Working capital (3)	178,531	178,531	
Total assets	231,379	231,379	
Total liabilities	18,055	18,055	
Convertible preferred stock	348,673	—	
Accumulated deficit	(146,966)	(146,966)	
Total stockholders' equity (deficit)	(135,349)	213,324	

(1) The pro forma balance sheet data in the table above reflects the conversion of our outstanding shares of our convertible preferred stock into 234,401,367 shares of our common stock, which will occur immediately prior to the closing of this offering and the filing and effectiveness of our amended and restated certificate of incorporation.

(2) The pro forma as adjusted balance sheet data in the table above reflects the pro forma adjustments described in footnote (1) above plus the sale and issuance by us of shares of our common stock in this offering, based upon the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and marketable securities, working capital, total assets and total stockholders' equity (deficit) by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of one million shares in the number of shares offered by us would increase (decrease) each of cash, cash equivalents and marketable securities, working capital, total assets and stockholders' equity (deficit) by approximately $ million, assuming the assumed initial public offering price of $ per share remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

(3) We define working capital as current assets less current liabilities. See our condensed consolidated financial statements for further details regarding our current assets and current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this prospectus, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Business, Financial Condition and Capital Requirements

We are in the early stages of clinical drug development and have a very limited operating history and no products approved for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are an early clinical-stage biopharmaceutical company with a limited operating history, focused on developing therapeutics for neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis, or ALS. We commenced operations in May 2015, have no products approved for commercial sale and have not generated any revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have only recently begun a Phase 1 clinical trial for our most advanced product candidate, DNL201, which is in our LRRK2 core program, and have not initiated clinical trials for any of our other current product candidates. To date, we have not initiated or completed a pivotal clinical trial, obtained marketing approval for any product candidates, manufactured a commercial scale product, or arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful product commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

We have incurred net losses in each reporting period since our inception, including net losses of $86.7 million and $16.8 million for the years ended December 31, 2016 and 2015, respectively, and $43.5 million for the six months ended June 30, 2017. As of June 30, 2017, we had an accumulated deficit of $147.0 million.

We have invested significant financial resources in research and development activities, including for our preclinical and clinical product candidates and our blood-brain barrier, or BBB, platform technology. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and our ability to generate revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We expect to continue to incur significant expenses and increasingly higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and discovery activities;

- continue the development of our BBB platform technology;
- progress our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical or other studies for our product candidates;
- work with our contract manufacturers to scale up the manufacturing processes for our product candidates or, in the future, establish and operate a manufacturing facility;
- change or add additional contract manufacturers or suppliers;
- seek regulatory approvals and marketing authorizations for our product candidates;
- establish sales, marketing and distribution infrastructure to commercialize any products for which we obtain approval;
- acquire or in-license product candidates, intellectual property and technologies;
- make milestone, royalty or other payments due under any license or collaboration agreements;
- obtain, maintain, protect and enforce our intellectual property portfolio, including intellectual property obtained through license agreements;
- attract, hire and retain qualified personnel;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- experience any delays or encounter other issues related to our operations;
- meet the requirements and demands of being a public company; and
- defend against any product liability claims or other lawsuits related to our products.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have never generated any revenue from product sales, and we may never generate revenue or be profitable.

We have no products approved for commercial sale and have not generated any revenue from product sales. We do not anticipate generating any revenue from product sales until after we have successfully completed clinical development and received regulatory approval for the commercial sale of a product candidate, if ever.

Our ability to generate revenue and achieve profitability depends significantly on many factors, including:

- successfully completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development and clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, including those that utilize our BBB platform technology, as well as establishing and

maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand of our product candidates;

- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- launching and successfully commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining an adequate price for our product candidates, both in the United States and in foreign countries where our products are commercialized;
- obtaining adequate reimbursement for our product candidates from payors;
- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding and enforcing our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with drug development, we are unable to predict the timing or amount of our expenses, or when we will be able to generate any meaningful revenue or achieve or maintain profitability, if ever. In addition, our expenses could increase beyond our current expectations if we are required by the U.S. Food and Drug Administration, or FDA, or foreign regulatory agencies, to perform studies in addition to those that we currently anticipate, or if there are any delays in any of our or our future collaborators' clinical trials or the development of any of our product candidates. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and ongoing compliance efforts.

Even if we are able to generate revenue from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Revenue from the sale of any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. If the number of addressable patients is not as significant as we anticipate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock, all or any of which may adversely affect our viability.

If we fail to obtain additional financing, we may be unable to complete the development and, if approved, commercialization of our product candidates.

Our operations have required substantial amounts of cash since inception. To date, we have financed our operations primarily through the sale of equity securities. We are currently advancing one

product candidate, DNL201, through clinical development and have several other product candidates in preclinical development, as well as early-stage research projects. Developing our product candidates is expensive, and we expect to continue to spend substantial amounts as we fund our early-stage research projects, continue preclinical development of our seed programs and, in particular, advance our core programs through preclinical development and clinical trials. Even if we are successful in developing our product candidates, obtaining regulatory approvals and launching and commercializing any product candidate will require substantial additional funding beyond the net proceeds of this offering.

As of June 30, 2017, we had $212.8 million in cash, cash equivalents and marketable securities. We estimate that our net proceeds from this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our projected operations through at least the next 12 months. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be available to fund our operations is based on assumptions that may be proved inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

We will require additional capital for the further development and, if approved, commercialization of our product candidates. Additional capital may not be available when we need it, on terms acceptable to us or at all. We have no committed source of additional capital. If adequate capital is not available to us on a timely basis, we may be required to significantly delay, scale back or discontinue our research and development programs or the commercialization of any product candidates, if approved, or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations and cause the price of our common stock to decline.

Due to the significant resources required for the development of our programs, and depending on our ability to access capital, we must prioritize development of certain product candidates. Moreover, we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Our current total portfolio consists of 11 programs. We designate certain programs as core programs and others as seed programs. Together, these programs require significant capital investment. We currently have six core programs which are at various stages of preclinical and early clinical development, and our seed programs are in the research, discovery and preclinical stages of development. We seek to maintain a process of prioritization and resource allocation to maintain an optimal balance between aggressively advancing lead programs and ensuring replenishment of our portfolio. We regularly review the designation of each program as core or seed, and terminate those programs which do not meet our development criteria, which we have done with three programs in the past two years.

Due to the significant resources required for the development of our programs, we must focus our programs on specific diseases and disease pathways and decide which product candidates to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation

of research, development, collaboration, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain programs may subsequently also prove to be suboptimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biopharmaceutical industry, in particular for neurodegenerative diseases, our business, financial condition and results of operations could be materially adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights. We regularly review the designation of each program as core or seed, and terminate those programs which do not meet our development criteria.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Research and development of biopharmaceutical products is inherently risky. We are heavily dependent on the successful development of our BBB platform technology and the product candidates currently in our core programs, which are in the early stages of preclinical and clinical development. We cannot give any assurance that any of our product candidates will receive regulatory, including marketing, approval, which is necessary before they can be commercialized.

We are at an early stage of development of the product candidates currently in our programs and are further developing our BBB platform technology. To date, we have invested substantially all of our efforts and financial resources to identify, acquire intellectual property for, and develop our BBB platform technology and our programs, including conducting preclinical studies and early-stage clinical trials in our core programs, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;
- our platform technology to deliver large molecule therapeutics across the BBB may not be clinically viable;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- our competitors may develop platform technologies to deliver large molecule therapeutics across the BBB that render our platform technology obsolete or less attractive;
- the product candidates and BBB platform technology that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the product candidates and BBB platform technology that we develop may be covered by third parties' patents or other intellectual property or exclusive rights;

- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may not be successful in our efforts to further develop our BBB platform technology and current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

We have never completed a clinical development program. In the past two years, we have discontinued the development of three programs prior to completion of preclinical development because we did not believe they met our criteria for potential clinical success. We currently have one product candidate, DNL201, in a Phase 1 clinical trial in healthy volunteers in the United States. None of our product candidates have advanced into late-stage development or a pivotal clinical trial and it may be years before any such trial is initiated, if at all. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. For instance, in 2016, we initiated a Phase 1 clinical trial in a former RIPK1 inhibitor product candidate, DNL104, which we subsequently discontinued based on liver test abnormalities in some clinical trial healthy volunteer participants. We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion.

If any of our product candidates successfully complete clinical trials, we generally plan to seek regulatory approval to market our product candidates in the United States, the European Union, or EU, and in additional foreign countries where we believe there is a viable commercial opportunity. We have never commenced, compiled or submitted an application seeking regulatory approval to market any product candidate. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the United States, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. We may also rely on our collaborators or partners to conduct the required activities to support an application for regulatory approval, and to seek approval, for one or more of our product candidates. We cannot be sure that our collaborators or partners will conduct these activities or do so within the timeframe we desire. Even if we (or our collaborators or partners) are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative diseases or other diseases, we cannot assure you that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

We may not be successful in our efforts to continue to create a pipeline of product candidates or to develop commercially successful products. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional product candidates. We currently have five seed programs, all of which are in the research, discovery and preclinical stages of development. Identifying, developing, obtaining regulatory approval and commercializing additional product candidates for the treatment of neurodegenerative diseases will require substantial additional funding beyond the net proceeds of this offering and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully identify or acquire additional product candidates, advance any of these additional product candidates through the development process, successfully commercialize any such additional product candidates, if approved, or assemble sufficient resources to identify, acquire, develop or, if approved, commercialize additional product candidates. If we are unable to successfully identify, acquire, develop and commercialize additional product candidates, our commercial opportunity may be limited.

We have concentrated our research and development efforts on the treatment of neurodegenerative diseases, a field that has seen limited success in drug development. Further, our product candidates are based on new approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have focused our research and development efforts on addressing neurodegenerative diseases. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen limited successes in drug development. There are few effective therapeutic options available for patients with Alzheimer’s disease, Parkinson’s disease, ALS and other neurodegenerative diseases. Our future success is highly dependent on the successful development of our BBB platform technology and our product candidates for treating neurodegenerative diseases. Developing and, if approved, commercializing our product candidates for treatment of neurodegenerative diseases subjects us to a number of challenges, including engineering product candidates to cross the BBB to enable optimal concentration of the therapeutic in the brain and obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on.

Our approach to the treatment of neurodegenerative diseases aims to identify and select targets with a genetic link to neurodegenerative diseases, identify and develop molecules that engage the intended target, identify and develop biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our molecules, and engineer our molecules to cross the BBB and act directly in the brain. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to novel treatments.

We may encounter substantial delays in our clinical trials, or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an investigational new drug application, or IND, or a clinical trial application, or CTA, will result in the FDA or European Medicines Agency, or EMA, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROS, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting and training suitable clinical investigators;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including after review of an IND or amendment, CTA or amendment, or equivalent application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; a negative finding from an inspection of our clinical trial operations or study sites; developments on trials conducted by competitors for related technology that raises FDA or EMA concerns about risk to patients of the technology broadly; or if the FDA or EMA finds that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in identifying, recruiting and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's current good clinical practices, or cGCPs, requirements, or applicable EMA or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs;
- transfer of manufacturing processes from our academic collaborators to larger-scale facilities operated by a contract manufacturing organization, or CMO, or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to or we may elect to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such trial or by the FDA, EMA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Our most advanced product candidate, DNL201, which is currently in a Phase 1 clinical trial in healthy volunteers in the United States, is subject to a partial clinical hold instituted by the FDA due to histological findings observed in our preclinical studies. This partial clinical hold relates to the FDA's decision to impose an exposure cap in our Phase 1 healthy volunteer clinical trial. The partial clinical hold prohibits evaluation of DNL201 above a specific dose cap level. The FDA may re-evaluate the exposure cap for this trial, and may potentially raise it, based on the safety and tolerability data generated by the trial as well as data supporting the monitorability of the effects of the trial. We cannot assure you that the FDA will deem our response to be a complete response or that it will determine to lift or change the exposure cap imposed, and ultimately lift this partial clinical hold. Any inability to continue or complete our clinical trial of DNL201, as a result of the partial clinical hold or otherwise, will delay our clinical development plans for DNL201, may require us to incur additional clinical development costs and could impair our ability to ultimately obtain FDA approval for DNL201. We cannot assure you that DNL201 or our other product candidates will not be subject to new, partial or full clinical holds in the future.

We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, such as we did for DNL104, which could adversely affect our business.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the proximity of patients to a trial site;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. For those product candidates that are subject to regulation as biological drug products, we will need to demonstrate that they are safe, pure, and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our product candidates may not be predictive of the results of early-stage or later-stage

clinical trials, and results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in neurodegenerative diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidate, which may also limit its commercial potential.

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours, which may negatively impact our ability to successfully market or commercialize any product candidates we may develop and ultimately harm our financial condition.

The development and commercialization of new drug products is highly competitive. Moreover, the neurodegenerative field is characterized by strong and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of products for the treatment of the neurodegenerative disease indications for which we have research programs, including Alzheimer’s disease, Parkinson’s disease and ALS. Companies that we are aware are developing therapeutics in the neurodegenerative disease area include large companies with significant financial resources, such as AbbVie, AstraZeneca, Biogen, Celgene, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, Pfizer, Roche, Sanofi and Takeda.

In addition to competition from other companies targeting neurodegenerative indications, any products we may develop may also face competition from other types of therapies, such as gene-editing therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours and may obtain orphan product exclusivity from the FDA for indications our product candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. See "Risks Related to Our Intellectual Property."

The manufacture of our product candidates, particularly those that utilize our BBB platform technology, is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our drug and biological product candidates, particularly those that utilize our BBB platform technology, are complex, expensive, highly-regulated and subject to multiple risks. Additionally, the manufacture of biologics involves complex processes, including developing cells or cell systems to produce the biologic, growing large quantities of such cells, and harvesting and purifying the biologic produced by them. As a result, the cost to manufacture a biologic is generally far higher than traditional small molecule chemical compounds, and the biologics manufacturing process is less reliable and is difficult to reproduce. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. Further, as product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development

program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In order to conduct clinical trials of our product candidates, or supply commercial products, if approved, we will need to manufacture them in small and large quantities. Our manufacturing partners may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risks would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any products that we may develop is subject to FDA, EMA and foreign regulatory authority approval processes, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with current Good Manufacturing Practices, or cGMPs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be

costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved.

Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. Even if any product candidates we may develop receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors, and others in the medical community. The degree of market acceptance of any product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in pivotal clinical trials and published in peer-reviewed journals;
- the potential and perceived advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- the ability to offer appropriate patient access programs, such as co-pay assistance;
- the extent to which physicians recommend our products to their patients;
- convenience and ease of dosing and administration compared to alternative treatments;

- the clinical indications for which the product candidate is approved by FDA, EMA or other regulatory agencies;
- product labeling or product insert requirements of the FDA, EMA or other comparable foreign regulatory authorities, including any limitations, contraindications or warnings contained in a product's approved labeling;
- restrictions on how the product is distributed;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If any product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenue, and we may not become profitable.

Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to successfully commercialize any products that we may develop also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs, or VA, hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to get reimbursement, physicians may need to show that patients have

superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize product candidates, and our overall financial condition.

If any of our product candidates that are small molecules obtain regulatory approval, additional competitors could enter the market with generic versions of such drugs, which may result in a material decline in sales of affected products.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved, small molecule innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application, or NDA, under section 505(b)(2) that references the FDA's prior approval of the small molecule innovator product. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. These include, subject to certain exceptions, the period during which an FDA-approved drug is subject to orphan drug exclusivity. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its product before expiration of the patents must include in the ANDA a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if any of our small molecule product candidates are approved, competitors could file ANDAs for generic versions of our small molecule drug products or 505(b)(2) NDAs that reference our

small molecule drug products, respectively. If there are patents listed for our small molecule drug products in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict which, if any, patents in our current portfolio or patents we may obtain in the future will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected. See “Risks Related to Our Intellectual Property.”

Our biologic, or large molecule, product candidates for which we intend to seek approval may face competition sooner than anticipated.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, our large molecule product candidates may face competition from biosimilar products. In the United States, our large molecule product candidates are regulated by the FDA as biologic products and we intend to seek approval for these product candidates pursuant to the biologics license application, or BLA, pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our large molecule product candidates.

We believe that any of our large molecule product candidates approved as a biologic product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get it on the market until 10 years after the time of

approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our large molecule product candidates, if approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk when and if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased or interrupted demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Moreover, the FDA, EMA or other regulatory authorities may fail to approve companion diagnostics that we contemplate using with our therapeutic product candidates. We have not submitted for, or obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA, BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- we may be unable to demonstrate to the FDA, EMA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other comparable foreign regulatory authorities.

Our most advanced product candidate, DNL201, is currently our only clinical stage product candidate. In June 2017, we initiated a Phase 1 clinical trial of DNL201 in healthy volunteers in the United States and, to date, it has been well tolerated. However, adverse events and other side effects may result from higher dosing, repeated dosing and/or longer-term exposure to DNL201 and could lead to delays and/or termination of the development of this product candidate.

In 2016, we initiated a Phase 1 clinical trial in a former RIPK1 inhibitor product candidate, DNL104, which we subsequently discontinued based on liver test abnormalities in some clinical trial healthy volunteer participants.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and/or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our license agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a Risk Evaluation and Mitigation Strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

We may in the future conduct clinical trials for our product candidates outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.

We may in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any partner we work with fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to extensive regulatory scrutiny.

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, BLA or marketing authorization application, or MAA. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates will be subject to limitations on the approved indicated uses for which the product may be marketed and promoted or to the conditions of approval (including the requirement to implement a Risk Evaluation and Mitigation Strategy), or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have approval. The holder of an approved NDA, BLA, or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;

- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products; or
- require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

We plan to seek orphan drug designation for some product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. We plan to seek orphan drug designations for some product candidates and may be unable to obtain such designations.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other NDA or BLA applications to market the same drug or biologic for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the drug was designated. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Furthermore, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Affordable Care Act, or ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate

Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research. Recent changes in the U.S. administration could lead to repeal of or changes in some or all of the ACA, and complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business. Until the ACA is fully implemented or there is more certainty concerning the future of the ACA, it will be difficult to predict its full impact and influence on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013, and will remain in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidates, if approved.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and negligent conduct that fails to: comply with the laws of the FDA, EMA and other comparable foreign regulatory authorities; provide true, complete and accurate information to the FDA, EMA and other comparable foreign regulatory authorities; comply with

manufacturing standards we have established; comply with healthcare fraud and abuse laws in the United States and similar foreign fraudulent misconduct laws; or report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. In particular, research, sales, marketing, education and other business arrangements in the healthcare industry are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, educating, marketing and promotion, sales and commission, certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial conditions could be adversely affected.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be subject to various federal and state fraud and abuse laws. The laws that may impact our operations include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil “qui tam” or “whistleblower” actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying,

concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal Physician Payment Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services under the Open Payments Program, information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission, or SEC, and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to

obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Risks Related to Our Reliance on Third Parties

We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we may develop. If any such collaborations are not successful, we may not be able to realize the market potential of those product candidates.

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we may develop. For example, we have a collaboration with F-star, among others, to further our development of product candidates and to enhance our research efforts directed to better understanding neurodegenerative diseases. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic institutions. If we enter into any such arrangements with any third parties, we will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs, or any product candidates we may develop, pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or research programs or may use our proprietary information in such a way as to expose us to potential litigation or other intellectual property related proceedings, including proceedings challenging the scope, ownership, validity and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property covering our product candidates or research programs that results from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates or research programs;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our product candidates or research programs or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborators may decide to not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates or research programs if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may undergo a change of control and the new owners may decide to take the collaboration in a direction which is not in our best interest;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, know-how or intellectual property of the collaborator relating to our products, product candidates or research programs;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or our BBB platform technology; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our development or commercialization program under such collaboration could be delayed, diminished, or terminated.

We may face significant competition in seeking appropriate collaborations. Recent business combinations among biotechnology and pharmaceutical companies have resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elects not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our

agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section also apply to the activities of our collaborators and any negative impact on our collaborators may adversely affect us.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with cGCPs for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of materials for our research programs and preclinical studies and expect to continue to do so for clinical trials and for commercialization of any product candidates that we may develop. This reliance on third parties carries and may increase the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely on third-party manufacturers for the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials and for commercial supply of any product candidates that we may develop.

We may be unable to establish any further agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for any of our product candidates. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the raw materials required for the production of our product candidates. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop and for our BBB platform technology, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our BBB platform technology and any proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by in-licensing intellectual property and filing patent applications in the United States and abroad relating to our BBB platform technology, core programs and product candidates, as well as other technologies that are important to our business. Given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. For example, we do not own or in-license any issued patents in the United States directed to the composition of matter of any of the antibodies or enzymes that we have thus far developed using our BBB platform technology or that cover the composition of matter of our DNL151 product candidate, which is in our LRRK2 core program. In addition, we do not own or in-license any issued patents covering the Fc domain portion of our BBB platform technology that binds to transferrin receptor, or any issued patents that cover our RIPK1, TREM2, aSyn, or IDS core programs. We have filed or intend to file patent applications on these aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our BBB platform technology, core programs and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such BBB platform technology, core programs, product candidates and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our BBB platform technology, core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If any of our owned or in-licensed patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a

reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our owned or in-licensed pending and future patent applications may not result in patents being issued which protect our BBB platform technology, product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we own or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether our BBB platform technology, product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. We or our licensors may be subject to a third party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review, or interference proceedings or other similar proceedings challenging our owned or licensed patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our owned or in-licensed patent rights, allow third parties to commercialize our BBB platform technology, product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our or our licensor’s priority

of invention or other features of patentability with respect to our owned or in-licensed patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our BBB platform technology, product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. For example, we currently, and may in the future, co-own certain patents and patent applications relating to our BBB platform technology with F-star. In addition, certain of our licensors co-own the patents and patent applications we in-license with other third parties with whom we do not have a direct relationship. Our exclusive rights to certain of these patents and patent applications are dependent, in part, on inter-institutional or other operating agreements between the joint owners of such patents and patent applications, who are not parties to our license agreements. For example, under our license agreement with VIB, we license certain patents and patent applications co-owned by VIB and KU Leuven. Our rights to KU Leuven's interest in such patents and patent applications depends on an operating agreement between VIB and KU Leuven, pursuant to which VIB controls the licensing of such patents and patent applications. If our licensors do not have exclusive control of the grant of licenses under any such third-party co-owners' interest in such patents or patent applications or we are otherwise unable to secure such exclusive rights, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our rights to develop and commercialize our BBB platform technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our BBB platform technology and product candidates. For example, in June 2016, we entered into an exclusive license agreement with Genentech pursuant to which we received an exclusive license to certain of Genentech's intellectual property relating to our LRRK2 program, including our DNL201 and DNL151 product candidates. In March 2017, we entered into an exclusive license agreement with VIB pursuant to which we received exclusive and non-exclusive licenses to certain patent rights and related know-how pertaining to antibodies that target BACE1. In addition, in August 2016, we entered into a collaboration with UK-based F-star, a biopharmaceutical company developing novel bispecific antibodies, focused on research and development of our BBB platform technology. The agreement with F-star includes certain non-exclusive licenses to F-star's modular antibody technology to research and develop certain antibodies, as well as options for us to obtain exclusive rights to develop and commercialize certain antibodies by exercising an option to obtain certain exclusive licenses or to buy-out all of the outstanding shares of F-star Gamma. See the section titled "Business—Licenses and Collaborations—F-star License and Collaboration Agreement" for additional information. However, we will not obtain exclusive rights to commercialize and exploit such antibodies unless we exercise our options to obtain

such exclusive rights within specified periods of time. If we do not exercise our options with respect to a particular antibody in a timely manner or at all, or fail to satisfy any conditions upon which our options are contingent, F-star may offer such exclusive rights to other third parties. In addition, F-star may breach our agreement and attempt to license such patents and patent applications to other third parties, including our competitors, before or after we exercise our options. If we are unable to secure exclusive rights to F-star's modular antibody technology to commercialize and exploit our antibodies, our competitive position, business, financial condition, results of operations, and prospects may be materially harmed.

Our agreement with F-star and other license agreements may not provide exclusive rights to use the licensed intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, F-star retains the right to use itself, and to license to others, its modular antibody technology for any purpose other than the targets and antibodies which we have agreed with F-star would or may be exclusively available to us. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products that also utilizes technology that we have in-licensed.

In addition, subject to the terms of any such license agreements, we do not have the right to control the preparation, filing, prosecution and maintenance, and we may not have the right to control the enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, under our agreements with F-star and Genentech, the licensors control prosecution and, in the case of F-star and in specified circumstances, enforcement of certain of the patents and patent applications licensed to us. We cannot be certain that our in-licensed patents and patent applications that are controlled by our licensors will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, our right to develop and commercialize our BBB platform technology and any of our product candidates that are subject of such licensed rights could be adversely affected, and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, our license to certain intellectual property owned by Genentech is subject to certain research rights Genentech granted to third parties prior to our license agreement. In addition, certain of our in-licensed intellectual property relating to RIPK1 was funded in part by the U.S. government. As a result, the U.S. government may have certain rights to such intellectual property. When new technologies are developed with U.S. government funding, the U.S. government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the U.S. government to use the invention or to have others use the invention on its behalf. The U.S. government's rights may also permit it to disclose the funded inventions and technology to third parties and to exercise march-in rights to use or allow third parties to use the technology we have licensed that was developed using U.S. government funding. The U.S. government may exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States in certain circumstances and if this requirement is not waived. Any exercise by the U.S. government of such rights or by any third party of its reserved rights could have a

material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of product candidates we may develop or our BBB platform technology. It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates or continue to utilize our existing BBB platform technology, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, including our BBB platform technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In addition, each of our license agreements, and we expect our future agreements, will impose various development, diligence, commercialization, and other obligations on us. Certain of our license agreements also require us to meet development timelines, or to exercise commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the licenses. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties would have the freedom to seek regulatory approval of, and to market, products identical to ours and we may be required to cease our development and commercialization of certain of our product candidates or of our current BBB platform technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Moreover, disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on our BBB platform technology, product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our BBB platform technology, product candidates or other technologies or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents

Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Issued patents covering our BBB platform technology, product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering our BBB platform technology, product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may raise claims challenging the validity or enforceability of our owned or in-licensed patents before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our BBB platform technology, product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our BBB platform technology, product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our owned or in-licensed U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permit a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent

Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our BBB platform technology, product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our BBB platform technology, product candidates and other technologies. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our BBB platform technology, product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that

technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining, through acquisitions, in-licenses or otherwise, necessary rights to our BBB platform technology, product candidates or other technologies.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop our BBB platform technology and product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of neurodegeneration and BBB technology and may have patents and have filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third party patents, we may find it necessary or prudent to obtain licenses to such patents from such third party intellectual property holders. We may also require licenses from third parties for certain BBB technologies that we are evaluating for use with our current or future product candidates. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our current or future product candidates and our BBB platform technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our licensors, competitors and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring

against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Third-party claims of intellectual property infringement, misappropriation or other violation against us, our licensors or our collaborators may prevent or delay the development and commercialization of our BBB platform technology, product candidates and other technologies.

The field of discovering treatments for neurodegenerative diseases, especially using BBB technology, is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. As such, there may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our, our licensors' and our collaborators' ability to avoid infringing, misappropriating and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist relating to BBB technology and in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our BBB platform technology, product candidates and other technologies may give rise to claims of infringement of the patent rights of others. We cannot assure you that our BBB platform technology, product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our BBB platform technology, product candidates, and other technologies might assert are infringed by our current or future BBB platform technology, product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our BBB platform technology, product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our BBB platform technology, product candidates or other technologies, could be found to be infringed by our BBB platform technology, product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our BBB platform technology, product candidates or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our BBB platform technology, product candidates or other technologies infringes upon these patents. In the event that any third party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our BBB platform technology, product candidates or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable

patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our BBB platform technology, product candidates or other technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing BBB platform technology, product candidates or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our BBB platform technology, product candidates or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition or results of operations.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, priority or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent owned or in-licensed by us is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1), or may refuse to stop the other party from using the technology at issue on the grounds that our owned and in-licensed patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the

resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we license or may own;
- we, or our current or future licensors or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or own now or in the future;
- we, or our current or future licensors or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our current or future pending owned or licensed patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Operations

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, particularly our Chief Executive Officer, Dr. Ryan Watts, and our scientific and medical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

We conduct our operations at our facility in South San Francisco, California, in a region that is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region, and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided restricted stock and stock option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of all of these individuals or the lives of any of our other employees. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As of June 30, 2017, we had approximately 120 employees, all of whom were full-time. As our development plans and strategies develop, and as we transition into operating as a public company, we must add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;

- expanding our operational, financial and management controls, reporting systems, and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities. Our ability to successfully manage our expected growth is uncertain given the fact that all of our executive officers have joined us since February 2015. This lack of long-term experience working together as a company may adversely impact our senior management team's ability to effectively manage our business and growth.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

If we engage in acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

We have in the past engaged in acquisitions and we may engage in various acquisitions and strategic partnerships in the future, including licensing or acquiring complementary products, intellectual property rights, technologies, or businesses. Any acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of indebtedness or contingent liabilities;
- the issuance of our equity securities which would result in dilution to our stockholders;
- assimilation of operations, intellectual property, products and product candidates of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such an acquisition or strategic partnership;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and

- our inability to generate revenue from acquired intellectual property, technology and/or products sufficient to meet our objectives or even to offset the associated transaction and maintenance costs.

In addition, if we undertake such a transaction, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

All of our operations including our corporate headquarters are located in a single facility in South San Francisco, California. Damage or extended periods of interruption to our corporate, development or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Although we maintain property damage and business interruption insurance coverage on these facilities, our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Our business is subject to economic, political, regulatory and other risks associated with international operations.

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and collaborative relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing and changing regulatory requirements in non-U.S. countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- potential liability under the FCPA or comparable foreign laws; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

These and other risks associated with our planned international operations may materially adversely affect our ability to attain profitable operations.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

As of December 31, 2016, we had federal net operating loss carryforwards of approximately $65.4 million, which will begin to expire in 2035. Under Sections 382 and 383 of the Internal Revenue Code, or Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change taxable income or taxes may be limited. As a result of our most recent private placements and other transactions that have occurred since our incorporation, we may have experienced, and, in connection with this offering, may experience, such an ownership change. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change taxable income or taxes may be subject to limitation.

Risks Related to This Offering and Ownership of Our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be volatile, which could result in substantial losses for investors purchasing shares in this offering.

The initial public offering price for our common stock will be determined through negotiations with the underwriters. This initial public offering price may differ from the market price of our common stock after the offering. As a result, you may not be able to sell your common stock at or above the initial public offering price. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- failure to develop our BBB platform technology;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- expiration of market standoff or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;

- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our stock shortly following this offering. Following periods of such volatility in the market price of a company’s securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management’s attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, upon the expiration of the market standoff and lock-up agreements, the early release of these agreements, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. After this offering and after giving effect to the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock upon the closing of this offering, we will have shares of common stock outstanding based on shares of our common stock outstanding as of , 2017. Of these shares, the shares we are selling in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining shares, or % of our outstanding shares after this offering, are currently prohibited or otherwise restricted under securities laws, market standoff agreements entered into by our stockholders with us or lock-up agreements entered into by our stockholders with the underwriters; however, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, these shares will be able to be sold in the public market beginning 180 days after the date of this prospectus. The representatives may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. In addition, shares of unvested restricted stock were issued and outstanding as of will become available for sale immediately upon the vesting of such shares, as applicable, and the expiration of any applicable market standoff or lock-up agreements. Shares issued upon the exercise of stock options outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale

in the public market to the extent permitted by the provisions of applicable vesting schedules, any applicable market standoff and lock-up agreements, and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act. See the section titled “Shares Eligible for Future Sale” for additional information.

Moreover, after this offering, holders of an aggregate of shares of our common stock will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also plan to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in the section titled “Underwriting” in this prospectus. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $ per share, representing the difference between the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, and our pro forma net tangible book value per share after giving effect to this offering and the automatic conversion of all outstanding shares of our convertible preferred stock upon the closing of this offering. As of June 30, 2017, there were 23,816,215 shares subject to outstanding options with a weighted-average exercise price of $0.65 per share. To the extent that these outstanding options are ultimately exercised or the underwriters exercise their option to purchase additional shares, you will incur further dilution. See the section titled “Dilution” for a further description of the dilution you will experience immediately after this offering.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

Insiders will continue to have substantial influence over us after this offering, which could limit your ability to affect the outcome of key transactions, including a change of control.

After this offering, our directors and executive officers and their affiliates will beneficially own shares representing approximately % of our outstanding common stock. As a result, these

stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This concentration of ownership may have the effect of delaying or preventing a change in control of our company and might affect the market price of our common stock.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. As a result, the information we provide stockholders will be different than the information that is available with respect to other public companies. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. The SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of , and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are

often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the SEC after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we are unable to maintain effective internal controls, our business, financial position and results of operations could be adversely affected.

As a public company, we will be subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, including the requirements of SOX Section 404, which require annual management assessments of the effectiveness of our internal control over financial reporting. However, our auditors will not be required to formally attest to the effectiveness of our internal control over financial reporting pursuant to SOX Section 404 until we are no longer an emerging growth company if we continue to take advantage of the exemptions available to us through the JOBS Act.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act of 2002. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position and results of operations.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We cannot specify with certainty the particular uses of the net proceeds we will receive from this offering. Our management will have broad discretion in the application of the net proceeds, including

for any of the purposes described in the section titled “Use of Proceeds” in this prospectus. Our management may spend a portion or all of the net proceeds from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business, financial condition, results of operations and prospects. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We do not expect to pay any dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future credit facility may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Delaware law and provisions in our amended and restated certificate of incorporation and bylaws that will become effective upon the closing of this offering might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and bylaws that will become effective upon the closing of this offering may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our charter documents will:

- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered three year terms;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- provide that our directors may only be removed for cause;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issues shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- provide our board of directors with the exclusive right to elect a director to fill a vacancy or newly created directorship;
- permit stockholders to only take actions at a duly called annual or special meeting and not by written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend the bylaws; and

- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware, or DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering provides that the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the success, cost and timing of our development activities, preclinical studies and clinical trials, and in particular the development of our BBB platform technology, core programs and biomarkers;
- the expected potential benefits of strategic collaboration agreements and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the timing or likelihood of regulatory filings and approvals;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- the terms and conditions of licenses granted to us and our ability to license additional intellectual property relating to our product candidates and BBB platform technology;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our product candidates;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain approval;
- future agreements with third parties in connection with the commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- existing regulations and regulatory developments in the United States and foreign countries;
- potential claims relating to our intellectual property and third-party intellectual property;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing and reimbursement of our product candidates, if approved;

- the success of competing products or platform technologies that are or may become available;
- our ability to attract and retain key managerial, scientific and medical personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act; and
- our anticipated use of the proceeds from this offering.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate, and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

MARKET, INDUSTRY AND OTHER DATA

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. We obtained the industry, market and similar data set forth in this prospectus from our own internal estimates and research and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe that the data we use from third parties are reliable, we have not separately verified these data. Further, while we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections and estimates.

In some cases, we do not expressly refer to the sources from which data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

The sources of industry and market data contained in this prospectus are listed below:

(1) *Science*, “RIPK1 Mediates Axonal Degeneration by Promoting Inflammation and Necroptosis in ALS,” Volume 353, Issue 6299, August 5, 2016

(2) The Alzheimer’s Association, “2017 Alzheimer’s Disease Facts and Figures”

(3) The Alzheimer’s Association, “Fact Sheet,” March 2017

(4) The National MPS Society, “MPS II”

(5) The Parkinson’s Disease Foundation, “Statistics on Parkinson’s”

(6) The ALS Association, “Facts You Should Know”

(7) The Michael J. Fox Foundation for Parkinson’s Research, “LRRK2 Kinase Inhibitors of Different Structural Classes Induce Abnormal Accumulation of Lamellar Bodies in Type II Pneumocytes in Non-Human Primates but are Reversible and Without Pulmonary Functional Consequences”

(8) The World Health Organization, “Dementia Fact Sheet,” May 2017

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million, assuming an initial public offering price of per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $ million.

A $1.00 increase (decrease) in the assumed initial public offering price of per share would increase (decrease) the aggregate net proceeds to us from this offering by approximately million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial public offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

The principal purposes of this offering are to obtain additional capital to support our operations, establish a public market for our common stock and facilitate our future access to the public capital markets. We currently anticipate that we will use the net proceeds from this offering, together with our existing resources, through 2019 as follows:

- approximately $ million to fund the costs of Phase 1 trials in healthy volunteers for each of DNL201 and DNL151 and a Phase 1b study in LRRK2 mutation-carrying Parkinson's disease patients, as well as preparation for a potential future Phase 2 clinical trial;
- approximately $ million to fund the costs to advance our RIPK1 program through Phase 1 and early Phase 2 clinical development, substantially represented by the planned Phase 1 clinical trial in healthy volunteers for DNL747 and a Phase 2a clinical trial in ALS patients and a Phase 2a clinical trial in Alzheimer's disease patients;
- approximately $ million to optimize and broaden our ATV and ETV platform technologies and to advance our four core antibody and enzyme replacement programs through preclinical development and IND-enabling activities;
- if we exercise our option to acquire all outstanding shares of F-star Gamma, in the aggregate, approximately $18.0 million to $50.0 million to fund the initial exercise payments; and
- the remainder to fund seed programs, general research and development activities, working capital and other general corporate activities.

We believe opportunities may exist from time to time to expand our current business through license or acquisitions of, or investments in, complementary businesses, products or technologies. While we currently have no agreements or commitments to complete any such transaction at this time, we may use a portion of the net proceeds for these purposes.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical

trials, as well as any collaborations that we may enter into with third parties for our programs, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds. We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including interest-bearing, investment-grade instruments and U.S. government securities.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements and contractual restrictions of then-existing debt instruments and other factors that our board of directors deems relevant.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of June 30, 2017, as follows:

- on an actual basis;
- on a pro forma basis to reflect (1) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 234,401,367 shares of common stock upon the closing of this offering and (2) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering, as if such conversion had occurred on June 30, 2017; and
- on a pro forma as adjusted basis to further reflect our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information in conjunction with our consolidated financial statements and the related notes and the sections titled "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" that are included elsewhere in this prospectus.

	As of June 30, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted (1)
	(in thousands, except share and per share amounts)		
Cash, cash equivalents and marketable securities	$ 212,839	$ 212,839	$
Convertible preferred stock, par value $0.01 per share; 253,153,867 shares authorized, 234,401,367 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 348,673	$ —	$
Stockholder's equity (deficit):			
Common stock, par value $0.01 per share; 334,349,451 shares authorized, 54,273,036 shares issued and outstanding, actual; shares authorized, 288,674,403 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	400	2,744	
Additional paid-in capital	11,594	357,923	
Accumulated other comprehensive loss	(377)	(377)	
Accumulated deficit	(146,966)	(146,966)	
Total stockholders' equity (deficit)	(135,349)	213,324	
Total capitalization	$ 213,324	$ 213,324	$

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted cash, cash equivalents and marketable securities, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately $ million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses

payable by us. Each increase (decrease) of 1.0 million shares in the number of shares of common stock offered by us would increase (decrease) our pro forma as adjusted cash, cash equivalents and marketable securities, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately $ million, assuming the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The number of shares of common stock that will be outstanding after this offering is based on 288,674,403 shares of common stock (including our convertible preferred stock on an as-converted basis) outstanding as of June 30, 2017, and excludes the following:

- 23,816,215 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of June 30, 2017, at a weighted-average exercise price of $0.65 per share;
- 1,320,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after June 30, 2017, at a weighted-average exercise price of $2.40 per share;
- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
  - 1,461,675 shares of common stock reserved for future issuance under our 2015 Stock Incentive Plan, or 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Equity Incentive Plan, or 2017 Plan;
  - shares of common stock reserved for future issuance under our 2017 Plan (excluding the 1,461,675 shares to be transferred from our 2015 Plan), which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled "Executive Compensation—Employee Benefit and Stock Plans;" and
  - shares of common stock reserved for future issuance under our 2017 Employee Stock Purchase Plan, or ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled "Executive Compensation—Employee Benefit and Stock Plans."

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of June 30, 2017 was $(135.3) million, or $(2.49) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and convertible preferred stock, which is not included within our stockholders' equity (deficit). Historical net tangible book value per share represents historical net tangible book value (deficit) divided by the number of shares of our common stock outstanding as of June 30, 2017.

Our pro forma net tangible book value as of June 30, 2017 was $213.3 million, or $0.74 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 234,401,367 shares of common stock upon the completion of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of June 30, 2017, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 234,401,367 shares of our common stock upon the completion of this offering.

After giving further effect to our sale of shares of common stock in this offering at the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of would have been approximately $ million, or approximately $ per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $ to our existing stockholders and an immediate dilution in pro forma as adjusted net tangible book value per share of approximately $ to new investors purchasing common stock in this offering. Dilution per share to new investors purchasing common stock in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors.

The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of June 30, 2017	$(2.49)	
Pro forma increase in net tangible book value (deficit) per share as of June 30, 2017	$ 3.23	
Pro forma net tangible book value per share as of June 30, 2017	$ 0.74	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new investors purchasing shares in this offering		$

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share

after this offering by $ per share and the dilution to new investors purchasing common stock in this offering by $ per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase of 1.0 million shares in the number of shares offered by us would increase the pro forma as adjusted net tangible book value per share after this offering by $ and decrease the dilution per share to new investors participating in this offering by $, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A decrease of 1.0 million shares in the number of shares offered by us would decrease the pro forma as adjusted net tangible book value per share after this offering by $ and increase the dilution per share to new investors participating in this offering by $, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares of common stock in this offering in full at the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover of this prospectus, and assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, and the dilution in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering would be $ per share.

The following table summarizes, on a pro forma as adjusted basis, as of June 30, 2017, the number of shares of common stock purchased from us on an as converted to common stock basis, the total consideration paid, or to be paid, and the weighted-average price per share paid, or to be paid, by existing stockholders and by new investors in this offering at the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Weighted Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders before this offering		%	$	%	$
Investors participating in this offering					
Total		100%	$	100%	$

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to % of the total number of shares outstanding after this offering.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the estimated offering price range set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the total consideration paid by new investors by $ million, assuming no change in the assumed initial public offering price.

The number of shares of common stock that will be outstanding after this offering is based on 288,674,403 shares of common stock (including convertible preferred stock on an as-converted basis) outstanding as of June 30, 2017, and excludes the following:

- 23,816,215 shares of common stock issuable upon exercise of options to purchase shares of our common stock outstanding as of June 30, 2017, at a weighted-average exercise price of $0.65 per share;
- 1,320,000 shares of common stock issuable upon exercise of options to purchase shares of our common stock that were granted after June 30, 2017, at a weighted-average exercise price of $2.40 per share;
- shares of common stock reserved for future issuance under our stock-based compensation plans, consisting of:
  - 1,461,675 shares of common stock reserved for future issuance under our 2015 Plan, which shares will be added to the shares to be reserved under our 2017 Plan;
  - shares of common stock reserved for future issuance under our 2017 Plan (excluding the 1,461,675 shares to be transferred from our 2015 Plan), which will become effective in connection with this offering, and any additional shares that become available under our 2017 Plan pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans;” and
  - shares of common stock reserved for future issuance under our ESPP, which will become effective in connection with this offering, and any additional shares that become available under our ESPP pursuant to provisions thereof that automatically increase the share reserve under the plan each year, as more fully described in the section titled “Executive Compensation—Employee Benefit and Stock Plans.”

To the extent that any outstanding options are exercised or new options are issued under the equity benefit plans, or we issue additional shares of common stock or convertible securities in the future, there will be further dilution to investors participating in this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables summarize our selected consolidated financial data for the periods and as of the dates indicated. We have derived our selected consolidated statements of operations and comprehensive loss data for the years ended December 31, 2015 and 2016, and the consolidated balance sheets data as of December 31, 2015 and 2016, from our audited consolidated financial statements and related notes included elsewhere in this prospectus. We have derived the selected consolidated statements of operations and comprehensive loss data for the six months ended June 30, 2016 and 2017, and the consolidated balance sheet data as of June 30, 2017, from our unaudited interim condensed consolidated financial statements and related notes included elsewhere in this prospectus. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements and reflect, in the opinion of management, all adjustments, which include only normal, recurring adjustments that are necessary to present fairly the unaudited interim condensed consolidated financial statements. Our historical results are not necessarily indicative of the results that may be expected in the future, and the results for the six months ended June 30, 2017, are not necessarily indicative of results to be expected for the full year or any other period. You should read the consolidated financial and other data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share amounts)			
Consolidated Statements of Operations and Comprehensive Loss Data:				
Operating expenses:				
Research and development	$ 11,571	$ 75,702	$ 31,153	$ 37,474
General and administrative	5,108	11,731	5,572	6,838
Total operating expenses	16,679	87,433	36,725	44,312
Loss from operations	(16,679)	(87,433)	(36,725)	(44,312)
Interest income (expense), net	(109)	781	38	858
Net loss	(16,788)	(86,652)	(36,687)	(43,454)
Other comprehensive income (loss)	—	(373)	16	(4)
Comprehensive loss	$ (16,788)	$ (87,025)	$ (36,671)	$ (43,458)
Net loss per share, basic and diluted (1)	$ (1.40)	$ (3.37)	$ (1.69)	$ (1.16)
Weighted average number of shares outstanding, basic and diluted (1)	12,025,514	25,698,880	21,742,166	37,380,492
Pro forma net loss per share, basic and diluted (unaudited) (1)		$ (0.44)		$ (0.16)
Pro forma weighted-average common shares outstanding, basic and diluted (unaudited) (1)		195,696,975		271,781,859

(1) See the consolidated statements of operations and Note 12 to our consolidated financial statements, and the condensed consolidated statements of operations and Note 8 to our

unaudited condensed consolidated financial statements, for further details on the calculation of net loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts and unaudited pro forma information.

	As of December 31,		As of June 30,
	2015	2016	2017
	(in thousands)		
Consolidated Balance Sheets Data:			
Cash, cash equivalents and marketable securities	$ 30,740	$ 250,911	$ 212,839
Working capital (1)	29,950	172,849	178,531
Total assets	36,683	271,067	231,379
Total liabilities	4,009	16,548	18,055
Convertible preferred stock	48,308	348,673	348,673
Accumulated deficit	(16,860)	(103,512)	(146,966)
Total stockholders' deficit	(15,634)	(94,154)	(135,349)

(1) We define working capital as current assets less current liabilities. See our consolidated financial statements and condensed consolidated financial statements for further details regarding our current assets and current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section titled "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes to those statements included elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives, expectations, forecasts and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under the section titled "Risk Factors" and elsewhere in this prospectus. You should carefully read the "Risk Factors" to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We discover and develop therapeutics to defeat degeneration.

Our strategy is guided by three overarching principles:

- **Genetic Pathway Potential**: We select our therapeutic targets and disease pathways based on degenogenes, which are genes that when mutated cause, or are major risk factors for, neurodegenerative diseases.
- **Engineering Brain Delivery**: We engineer our product candidates to cross the BBB and act directly in the brain.
- **Biomarker-Driven Development**: We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates.

Our total portfolio currently consists of eleven programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have six core programs and five seed programs. Our core programs are at various stages of clinical and preclinical development. Our most advanced core programs are our LRRK2 inhibitor program to address Parkinson's disease and our RIPK1 inhibitor program to address Alzheimer's disease and ALS. The two most advanced product candidates in our LRRK2 program, DNL201 and DNL151, are potent, selective and brain penetrant small molecule LRRK2 inhibitor product candidates for Parkinson's disease. DNL201 is currently in a Phase 1 clinical trial in healthy volunteers in the United States and DNL151 has completed IND-enabling preclinical studies and we plan to file an IND or CTA in the fourth quarter of 2017. The most advanced product candidate in our RIPK1 inhibitor program, DNL747, is a potent, selective and brain penetrant small molecule RIPK1 inhibitor product candidate for ALS and Alzheimer's disease. DNL747 is in IND-enabling preclinical studies and we plan to submit an IND or CTA in early 2018.

We have also developed proprietary drug delivery platform technology designed to deliver large molecules across the BBB. We are currently optimizing and broadening this platform technology. Our ATV and ETV platforms are modular BBB delivery technologies for large molecule therapeutics, including antibodies, enzyme and other proteins. We plan to have multiple product candidates that utilize our ATV or ETV platforms enter clinical development in 2019 and 2020, including molecules targeting aSyn, IDS, TREM2, BACE1 and Tau.

To complement our internal capabilities, we have entered into arrangements with biopharmaceutical companies, patient-focused data companies, numerous leading academic institutions and foundations to gain access to new product candidates, enable and accelerate the development of our existing programs and deepen our scientific understanding of certain areas of biology. We rely on third-party contract manufacturers to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates. We currently do not need commercial manufacturing capacity.

Since we commenced operations in May 2015, we have devoted substantially all of our resources to discovering, acquiring and developing product candidates, building our BBB platform technology and assembling our core capabilities in neurodegenerative disease pathways. Key operational and financing milestones include:

- In May 2015, we commenced operations and began assembling a team with a deep set of scientific, clinical and business capabilities.
- In May 2015, we entered into a preferred stock purchase agreement, which was subsequently amended, pursuant to which we raised aggregate proceeds of $219.3 million from issuances of our Series A-1 convertible preferred stock and Series A-2 convertible preferred stock in multiple closings between May 2015 and June 2016.
- In June 2015, in order to acquire certain patent rights and a product candidate, we acquired Incro Pharmaceuticals, or Incro, for $1.5 million, which consisted of $0.9 million in assumed liabilities and $0.6 million in shares of our common stock. In September 2016, following the satisfaction of certain milestones, we issued an additional $5.3 million in shares of common stock in connection with this acquisition.
- In June 2016, we entered into an exclusive license agreement with Genentech for the rights to certain patents, other intellectual property and a product candidate to expand and further progress our LRRK2 program.
- In June 2016, we amended our preferred stock purchase agreement, pursuant to which we raised an additional $130.0 million in proceeds from issuances of our Series B-1 convertible preferred stock in multiple closings between June 2016 and August 2016.
- In August 2016, we entered into a license and collaboration agreement with F-star. The goal of the collaboration is the development of certain constant Fc-domains of an antibody with non-native antigen binding activity, or Fcabs, to enhance delivery of therapeutics across the BBB into the brain. In connection with the entry into the license and collaboration agreement, we purchased an option to acquire all outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement.
- In April 2017, we filed an IND with the FDA for our most advanced therapeutic product candidate, DNL201, and we initiated a Phase 1 clinical trial of DNL201 in healthy volunteers in the United States in June 2017.

We do not have any products approved for sale and have not generated any product revenue since our inception. To date, we have funded our operations primarily with proceeds from the sale and issuance of convertible preferred stock. From our inception through June 30, 2017, we have raised aggregate cash proceeds of $349.3 million from the issuance of our convertible preferred stock.

We have incurred significant operating losses to date and expect to continue to incur operating losses for the foreseeable future. Our ability to generate product revenue will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $86.7 million and $16.8 million for the years ended December 31, 2016 and 2015, respectively, and

$43.5 million for the six months ended June 30, 2017. As of June 30, 2017, we had an accumulated deficit of $147.0 million. We expect to continue to incur significant expenses and operating losses as we advance our LRRK2 and RIPK1 programs through preclinical and clinical trials; broaden and improve our BBB platform technology; acquire, discover, validate and develop additional product candidates; obtain, maintain, protect and enforce our intellectual property portfolio; and hire additional personnel. In addition, upon the completion of this offering we expect to incur additional costs associated with operating as a public company.

License and Collaboration Agreements

F-star

On August 24, 2016, we entered into a License and Collaboration Agreement, or the Collaboration Agreement, with F-star. The goal of the collaboration is the development of Fcabs to enhance delivery of therapeutics across the BBB into the brain. The collaboration leverages F-star's modular antibody technology and our expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the Collaboration Agreement, we can nominate up to three Fcab targets, or Accepted Fcab Targets, within the first three years of the date of the Collaboration Agreement; and we have selected TfR as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, we can nominate up to eight Fab targets, or Accepted Fab Targets, which are targets bound by the variable domains of an antibody or other therapeutic modalities, or Fabs. Under the terms of the Collaboration Agreement, we paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target under the Collaboration Agreement. We are obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target we select, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. We are also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

In connection with the entry into the Collaboration Agreement, we also purchased an option for an upfront option fee of $0.5 million, or the buy-out option, to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement, or the Option Agreement. If we exercise this buy-out option, we will be required to make initial exercise payments ranging from, in the aggregate, approximately $18.0 million to $50.0 million, plus a payment for the estimated net cash held by F-star Gamma at the time of such exercise. In addition to these initial exercise payments, we would be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by us or solely by F-star or jointly by us and F-star and the timing of our exercise of the buy-out option. Following exercise of the buy-out option, we will not be required to make any further milestone or royalty payments under the Collaboration Agreement.

We recognized the entire $5.5 million upfront fee in research and development expense for the year ended December 31, 2016. We recognized an additional $0.3 million of research and development expense related to the funding of F-star Gamma research costs during the year ended December 31, 2016.

Genentech

On June 17, 2016, we entered into an Exclusive License Agreement with Genentech. The agreement gives us access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress our in-house LRRK2 program for Parkinson's disease. As consideration, we paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million, both of which are included in research and development expense for the year ended December 31, 2016 as there is no alternative future use of the rights acquired in other research and development projects.

We may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by us, (ii) the date a compound was first discovered, derived or optimized by us, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. We also have the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, up to a maximum reduction of fifty percent. The first clinical milestone of $2.5 million became due upon first patient dosing in the Phase 1 clinical trial for DNL201. The full amount was recognized in research and development expense in the six months ended June 30, 2017.

Unless earlier terminated, the agreement with Genentech will continue in effect until all of our royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, we will retain the licenses under the intellectual property Genentech licensed to us on a non-exclusive, royalty-free basis.

Components of Operating Results

Operating Expenses

Research and Development

Research and development activities account for a significant portion of our operating expenses. We record research and development expenses as incurred. Research and development expenses incurred by us for the discovery and development of our product candidates and BBB platform technology include:

- external research and development expenses, including:
  - expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants;
  - expenses to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use;
  - fees related to our license and collaboration agreements;
- personnel related expenses, including salaries, benefits and non-cash stock-based compensation expense; and
- other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

A portion of our research and development expenses are direct external expenses, which we track on a program-specific basis once a program has commenced a late-stage IND-enabling study. Program expenses include expenses associated with our most advanced product candidates and the discovery and development of backup or next-generation molecules. We also track external expenses associated with our BBB platform technology. All external costs associated with earlier stage programs, or that benefit the entire portfolio, are tracked as a group. We do not track personnel or other operating expenses incurred for our research and development programs on a program-specific basis. These expenses primarily relate to salaries and benefits, stock-based compensation, facility expenses including depreciation and lab consumables.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales or licensing of our product candidates. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of:

- our ability to add and retain key research and development personnel;
- our ability to establish an appropriate safety profile with IND-enabling toxicology studies;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our successful enrollment in and completion of clinical trials;
- the costs associated with the development of any additional product candidates we identify in-house or acquire through collaborations;
- our ability to discover, develop and utilize biomarkers to demonstrate target engagement, pathway engagement and the impact on disease progression of our molecules;
- our ability to establish agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved;
- our receipt of marketing approvals from applicable regulatory authorities;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others; and
- the continued acceptable safety profiles of the product candidates following approval.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We expect our research and development expenses to increase at least over the next several years as we continue to implement our business strategy, advance our current programs, expand our research and development efforts, seek regulatory approvals for any product candidates that successfully complete clinical trials, access and develop additional product candidates and incur expenses associated with hiring additional personnel to support our research and development efforts. In addition, product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative

General and administrative expenses include personnel related expenses, such as salaries, benefits, travel and non-cash stock-based compensation expense, expenses for outside professional services and allocated expenses. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent expenses related to our office and research and development facility not otherwise included in research and development expenses.

We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services. We also expect to increase our administrative headcount when operating as a public company and as we advance our product candidates through clinical development, which will also likely require us to increase our general and administrative expenses.

Interest Income (Expense), Net

Interest income (expense), net, consists primarily of interest income and investment income earned on our cash, cash equivalents and marketable securities.

Results of Operations

Comparison of the Six Months Ended June 30, 2016 and 2017

The following table sets forth the significant components of our results of operations (in thousands):

	Six Months Ended June 30,		
	2016	2017	Change
Operating expenses:			
Research and development	$ 31,153	$ 37,474	$ 6,321
General and administrative	5,572	6,838	1,266
Total operating expenses	36,725	44,312	7,587
Loss from operations	(36,725)	(44,312)	(7,587)
Interest income, net	38	858	820
Net loss	$(36,687)	$(43,454)	$(6,767)

Research and development expenses. Research and development expenses were $31.2 million for the six months ended June 30, 2016 compared to $37.5 million for the six months ended June 30, 2017.

The following table summarizes our research and development expenses (in thousands):

	Six Months Ended June 30,		
	2016	2017	Change
LRRK2 program external expenses (1)	$ 11,312	$ 9,749	$(1,563)
RIPK1 program external expenses	5,652	3,755	(1,897)
BBB platform external expenses	1,369	1,634	265
Other external research and development expenses	3,485	4,904	1,419
Personnel related expenses (2)	6,238	10,897	4,659
Other unallocated research and development expenses	3,097	6,535	3,438
Total research and development expenses	$31,153	$37,474	$ 6,321

(1) Payments under the license agreement with Genentech for an upfront payment and technology transfer fee totaling $8.8 million and a milestone payment of $2.5 million are included in the amounts for the six months ended June 30, 2016 and 2017, respectively.
(2) Personnel related expenses include stock-based compensation expense of $0.6 million for the six months ended June 30, 2016 and $1.2 million for the six months ended June 30, 2017, reflecting an increase of $0.6 million.

The increase in total research and development expenses of $6.3 million was primarily attributable to a $4.7 million increase in personnel related expenses due to an increase in our research and development headcount and a $3.4 million increase in other unallocated research and development expenses. The increase in other unallocated research and development expenses consisted of an increase in lab consumable expenses of $1.6 million and an increase in facilities related expenses of $1.8 million, attributable to increases in research and development headcount and the move to our new headquarters in August 2016 which allowed us to significantly increase our lab space capacity, including the addition of a vivarium.

These increases were partially offset by a $1.6 million decrease in LRRK2 program external expenses and a $1.9 million decrease in RIPK1 program external expenses. The decrease in LRRK2 program external expenses is primarily attributable to $8.8 million in upfront expenses incurred in the six months ended June 30, 2016 related to our license agreement with Genentech, partially offset by the milestone payment of $2.5 million under such license agreement and increases in external program expenses in the six months ended June 30, 2017, due to activities associated with preparing for an IND filing for DNL201. The decrease in RIPK1 program external expenses is primarily due to the termination of the clinical trial for DNL104 in April 2017.

General and administrative expenses. General and administrative expenses were $5.6 million for the six months ended June 30, 2016 compared to $6.8 million for the six months ended June 30, 2017. The increase of $1.2 million was primarily attributable to a $0.6 million increase in patent expenses and professional services to support our ongoing operations and $0.2 million related to increased facilities expenses attributable to general and administrative expenses resulting from the move to our new headquarters in August 2016.

Interest income, net. Interest income, net was immaterial for the six months ended June 30, 2016 compared to $0.9 million for the six months ended June 30, 2017. We began investing our excess cash in marketable securities in June 2016. As such, the increase of $0.8 million reflects that the six months ended June 30, 2016 includes less than one month of income from marketable securities, compared to the six months ended June 30, 2017, which includes six months of income from marketable securities.

Comparison of the Years Ended December 31, 2015 and 2016

The following table sets forth the significant components of our results of operations (in thousands):

	Year Ended December 31,		
	2015	2016	Change
Operating expenses:			
Research and development	$ 11,571	$ 75,702	$ 64,131
General and administrative	5,108	11,731	6,623
Total operating expenses	16,679	87,433	70,754
Loss from operations	(16,679)	(87,433)	(70,754)
Interest income (expense), net	(109)	781	890
Net loss	$(16,788)	$(86,652)	$(69,864)

Research and development expenses. Research and development expenses were $11.6 million for the year ended December 31, 2015 compared to $75.7 million for the year ended December 31, 2016.

The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,		
	2015	2016	Change
LRRK2 program external expenses (1)	$ 777	$ 16,770	$ 15,993
RIPK1 program external expenses (2)	2,256	19,106	16,850
BBB platform external expenses (3)	33	8,016	7,983
Other external research and development expenses	3,305	8,020	4,715
Personnel related expenses (4)	2,943	14,974	12,031
Other unallocated research and development expenses	2,257	8,816	6,559
Total research and development expenses	$ 11,571	$ 75,702	$ 64,131

(1) The amount for the year ended December 31, 2016 includes an upfront payment and technology transfer license payment to Genentech totaling $10.0 million.
(2) The amount for the years ended December 31, 2015 and 2016 include $1.5 million and $5.3 million in expenses related to initial and contingent stock consideration, respectively, both issued in connection with our acquisition of Incro.
(3) The amount for the year ended December 31, 2016 includes $5.5 million in expenses related to a payment made under our license and collaboration agreement with F-star.
(4) Personnel related expenses include stock-based compensation expense of $0.1 million in 2015 and $2.1 million in 2016, with the increase driven by higher headcount and a higher estimated fair value of our common stock.

The increase in research and development expenses of $64.1 million is a result of several factors. The increase was attributable to a $16.9 million increase in our RIPK1 program external expenses, a $16.0 million increase in our LRRK2 program external expenses, an $8.0 million increase in our BBB platform technology external expenses and a $12.0 million increase in personnel related expenses. In addition, the increase reflects the fact that the expenses in the year ended December 31, 2015 only include seven months of operations, as we commenced operations in May 2015.

The increase in our RIPK1 program external expenses is primarily attributable to the increased fair value and number of shares of our common stock issued during 2016 to former shareholders of Incro as contingent consideration for our acquisition of Incro, as well as the expenses incurred for the preparation for and initiation of the DNL104 Phase 1 clinical trial. The increase in our LRRK2 program external expenses is primarily attributable to an upfront payment and a technology transfer license payment to Genentech totaling $10.0 million in the year ended December 31, 2016, as well as increased external research services to progress DNL201 and other LRRK2 molecules into development. The increase in our BBB platform technology external expenses is primarily attributable to the $5.5 million upfront fee payment to F-star Gamma in the year ended December 31, 2016. The increase in personnel related expenses is attributable to a $10.0 million increase in salaries and benefits and a $2.0 million increase in stock-based compensation expense, both due primarily to an increase in our research and development headcount.

Furthermore, there was a $6.6 million increase in other unallocated research and development expenses. This was primarily composed of an increase in lab consumable expenses of $3.4 million and an increase in facilities related expenses of $2.7 million. These increases are partially attributable to the fact that these expenses include seven and twelve months of expenses in the years ended December 31, 2015 and 2016, respectively, and also reflect increases in research and development headcount and increased expenses related to the move to our new headquarters in August 2016.

General and administrative expenses. General and administrative expenses were $5.1 million for the year ended December 31, 2015 compared to $11.7 million for the year ended December 31, 2016. The increase of $6.6 million was primarily attributable to a $2.8 million increase in employee salaries and benefits as we expanded our headcount, a $2.5 million increase in patent and professional services to support our ongoing operations, a $0.5 million increase in stock-based compensation expense and $0.3 million related to increased facilities related expenses resulting from the move to our new headquarters in August 2016 and reflects the fact that the expenses in the year ended December 31, 2015 include only seven months of operations, as we commenced operations in May 2015.

Interest income (expense), net. Interest expense was $(0.1) million for the year ended December 31, 2015 compared to interest income of $0.8 million for the year ended December 31, 2016. The expense for the year ended December 31, 2015 represents interest expense on a $5.0 million promissory note outstanding from January 2015 until May 2015, at which time this note, along with the accrued interest, was converted into Series A-1 convertible preferred stock. The income for the year ended December 31, 2016 represents income from marketable securities earned in the period from June 2016 to December 2016, during which we invested our excess cash in marketable securities.

Liquidity and Capital Resources

Sources of Liquidity

From our inception through June 30, 2017, we have funded our operations primarily through the sale and issuance of our convertible preferred stock. From our inception through June 30, 2017, we raised aggregate cash proceeds of $349.3 million from the issuance of our convertible preferred stock. As of June 30, 2017, we had cash, cash equivalents and marketable securities in the amount of $212.8 million.

Future Funding Requirements

To date, we have not generated any revenue. We do not expect to generate any meaningful revenue unless and until we obtain regulatory approval of and commercialize any of our product

candidates or enter into collaborative agreements with third parties, and we do not know when, or if, either will occur. We expect to continue to incur significant losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are subject to all of the risks typically related to the development of new product candidates, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Moreover, following the completion of this offering, we expect to incur additional costs associated with operating as a public company. We anticipate that we will need substantial additional funding in connection with our continuing operations.

Until we can generate a sufficient amount of revenue from the commercialization of our product candidates or from collaborative agreements with third parties, if ever, we expect to finance our future cash needs through public or private equity or debt financings. Additional capital may not be available on reasonable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. Any of the foregoing could significantly harm our business, financial condition and prospects.

Since our inception, we have incurred significant losses and negative cash flows from operations. We have an accumulated deficit of $147.0 million through June 30, 2017. We expect to incur substantial additional losses in the future as we conduct and expand our research and development activities. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to enable us to fund our projected operations through at least the next 12 months.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. However, we have based these estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect.

The timing and amount of our operating expenditures will depend largely on:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of third parties with whom we have entered into license and collaboration agreements;
- our ability to maintain our current research and development programs and to establish new research and development, license or collaboration arrangements;
- our ability and success in securing manufacturing relationships with third parties or, in the future, in establishing and operating a manufacturing facility;
- the costs involved in prosecuting, defending and enforcing patent claims and other intellectual property claims;
- the cost and timing of regulatory approvals;

- our efforts to enhance operational, financial and information management systems and hire additional personnel, including personnel to support development of our product candidates; and
- the costs and ongoing investments to in-license and/or acquire additional technologies.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Cash Flows

The following table sets forth a summary of the primary sources and uses of cash for each of the periods presented below (in thousands):

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Cash used in operating activities	$(15,052)	$ (72,359)	$ (32,706)	$(36,378)
Cash provided by (used in) investing activities	(3,062)	(219,004)	(50,749)	37,457
Cash provided by financing activities	48,854	300,476	292,786	375
Net increase in cash and cash equivalents	$ 30,740	$ 9,113	$209,331	$ 1,454

Cash Used in Operating Activities

During the six months ended June 30, 2017, cash used in operating activities was $36.4 million, which consisted of a net loss of $43.5 million, adjusted by non-cash charges of $4.0 million and cash provided by changes in our operating assets and liabilities of $3.1 million. The non-cash charges consisted primarily of stock-based compensation expense of $1.8 million and depreciation expense of $1.5 million. The change in our operating assets and liabilities was primarily due to an increase of $2.4 million in accrued and other current liabilities and a decrease of $1.3 million in prepaid expenses and other current assets.

During the six months ended June 30, 2016, cash used in operating activities was $32.7 million, which consisted of a net loss of $36.7 million, adjusted by non-cash charges of $1.5 million and cash provided by changes in our operating assets and liabilities of $2.5 million. The non-cash charges consisted primarily of stock-based compensation expense of $1.1 million and depreciation expense of $0.4 million. The change in our operating assets and liabilities was primarily due to an increase of $1.9 million in accrued and other liabilities and an increase of $0.8 million in accounts payable.

During the year ended December 31, 2016, cash used in operating activities was $72.4 million, which consisted of a net loss of $86.7 million, adjusted by non-cash charges of $10.0 million and cash provided by changes in our operating assets and liabilities of $4.3 million. The non-cash charges consisted primarily of the expense recognized for the fair value of our common stock issued in connection with the acquisition of Incro of $5.3 million and stock-based compensation expense of $3.0 million. The change in our operating assets and liabilities was primarily due to an increase of $5.4 million of accrued and other liabilities. Our accrued liabilities increased due to employee bonuses and general business expenses, reflective of our increased headcount and expenses. This was partially

offset by an increase in restricted cash of $0.5 million associated with the lease for our new headquarters and an increase of $0.5 million in prepaid expenses and other assets mainly associated with prepayments made for ongoing research and development being conducted by third-party service providers.

During the year ended December 31, 2015, cash used in operating activities was $15.1 million, which consisted of a net loss of $16.8 million, adjusted by non-cash charges of $1.3 million and cash provided by changes in our operating assets and liabilities of $0.4 million. The non-cash charges consisted primarily of the expense recognized for the fair value of our common stock issued in connection with the acquisition of Incro of $0.6 million, and stock-based compensation expense of $0.5 million. The change in our operating assets and liabilities was primarily due to an increase of $3.3 million of accounts payable, accrued and other liabilities. Our accrued liabilities increased due to employee bonuses and general business expenses, reflective of the increased headcount and expenses. This was partially offset by an increase in prepaid expenses and other assets of $2.7 million primarily associated with prepayments made for ongoing research and development being conducted by third-party service providers and the deferral of employee bonuses.

Cash Provided by (Used in) Investing Activities

During the six months ended June 30, 2017, cash provided by investing activities was $37.5 million, which consisted of $67.1 million in proceeds from the maturity of marketable securities, partially offset by $28.2 million of purchases of short-term marketable securities and $1.4 million of capital expenditures to purchase property and equipment.

During the six months ended June 30, 2016, cash used in investing activities was $50.7 million, which consisted of $49.3 million of purchases of short-term marketable securities and $1.5 million of capital expenditures to purchase property and equipment.

During the year ended December 31, 2016, cash used in investing activities was $219.0 million, which consisted of $226.4 million of purchases of marketable securities, $6.1 million of capital expenditures to purchase property and equipment and $0.5 million of purchases of intangible assets, partially offset by $14.0 million in proceeds from the maturity of marketable securities.

During the year ended December 31, 2015, cash used in investing activities was $3.1 million, all of which related to capital expenditures to purchase property and equipment.

Cash Provided by Financing Activities

During the six months ended June 30, 2017, cash provided by financing activities was $0.4 million, consisting of net proceeds in connection with exercises of common stock options.

During the six months ended June 30, 2016, cash provided by financing activities was $292.8 million, primarily consisting of net proceeds from the issuances of shares of our convertible preferred stock.

During the years ended December 31, 2015 and 2016, cash provided by financing activities was $48.9 million and $300.5 million, respectively, primarily consisting of net proceeds from the issuances of shares of our convertible preferred stock and convertible promissory note, which has since been converted to convertible preferred stock.

Since our inception through December 31, 2016, we have raised an aggregate of approximately $348.6 million in net proceeds, through the issuance of shares of our convertible preferred stock, net of

$0.7 million in issuance costs, which we have used to fund our operations. During 2016, net proceeds from our sale of Series A and Series B-1 convertible preferred stock were $300.4 million. During 2015, net proceeds from our sale of Series A-1 convertible preferred stock were $43.2 million and net proceeds from the sale and issuance of a convertible promissory note was $5.0 million.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements. Our license and collaboration agreements with F-star represent a variable interest in a variable interest entity, or VIE, F-star Gamma. However, we do not consolidate F-star Gamma in our consolidated financial statements because we are not considered to be its primary beneficiary.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2016 (in thousands):

	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease obligations (1)	$21,039	$ 2,510	$5,250	$5,574	$ 7,705
Total contractual obligations	$21,039	$ 2,510	$5,250	$5,574	$ 7,705

(1) We lease our former and current facilities under operating leases. In September 2015, we entered into a lease for our current laboratory and office space that commenced in August 2016 and expires in July 2024. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

In the normal course of business, we enter into various firm purchase commitments primarily related to research and development activities. As of December 31, 2016, we had noncancelable purchase commitments of $1.0 million and contractual obligations under license agreements of $0.2 million.

Pursuant to certain license agreements, including our agreements with Genentech and F-star, we have obligations to make future milestone and royalty payments to other parties. Additionally, we have an option to acquire all outstanding shares of F-star Gamma for initial exercise payments ranging from $18.0 million to $50.0 million in the aggregate, plus the estimated net cash held by F-star Gamma at the time of such purchase. In addition to these initial exercise payments, we would be required to make certain contingent payments up to a maximum amount of $447.0 million in the aggregate. However, we are unable to estimate the timing or likelihood of achieving the milestones or of exercising the option to purchase the outstanding shares of F-star Gamma and, therefore, any related payments are not included in the table above.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about

the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Research and Development Expenses

We record research and development expenses to operations as incurred. Research and development expenses represent costs incurred by us for the discovery and development of our product candidates and the development of our BBB platform technology and include: employee-related expenses, including salaries, benefits, travel and non-cash stock-based compensation expense; external research and development expenses incurred under arrangements with third parties, such as CROs, preclinical testing organizations, CMOs, academic and non-profit institutions and consultants; costs to acquire technologies to be used in research and development that have not reached technological feasibility and have no alternative future use; license fees; and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

As part of the process of preparing financial statements, we are required to estimate and accrue expenses. A portion of our research and development expenses are external costs, which we track on a program-specific basis once a program has commenced a late-stage IND-enabling study. We record the estimated expenses of research and development activities conducted by third-party service providers based upon the estimated amount of services provided within research and development expense in the statements of operations and comprehensive loss. These services include the conduct of preclinical studies and clinical trials, contract manufacturing activities and consulting services. If the costs have been prepaid, this expense reduces the prepaid expenses in the balance sheet, and if not yet invoiced, the costs are included in accrued liabilities in the balance sheet. These costs are a significant component of our research and development expenses. We record amortization of prepaid expenses or accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties.

Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks. We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from external clinical research organizations and other third-party service providers. To date, we have not experienced material differences between our accrued expenses and actual expenses. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Variable Interest Entities

We assess whether we are the primary beneficiary of a VIE at the inception of the arrangement and at each reporting date. This assessment is based on our power to direct the activities of the VIE that most significantly impact the VIE's economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Stock-Based Compensation

We have granted stock-based awards, consisting of stock options and restricted stock, to our employees, certain non-employee consultants and certain members of our board of directors. We measure stock-based compensation expense for restricted stock and stock options granted to our employees and directors on the date of grant and recognize the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We account for stock-based compensation arrangements with non-employee consultants using a fair value approach. The estimated fair value of unvested options granted to non-employee consultants is remeasured at each reporting date through the date of final vesting. As a result, the noncash charge to operations for nonemployee options with vesting conditions is affected in each reporting period by changes in the estimated fair value of our common stock. We adjust for actual forfeitures as they occur.

We have also granted stock options that vest in conjunction with certain performance and market conditions to certain key employees. At each reporting date, we are required to evaluate whether the achievement of the performance or market condition is probable. Compensation expense is recorded over the appropriate service period based on our assessment of accomplishing each performance or market provision or the occurrence of other events that may have caused the awards to accelerate and vest. See the section titled “Executive Compensation” for additional information.

We estimate the fair value of stock options granted to our employees and directors on the grant date, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

- *Expected Term*. Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term), as we do not have sufficient historical data to use any other method to estimate expected term.
- *Expected Volatility*. As there has been no public market for our common stock to date, and as a result we do not have any trading history of our common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies are chosen based on their similar size, stage in the life cycle or area of specialty.
- *Risk-Free Interest Rate*. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of the stock option grants.
- *Expected Dividend*. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we use an expected dividend yield of zero.

For options granted to non-employee consultants, the fair value of these options is also remeasured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option.

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors, with input from management, considering our most recently available third-party valuations of common stock and our board of directors’ assessment of additional objective and subjective factors that it believed were relevant, and

factors that may have changed from the date of the most recent valuation through the date of the grant. These factors include, but are not limited to: our most recently available valuations of our common stock by an unrelated third party; the prices at which we sold shares of our convertible preferred stock to outside investors in arms-length transactions; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; our results of operations, financial position and capital resources; current business conditions and projections; the lack of marketability of our common stock; the hiring of key personnel and the experience of management; the risk inherent in the development of our products; our stage of development and material risks related to its business; the fact that the option grants involve illiquid securities in a private company; and the likelihood of achieving a liquidity event, such as an initial public offering or sale, in light of prevailing market conditions.

We have periodically determined the estimated fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid. The Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, our board of directors considered the following methods:

- *Current Value Method.* Under the Current Value Method, or CVM, our value is determined based on our balance sheet. This value is then first allocated based on the liquidation preference associated with preferred stock issued as of the valuation date, and then any residual value is assigned to the common stock.
- *Option-Pricing Method.* Under the option-pricing method, or OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options.
- *Probability-Weighted Expected Return Method.* The probability-weighted expected return method, or PWERM, is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

Our common stock valuation as of May 31, 2015 was prepared using a hybrid between the CVM and OPM, the latter of which was based on the price at which we sold shares of our Series A-1 convertible preferred stock. The deemed fair value was determined by weighting these two methodologies differently resulting in an increased estimated fair value of our common stock for financial reporting purposes.

Our common stock valuations as of March 31, 2016, June 30, 2016, September 30, 2016, and December 31, 2016 were prepared using the back-solve method of OPM, which derives the implied equity value for one type of equity security from a contemporaneous transaction involving another type of security.

Our common stock valuations as of March 31, 2017 and June 30, 2017 were prepared using the hybrid method, which is a hybrid between the PWERM and OPM, consistent with how such hybrid method is described in the Practice Aid.

Our board of directors and management develop best estimates based on application of these approaches and the assumptions underlying these valuations, giving careful consideration to the

advice from our third-party valuation expert. Such estimates involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation could be materially different. Following the closing of this offering, our board of directors will determine the fair market value of our common stock based on its closing price as reported on the date of grant on the primary stock exchange on which our common stock is traded.

The intrinsic value of all outstanding options as of , 2017 was approximately $ million, based on the assumed initial public offering price of $ per share, which is the midpoint of the estimated initial public offering price range set forth on the cover page of this prospectus, of which approximately $ million is related to vested options and approximately $ million is related to unvested options.

JOBS Act

We are an emerging growth company under the JOBS Act. As an emerging growth company, we may delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have nonetheless irrevocably elected not to avail ourselves of this exemption and, as a result, upon completion of this offering we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We will remain an emerging growth company until the earliest of (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) the date on which we are deemed to be a “large accelerated filer” under the rules of the SEC with at least $700.0 million of outstanding equity securities held by non-affiliates, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the previous three years, or (iv) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering.

Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $212.8 million as of June 30, 2017, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short to intermediate term fixed income securities.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, according to our board-approved investment charter.

Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Foreign Currency Sensitivity

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily the Euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against the Euro affects the reported amounts of expenses, assets and liabilities associated with a limited number of preclinical

and clinical activities. We do not currently engage in any hedging activity to reduce our potential exposure to currency fluctuations, although we may choose to do so in the future. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board issued Accounting Standards Update, or ASU, No. 2014–09, Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12, which amends the existing accounting standards for revenue recognition. ASU 2014–09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non–public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While we continue to assess all potential impacts under ASU 2014-09, we do not believe adopting the new revenue recognition standard will materially impact the consolidated financial statements as we have not yet generated revenue.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The standard is effective for interim and annual periods beginning after December 15, 2019, with early adoption permitted. The ASU is expected to impact our consolidated financial statements as we have certain operating lease arrangements for which we are the lessee. We are currently in the process of evaluating the impact the adoption of ASU 2016-02 will have on our consolidated financial position or results of operations. We expect that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on our consolidated balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the consolidated balance sheet presentation is expected to change, we do not expect a material change to our consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. We are currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but do not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. We are currently evaluating the impact of adopting this standard on our consolidated financial statements and disclosures, but we do not expect it to have a significant impact.

FOUNDERS' VISION

We have embarked on a deeply personal journey to conquer neurodegenerative diseases. Collectively, these diseases represent one of the most significant medical challenges facing us today, impacting millions of people including our own families and friends. We are passionately dedicated to understanding these diseases. Our goal is nothing short of defeating neurodegeneration by harnessing the power of modern science and technology to discover and develop medicines that meaningfully improve the lives of patients and their families.

This is a formidable challenge and opportunity. Defeating degeneration – to us – is akin to summiting the tallest mountains. Hence the name Denali. For the longest time, mankind was unable to summit the highest peaks. But when the time was right, bold mountaineers succeeded, enabled by technological progress and a better understanding of the elements. We believe that the same is possible in neurodegeneration today.

We are well aware that we are taking on a major challenge, yet we believe that success is within our reach. Recent genetic insights, better diagnostic tools and the ability to engineer medicines to cross the blood-brain barrier are crucial components in defeating degeneration. We have contributed to and experienced firsthand the advances that are made possible by following breakthrough science. We believe that the field of neurodegeneration is now at the inflection point where oncology was years ago when genetic discoveries revealed biological pathways responsible for cancer growth that resulted in powerful drug targets, and biomarkers enabled the diagnosis and selection of patients for targeted treatment approaches. Similar success is within reach in neurodegeneration.

Just like the mountaineers who set out to conquer the highest peaks, it takes a courageous team with a singular focus and unrelenting persistence to succeed. At Denali, we have assembled an outstanding team of driven and passionate scientists and drug developers, and a powerful network of collaborators in academia and industry.

The science is breaking open, and the time is right to discover and develop effective medicines for neurodegeneration. Every day matters. To patients, to their families and to society at large. We invite you to join us on our journey to the summit.

Ryan Watts, Ph.D.
CEO and Co-Founder

Alexander Schuth, M.D.
COO and Co-Founder

Marc Tessier-Lavigne, Ph.D.
Director and Co-Founder

BUSINESS

Overview and Strategy

We discover and develop therapeutics to defeat degeneration.

Neurodegeneration represents one of the most significant unmet medical needs of our time, with few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, or ALS, and other neurodegenerative diseases. The disease burden is massive.

We believe the time is right to make a focused and ambitious effort to defeat neurodegeneration. We believe that we can succeed in a field that has seen limited success in the past. Why? In short, because of our team of passionately dedicated scientists and drug developers, our scientific strategy and engineering technology, and our focused yet diversified portfolio approach. We are unique in developing a broad therapeutic portfolio for neurodegenerative diseases with biomarker driven, targeted therapeutics enabled by our proprietary brain delivery technology.

Historical challenges in developing effective therapeutics for patients with neurodegenative diseases included a scarcity of therapeutic targets due to a limited understanding of disease biology, insufficient uptake of therapeutics into the brain because of the blood-brain barrier, or BBB, and few available biomarkers for target engagement, diagnosis, patient selection and tracking disease progression. In recent years, however, significant progress in each of these areas has been made, greatly increasing the odds of developing effective therapeutics for neurodegenerative diseases.

Our strategy is guided by three overarching principles. We believe that the application of these principles will significantly increase the probability of success and will accelerate the timing to bring effective therapeutics to patients with neurodegenerative diseases:

Genetic Pathway Potential	We use recent advances in understanding human genetics and cell biology in neurodegeneration to select our therapeutic targets, disease pathways and biomarkers. We focus on the degenogenes, which are genes that when mutated cause, or are major risk factors for, neurodegenerative diseases. These degenogenes directly point to important disease pathways, and we have initially selected three such pathways for which we have built significant scientific expertise: lysosomal function, glial biology and cellular homeostasis.
Engineering Brain Delivery	We engineer our product candidates to cross the blood-brain barrier and act directly in the brain. This engineering is designed to enable optimal concentration of a therapeutic in the brain in order to improve therapeutic target engagement. For large molecule product candidates, such as antibodies and enzymes, we have engineered a proprietary BBB platform technology. For small molecule product candidates, which are synthetically created therapeutics, we design and test appropriate molecular architectures to optimize their exposure in the brain.
Biomarker-Driven Development	We discover, develop and utilize biomarkers to select the right patient population and demonstrate target engagement, pathway engagement and impact on disease progression of our product candidates. These biomarkers can be used as endpoints of efficacy in early clinical trials, with the goal of accelerating clinical development timelines. In addition, each of our therapeutic programs includes a patient selection strategy using biomarkers to identify and segment patients in order to increase the likelihood of success.

Our total portfolio currently consists of eleven programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have six core programs and five seed programs. Our core programs are at various stages of clinical and preclinical development, and we believe that each of these programs has the potential to result in either first-in-class or best-in-class products for neurodegenerative diseases. We actively pursue combination therapies using bi-specific BBB platform technology.

In building and developing our portfolio, we are guided by the principles outlined above, which means that the therapeutic target or pathway for each program is genetically linked to neurodegenerative disease, our product candidates are being engineered to optimize brain delivery, and the clinical development plan will be enabled by biomarkers. We rigorously follow the science and employ the therapeutic modality that we believe is best suited to modulate the target pathway. Our product candidates currently include small molecules, antibodies and enzymes and may expand to include other modalities in the future.

To increase the probability of success, we make parallel investments in several product candidates and back-up candidates, and plan to advance only those candidates that show strong preclinical and early clinical data to the later stages of clinical development. We constantly strive to replenish, grow and optimize our portfolio through in-house discovery and external business development activities, in each case enabled by our strong internal research and development expertise and capabilities.

By developing a broad portfolio of product candidates, we can continuously apply learnings and tools across programs and leverage economies of scale in our research and development organization. Our target indications include diseases with large patient populations, such as Alzheimer's disease, as well as orphan indications, such as mucopolysaccharidosis type II, or MPS II, and ALS. We aim to increase the probability of success and accelerate clinical development timelines by using biomarkers and other tools to demonstrate an impact on relevant disease biology for proof of concept in early clinical trials.

We have development and commercialization rights to all of our core programs, and we have a broad patent portfolio supporting our core programs.

The following table summarizes key information about our core programs:

Program Target	Drug Candidate	Therapeutic Modality	Disease Indication	Preclinical Development	Clinical Development
Lysosomal Function Pathway					
LRRK2	DNL201	Small Molecule	Parkinson's disease	Phase 1	
	DNL151	Small Molecule	Parkinson's disease	IND-Enabling	
Alpha-Synuclein	ATV:aSyn	Antibody	Parkinson's disease, DLB, MSA	Preclinical	
Iduronate 2-sulfatase	ETV:IDS	Enzyme	MPS II (Hunter Syndrome)	Preclinical	
Glial Biology Pathway					
RIPK1	DNL747	Small Molecule	Alzheimer's disease, ALS	IND-Enabling	
TREM2	ATV:TREM2	Antibody	Alzheimer's disease	Preclinical	
Cellular Homeostasis Pathway					
BACE1 / TAU	ATV:BACE1/Tau	Antibody	Alzheimer's disease	Preclinical	

ATV: Antibody Transport Vehicle; **ETV**: Enzyme Transport Vehicle; **DLB**: Dementia with Lewy Bodies; **MSA**: Multiple System Atrophy; **MPS II**: Mucopolysaccharidosis Type II; **ALS**: Amyotrophic Lateral Sclerosis

Delivering therapeutics across the BBB has been a major obstacle to successful drug development in neurodegeneration, and is critical to enabling effective treatments. Protein therapeutics, such as antibodies, have revolutionized the treatment of many diseases, but this class of medicines does not effectively cross the BBB and, therefore, currently has very limited therapeutic application to the treatment of neurodegenerative diseases. To address this limitation, we have developed a proprietary BBB platform technology designed to deliver large molecules across the BBB. We are currently optimizing and broadening this platform technology.

Our Antibody Transport Vehicle, or ATV, and Enzyme Transport Vehicle, or ETV, platforms are modular BBB delivery technologies for large molecule therapeutics, including antibodies, enzyme and other proteins. These platforms are designed to engage specific BBB transport receptors, which are ubiquitously expressed in the brain capillaries and facilitate transport of proteins into the brain. In an animal model, an antibody engineered with our ATV technology has demonstrated over 20-fold greater brain penetration than a control antibody not enabled by this technology. This improvement in brain exposure may enable therapeutically relevant concentrations of our ATV antibody product candidates in the brain, making them potentially superior to traditional monoclonal antibody therapeutics. We are currently developing several product candidates for multiple programs to advance to Investigational New Drug, or IND, enabling studies in preparation for human clinical trials. We plan to have multiple product candidates that utilize our ATV or ETV platforms enter clinical development in 2019 and 2020, including molecules targeting alpha-synuclein, or aSyn; iduronate 2-sulfatase, or IDS; triggering receptor expressed in myeloid cells 2, or TREM2; beta-secretase 1, or BACE1; and Tau.

We also follow a rigorous approach to designing small molecules to cross the BBB. DNL201 and DNL151, our small molecule inhibitors of leucine-rich repeat kinase 2, or LRRK2, have been specifically designed to cross the BBB. LRRK2 is a degenogene that regulates lysosomal function, and mutations in LRRK2 are one of the most commonly known genetic causes of Parkinson's disease. DNL747 is a small molecule inhibitor of receptor interacting serine/threonine protein kinase 1, or RIPK1, that is designed to cross the BBB. RIPK1 is a regulator of microglial homeostasis and increased RIPK1 kinase activity drives neuroinflammation and cell necroptosis in immune cells and in the brain. RIPK1 inhibition in preclinical models has been shown to have beneficial effects in both Alzheimer's disease and ALS.

We have assembled a team with a deep set of scientific, clinical, business and leadership capabilities in biotechnology, and specifically in neurodegenerative diseases, who worked together at Genentech for many years prior to the founding of Denali. Our Co-Founder and Chief Executive Officer, Ryan J. Watts, Ph.D., is a world-leading drug developer and neuroscientist, with particular expertise in BBB therapeutic delivery. Dr. Watts most recently led the neuroscience research team at Genentech and has led multiple discovery teams, including programs in Alzheimer's disease, Parkinson's disease and ALS. Our Co-Founder and Chief Operating Officer, Alexander O. Schuth, M.D., MBA, held various operational and leadership roles at Genentech for nearly ten years, including leading the partnering groups for neuroscience as well as technology innovation and diagnostics. Dr. Schuth has led more than 35 partnering transactions and a clinical stage development program. Our Co-Founder and director, Marc Tessier-Lavigne, Ph.D., is a world-leading neuroscientist, was formerly Chief Scientific Officer at Genentech and serves as President of Stanford University. Carole Ho, M.D., our Chief Medical Officer, brings over a decade of clinical development experience, most recently as Vice President, Non-Oncology Early Clinical Development at Genentech. Dr. Ho has overseen or contributed to more than ten IND filings and three drug approvals. Our Chief Financial Officer, Steve E. Krognes, MBA, brings over two decades of operational and corporate finance experience, most recently serving six years as Chief Financial Officer and member of the Executive Committee at Genentech. Mr. Krognes has led more than 40 strategic deals and led or contributed to several capital raising transactions.

Our leadership team is joined by about 120 employees, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, they bring expertise across relevant disciplines, including neuroscience, BBB biology, genetics, oncology, immunology, translational science, antibody engineering, chemistry and biomarker development. Our development leadership team members have, collectively, led and contributed to more than 120 IND and clinical trial application, or CTA, filings. Our board of directors is comprised of several leaders from both academia and industry. Our directors include Vicki Sato, Ph.D. (Chair), retired Professor of Management at Harvard Business School, Doug Cole, M.D., Managing Director of Flagship Pioneering, Jay Flatley, Executive Chairman and retired Chief Executive Officer of Illumina, Robert T. Nelsen, co-founder and Managing Director of ARCH Venture Partners and David Schenkein, M.D., Chief Executive Officer of Agios Pharmaceuticals. Our directors collectively bring deep scientific knowledge and relevant industry experience.

Licenses and collaborations are central components of our strategy to build and advance our pipeline of product candidates. We have entered into arrangements with biopharmaceutical companies such as Genentech and F-star, patient-focused data companies such as 23andMe and Patients Like Me, numerous leading academic institutions such as Harvard University, Massachusetts General Hospital, Washington University in St. Louis, the University of California, San Diego and Vlaams Instituut voor Biotechnologie and foundations such as the Michael J. Fox Foundation to gain access to new product candidates, enable and accelerate the development of our existing programs and deepen our scientific understanding of certain areas of biology. We believe that accessing external innovation is important to our success and we plan to remain active in accessing external innovation through business development activities. Our goal is to be the most attractive partner for academic groups and companies in the field of neurodegeneration based on our singular focus, broad capabilities and ability to execute with scientific rigor and speed.

Our Approach to Defeating Neurodegeneration

Disease Overview

Neurodegenerative diseases are a collection of conditions defined by progressive nervous system dysfunction, degeneration and/or death of neurons causing cognitive decline, functional impairment and eventually death. Neurodegeneration represents one of the most significant unmet medical needs of our time, with an aging population and lack of effective therapeutic options yielding a rapidly growing patient population. The two most common neurodegenerative diseases are Alzheimer's disease, representing an estimated 60% to 70% of all dementias according to the World Health Organization, and Parkinson's disease. In the United States, 5.5 million people suffer from Alzheimer's disease, as many as one million people suffer from Parkinson's disease (with 60,000 new patients being diagnosed each year), and more than 20,000 patients suffer from ALS, according to estimates from the Alzheimer's Association, the Parkinson's Disease Foundation, and the ALS Association, respectively.

The cost to society from neurodegenerative disease is massive. The direct costs to American society of caring for those with Alzheimer's disease and other dementias will total an estimated $259 billion in 2017, and is projected to increase to $1.1 trillion by 2050, according to the Alzheimer's Association. In the United States, the total cost of care to patients suffering from Alzheimer's disease and other dementias far exceeds that of many other diseases, including cancer.

Genetic Pathway Potential

Advances in our understanding of the genetics, pathology and cell biology underlying chronic neurodegenerative diseases have identified pathways that trigger and/or contribute to disease onset and progression. Of particular importance is the progress in genetic sequencing where the dramatic reduction in the cost of DNA sequencing has recently led to the discovery of numerous genetic mutations that have been linked to neurodegeneration (Figure 1).

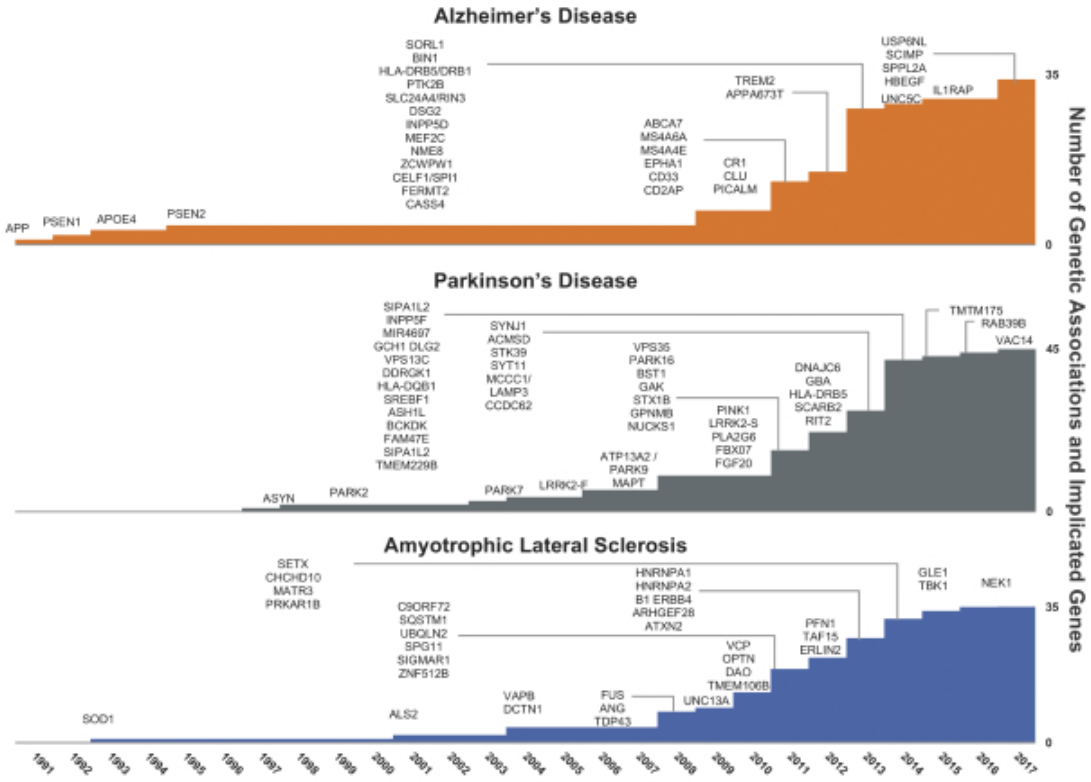
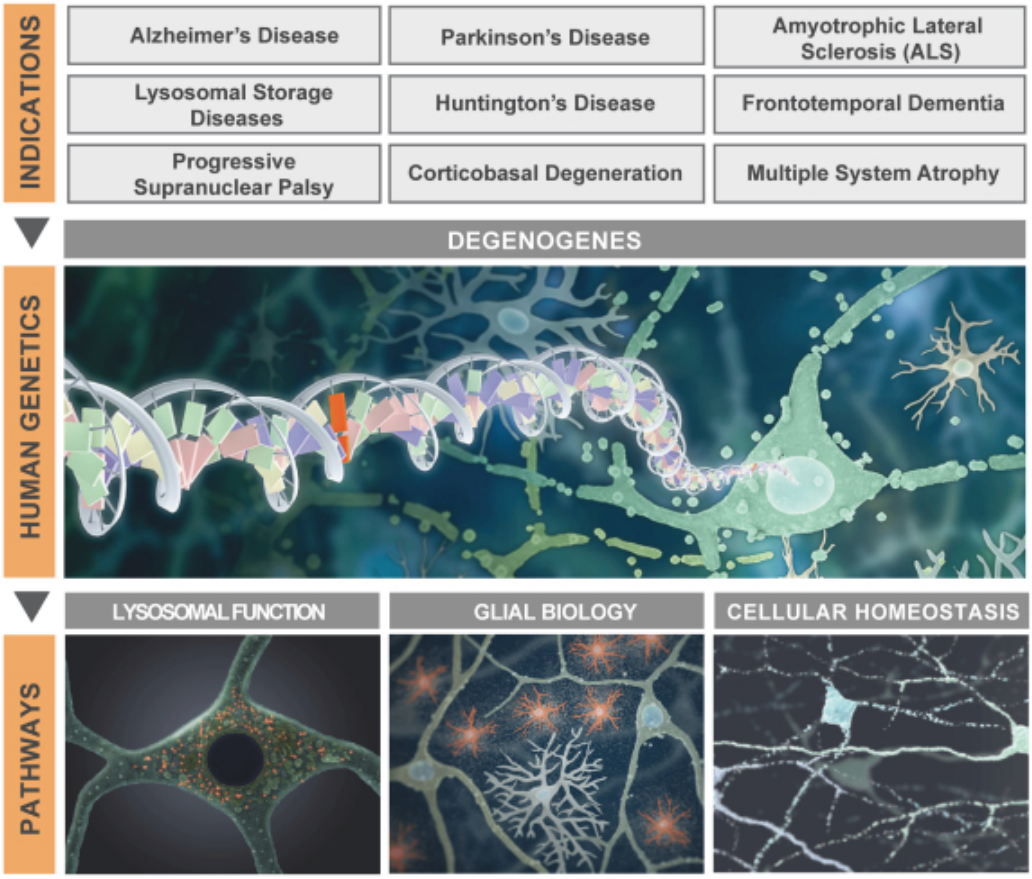


Figure 1: The number of associated genetic mutations linked to Alzheimer's disease, Parkinson's disease and ALS from 1991 to 2017. For genome-wide association studies, disease genes were selected based on genome-wide significance (p<5×10-8). Rare disease-causing and/or high penetrance mutations were included based on a p value of 1x10^-7 and replication in an independent cohort.

Human Genetics: Degenogenes

Prior to 2007, only a limited number of genetic mutations linked to Alzheimer's disease, Parkinson's disease and ALS had been identified. Since 2007, the number of genetic associations discovered in neurodegenerative diseases has grown rapidly, with more than 100 genes associated with these three neurodegenerative diseases collectively. The degenogenes directly point to important disease pathways that are disrupted in neurodegeneration, and are our scientific foundation for identifying and pursuing promising targets for drug development. We have chosen to initially focus on three such pathways: lysosomal function, glial biology and cellular homeostasis.



Disease Pathways

Lysosomal Function

The lysosomal system, the disposal and recycling compartment of the cell, is involved in the digestion and processing of proteins and lipids in brain cells. Dysfunction of the lysosomal system is associated with several neurodegenerative diseases, including Parkinson's disease and neurodegeneration in the context of lysosomal storage diseases, or LSDs. Degenogenes linked to lysosomal function include LRRK2, aSyn, and lysosomal enzymes, including IDS, and glucocerebrosidase, or GBA. Most LSDs result in rapid and aggressive neurodegeneration. We believe therapeutics designed to correct lysosomal dysfunction are a promising approach to broadly treat neurodegeneration.

Glial Biology

The human brain contains several types of glial cells, which are critical to healthy brain function. Specifically, microglial cells act as the resident immune system in the brain. It has been recently discovered that degenogenes implicate immune dysfunction in the brains of patients with Alzheimer's disease and other neurodegenerative diseases. These genes include TREM2 and numerous other genes that are highly expressed in inflamed microglia. We believe the impact of immune modulation in neurodegeneration is a promising approach to treating disease. Genetic and pathological data suggest

that reversing defects in glial biology may significantly delay or halt the progression of some neurodegenerative diseases, such as Alzheimer's disease and ALS. Specifically, we and others have recently discovered that RIPK1, a kinase downstream of the TNF receptor pathway, a highly validated biologic target in human disease, is overactive in inflamed microglia and several other cells in the brain. Blocking RIPK1 may reverse the hyper-inflamed nature of glia and restore normal function. Improving glial function and modulating the resident immune system in the brain represents a potentially attractive therapeutic strategy.

Cellular Homeostasis

Many degenogenes directly alter the homeostatic balance of brain cells. Specifically, defects in protein, RNA or metabolic homeostasis lead to the death of neurons and dysfunction of the nervous system. This includes spreading of protein aggregates resulting in proteinopathy in Alzheimer's and Parkinson's diseases, and the aggregation of RNA binding proteins disrupting cellular stress response in Alzheimer's disease and ALS. The clearance of macromolecules in the brain is particularly susceptible to imbalances that result in aggregation and degeneration in nerve cells. For example, Alzheimer's disease pathology is characterized by the presence of amyloid plaques and neurofibrillary tangles. Our approach is to create a bispecific antibody that targets both BACE1 and Tau, key proteins in the production of amyloid plaques and neurofibrillary tangles, which we believe will not only target both of these pathologies, but also has the potential for synergistic activity, restoring protein homeostasis with regards to the two most common Alzheimer's disease pathologies. We believe that therapies that correct defects in cellular homeostasis have the potential to halt or delay neurodegenerative disease progression.

Engineering Brain Delivery

The Blood-Brain Barrier Challenge

The human brain contains roughly 400 miles of blood vessels. These blood vessels are lined by a BBB that separates the brain from the blood and allows the transfer of nutrients and waste while protecting the brain from toxins. Entry of most small molecule drugs to the brain is restricted by efflux pumps on the BBB. The tight junctions of the BBB also prevent most proteins in the blood from reaching the brain, including therapeutic antibodies and enzymes. The concentration of most antibodies in the brain is only 0.1% of their concentration in blood plasma, and such restricted access to the brain has traditionally limited the efficacy of antibody therapeutics for neurodegenerative diseases (Figure 2).

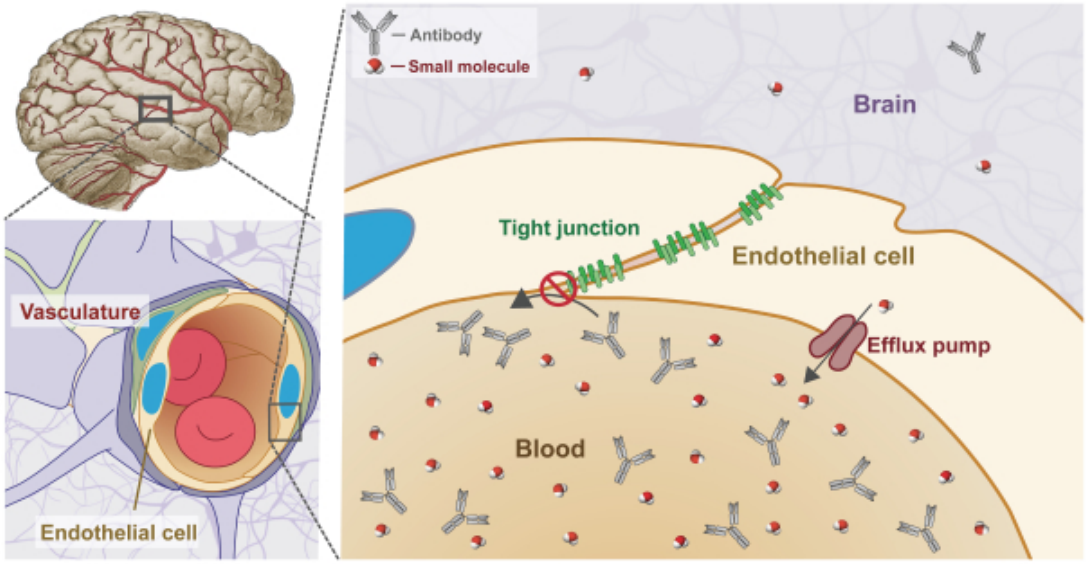


Figure 2. Schematic of the BBB. The specialized vessels of the brain represent a significant barrier of both small and large molecule therapeutics. Tight junctions between endothelial cells prevent the diffusion of large molecules while most small molecules are kept out of the brain by an efflux pump.

The protective nature of the BBB limits the passive uptake of small molecule and large molecule therapeutics in the brain. We believe that this is one of the major reasons for the low success rates of clinical trials in neurodegenerative diseases to date. Engineering brain delivery of product candidates is critical to our success in developing effective therapeutics for patients with neurodegenerative diseases. Our product candidates are engineered to reach their intended targets in the brain at exposure levels that will provide a therapeutic effect, while having an acceptable safety profile. We do not plan to bring a product candidate into late-stage clinical testing unless it has shown sufficient brain concentration and target engagement in the brain in preclinical models and early-stage clinical trials.

Engineering Large Molecule Brain Delivery

For large molecules, including therapeutic antibodies and enzymes, we are developing proprietary platform technologies to actively transport these molecules across the BBB through receptor-mediated transcytosis, or RMT. RMT through the BBB is the process by which macromolecules in the blood bind to receptors on the endothelial cells that make up the BBB and are actively transported and released into the brain. Our large molecule Transport Vehicle, or TV, platform technology engineers BBB receptor binding into an Fc domain (Figure 3). We have selected transferrin receptor, or TfR, which is a highly-expressed BBB receptor that we believe has the ability to substantially improve brain uptake of therapeutic molecules. This construct can be integrated and fused to therapeutic molecules as described below, without disrupting the binding of transferrin to TfR.

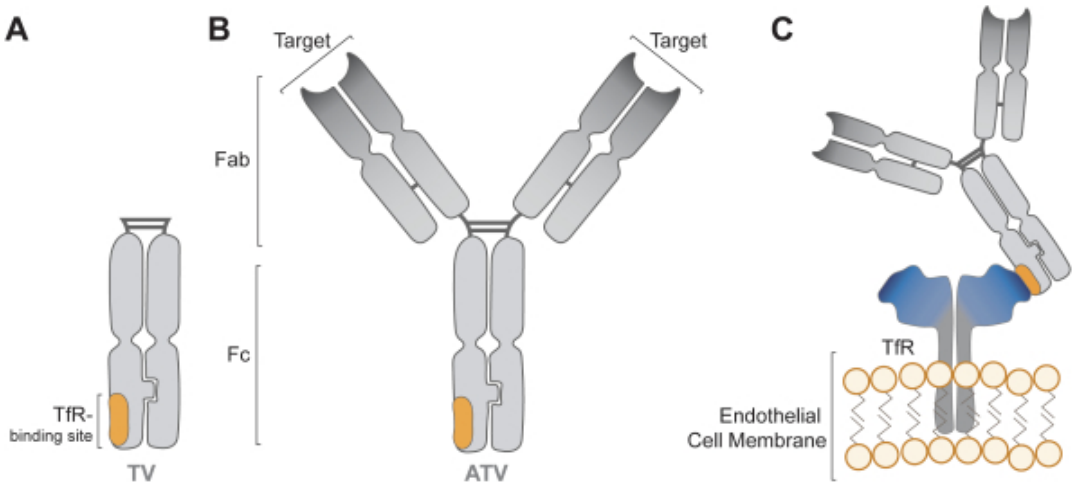


Figure 3. Schematic of receptor-mediated transport of ATV at BBB. ATV molecules engage TfR on the blood vessel wall in the brain. Once bound, ATV is brought into vesicles that are transported across the endothelial cell by RMT and released into the brain, thus substantially increasing antibody concentrations in brain.

Antibody Transport Vehicle

Our ATV platform technology utilizes the BBB receptor binding Fc domain to engineer bispecific and bivalent antibodies with improved brain delivery (Figure 4). This enables targeting of two pathologies for a given brain indication with a single therapeutic agent. This is potentially a significant advantage in treating diseases like Alzheimer's disease, where multiple pathologies are known to contribute to disease progression.

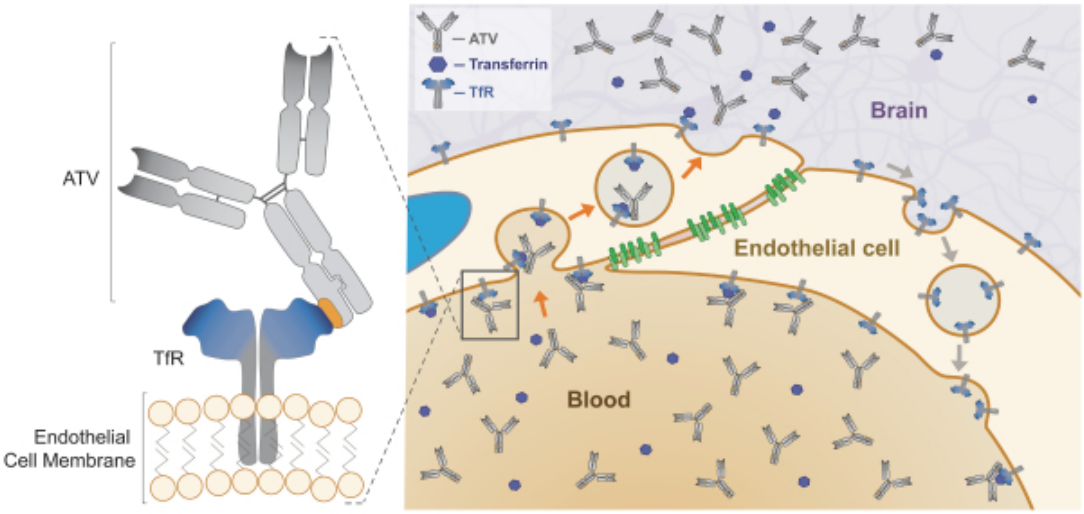


Figure 4. Schematic of receptor-mediated transport of ATV at the BBB. ATV molecules engage TfR on the blood vessel wall in the brain. Once bound, ATV is brought into vesicles that are transcytosed across the endothelial cell and released into the brain, thus substantially increasing antibody concentrations in brain. ATV binding to TfR does not disrupt the binding of transferrin to TfR.

We have achieved *in vivo* proof of concept for the ATV platform in mice whose genomes have been engineered to include a portion of the human TfR gene at a specific location, or human TfR knock-in mice. In this human TfR knock-in-mouse model, our preclinical studies have demonstrated over 20-fold increased antibody uptake in the brain, compared to a control antibody (Figure 5). This is equivalent to increasing antibody brain concentration from 0.1% to approximately 2%. As a result of a dramatic improvement in brain antibody uptake with the ATV, we observed a robust brain pharmacodynamic, or PD, response, as measured by reduction in brain amyloid-beta levels, which is one of the key pathologies in Alzheimer's disease. These data demonstrate that the brain concentrations achieved with the ATV platform are in excess of levels needed to mediate a therapeutic response. Without the ATV, the control antibody was unable to have a desired PD effect in the brain (Figure 5).

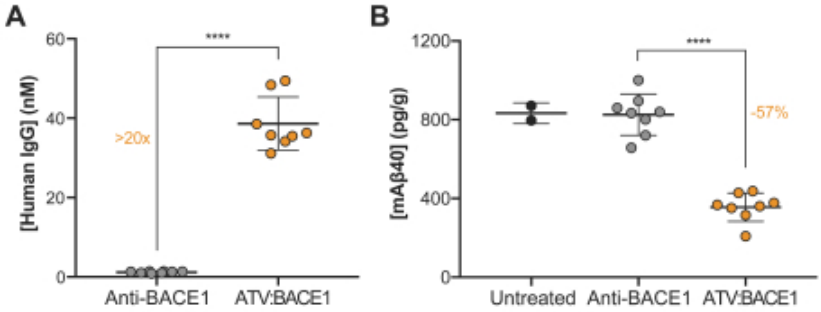


Figure 5: ATV therapeutics achieve robust brain uptake and pharmacodynamic activity in human TfR knock-in mice. Mice were injected with anti-BACE1 or ATV:BACE1, which were allowed to circulate for 24 hours. Brain antibody concentrations were compared between anti-BACE1 (1.2nM) and ATV:BACE1 (38.6nM). Reduction of brain Abeta levels for ATV:BACE1 (57%) as compared to anti-BACE1 (no reduction).

Enzyme Transport Vehicle

Our ETV platform utilizes the same approach as our ATV platform to deliver enzymes across the BBB. One potential application of this technology is the neurological component of LSDs. The ETV platform technology is an Fc-enzyme fusion in which the TfR binding is engineered into the Fc domain (Figure 6). The high modularity of the platform make it uniquely well suited for delivery of enzymes across the BBB. The ETV enables different fusion formats with one or two enzymes. The characteristics of the ETV platform are also applicable to proteins and peptides that may be fused to the platform for other indications.

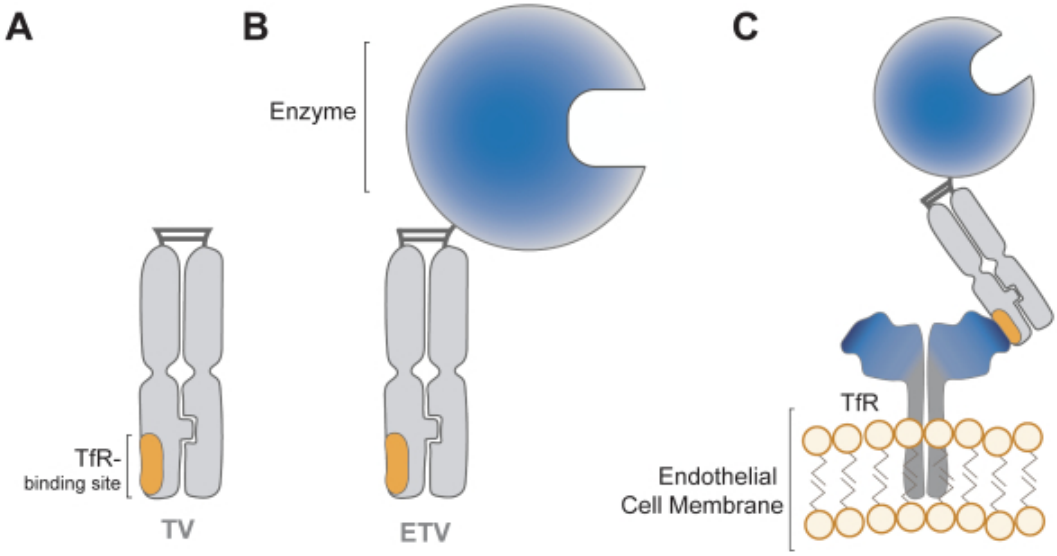


Figure 6: Engineering Brain Delivery using the ETV platforms. The ETV platform technology contains BBB receptor (TfR) binding in the Fc domain (A) fused to an enzyme (B) to enable transport of enzymes into the brain through TfR-mediated transcytosis (C).

Platform Technology Development and Applications

We are advancing our ATV and ETV platforms through further preclinical studies in mice and non-human primates. We plan to commence IND-enabling studies with multiple preclinical product candidates in 2018 and initiate clinical trials in 2019. We are also combining our proprietary human TfR knock-in-mice model with other disease-specific animal models in order to more precisely assess our ATV constructs in relevant diseases. We expect that this will give us the ability to perform PK/PD and efficacy studies in a single model without the need for surrogate molecules and to quantitatively demonstrate the advantages of antibodies and proteins delivered using our ATV platform technology.

To enable our development of our BBB platform technology, we have entered into a strategic licensing and collaboration agreement with F-star. This collaboration gives us the ability to obtain exclusive access to an intellectual property portfolio covering engineering of the Fc region of antibodies for use with specific targets, such as the TfR. The collaboration enhances our own protein engineering capabilities by leveraging F-star's more than 10 years of experience in this area. Our collaboration is focused on TfR binding with the option to expand the collaboration to develop two additional BBB receptor targets.

We believe that our ATV and ETV platforms are also broadly applicable beyond neurodegeneration and LSDs to improve delivery of antibodies to treat other brain diseases, including cancer. We currently are not pursuing these additional indications, but in the future, we may opportunistically pursue such indications independently or with partners.

Engineering Small Molecule Brain Delivery

We are focused on engineering small molecule therapeutics that achieve exposure levels in the brain sufficient to bind to protein targets and drive a therapeutic effect. An efficacious small-molecule medicine for brain diseases must be readily absorbed from the gut into the blood and penetrate the BBB while avoiding transporter-mediated efflux (Figure 7). It has been estimated that approximately 98% of small molecule drugs do not cross the BBB.

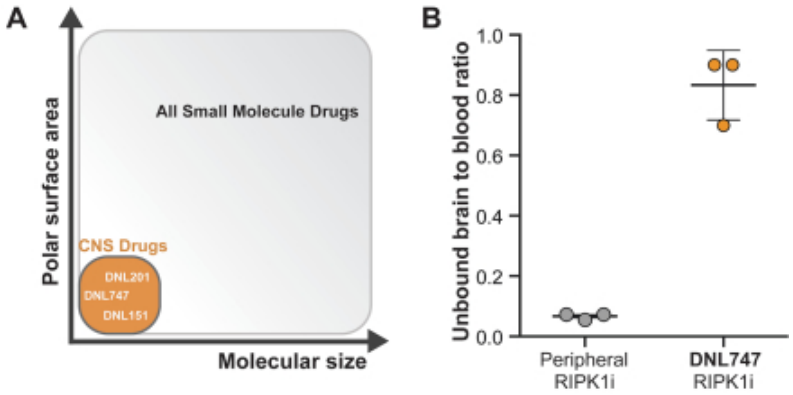


Figure 7: Generation of brain penetrant small molecules. The molecular properties compatible with CNS drugs are significantly more restricted than those generally used to design small molecule drugs, including tight restrictions on molecular weight and total polar surface area (A). This figure is not to scale. An example of how molecular properties influence brain penetration is shown in (B), where our lead RIPK1 inhibitor DNL747 displays a brain to blood ratio of ~0.8 while a benchmark periphery-restricted RIPK1 inhibitor displays a ratio of ~0.05.

Our small molecule drug discovery scientists have many years of experience designing small molecules for brain diseases, including DNL151, one of our lead LRRK2 inhibitors, and DNL747, our lead RIPK1 inhibitor, both of which have demonstrated strong brain exposure and confirmed target engagement in preclinical studies.

Biomarker-Driven Development

Translational science is the process of gathering and interpreting data obtained from cellular and animal models to inform the design and expected clinical outcome of future patient studies. In the field of neurodegeneration, this has been particularly difficult due to a lack of validated biomarkers and predictive animal models to confirm drug exposure and target engagement in brain tissue, as well as clinical disease progression and response. Historically, many programs have advanced into late-stage clinical trials prior to demonstrating a relevant biologic response.

We seek to increase the chances of success in early-stage patient clinical trials by defining biomarker goals at every phase of development, including prior to the filing of an IND. As molecules transition from the discovery phase to early clinical development, we focus on refining our understanding of the relationship between the PK/PD response and modulation of target biology using target engagement and other relevant biomarkers. This integrated approach allows for the design of rigorous and informative pharmacology experiments.

With this approach, we are seeking to make drug development more cost efficient by attempting to minimize avoidable errors in dose selection and study design that are impactful and costly in Phase 2 and Phase 3 clinical studies. In addition, we strive to develop for each of our programs a patient selection strategy guided by a genetic rationale and understanding of target biology.

Approach to Target Engagement and Dose Selection

As part of our strategy, we are using available reagents as well as developing proprietary reagents and assays to create biomarkers for each of our core programs. These biomarkers, which are relevant for both animal models and human trials, are critical for patient selection, measuring target engagement, supporting does selection and enabling decisions on progression of product candidates

to the next phase of development. Because potential targets of interest are in the brain, it is important to develop reagents that can assay specific biomarkers not only in the blood but also in the cerebral spinal fluid, or CSF, and the brain. By enabling biomarkers that are present in both animal models and humans, we are able to create a clinical strategy whereby measurements of exposure and target engagement in animals allows for better clinical translation and PK/PD modeling for human trials.

An example of this approach is reflected in our LRRK2 program. We developed a proprietary assay of LRRK2 kinase activity that measures phosphorylation of LRRK2 at Serine 935, or pS935. In a preclinical rat model, we have demonstrated that, following a single dose of a brain penetrant LRRK2 kinase inhibitor, there is a dose dependent reduction of LRRK2 kinase activity observed in the brain that is reflected in LRRK2 kinase inhibition in peripheral blood mononuclear cells, or PBMCs. Experiments such as this establish a relationship between peripheral (e.g. blood) and central (e.g. brain) target engagement, enabling the prediction of central target engagement in humans with measurements of blood and CSF drug exposure in conjunction with a peripheral assay for LRRK2 kinase activity.

Development of blood based assays potentially enables an assessment of target engagement in the clinic as early as first-in-human Phase 1 trials in healthy volunteer subjects. We have developed human assays using healthy control blood samples to assess performance of clinical candidates and continuously refine the reliability and quantitative rigor of our target engagement assays. After development of prototype assays, high sensitivity, high throughput, and quantitative platform based assays are developed for clinical use.

In the design of our Phase 1 trials, we plan to integrate our target engagement biomarker data with PK analysis from both the plasma and CSF to determine the relationship between dose, time and drug response. We develop an integrated exposure response model that enables tailoring of the dose selection for future patient studies. This model relies on the quantitative pharmacodynamic biomarkers assessment enabled by the development and refinement of reliable assays, described above. We plan to progress product candidates that show robust target engagement at safe and well-tolerated doses in early clinical development into our proof-of-concept trials.

We have identified target engagement biomarkers for all six of our core programs. Further, we are developing patient selection biomarkers for these programs.

Program Target	Research Target Engagement Biomarker	Clinical Target Engagement Biomarker	Patient Selection Biomarker
LRRK2	✓	✓	✓
Alpha Synuclein	✓	Development	Development
Iduronate 2-sulfatase	✓	✓	✓
RIPK1	✓	✓	Development
TREM2	✓	Development	Development
BACE1/TAU	✓	✓	✓

We plan to leverage the target engagement biomarker data resulting from Phase 1 healthy volunteer studies to determine target engagement and dose selection in patients. We have invested in

capabilities to obtain blood samples and other samples from patients with Alzheimer's disease, Parkinson's disease, and ALS to improve our prediction of relevant exposure-response relationships and support the design of future patient clinical trials. The data from these biomarker assessments via proprietary assays and PK analyses are critical to dose selection in the design of Phase 1b and Phase 2 clinical trials.

Approach to Pathway Engagement and Disease Progression

Our approach to building expertise in pathway biology enables identification of candidate pathway biomarkers that can be assessed in our clinical studies to understand pathway engagement and may serve as potential endpoints. An example of this approach is outlined in Figure 8. In this example, development of reagents for fluid biomarkers (for instance, Rabs) as well as imaging biomarkers (for instance, dopamine transporter imaging, or DAT) are being evaluated.

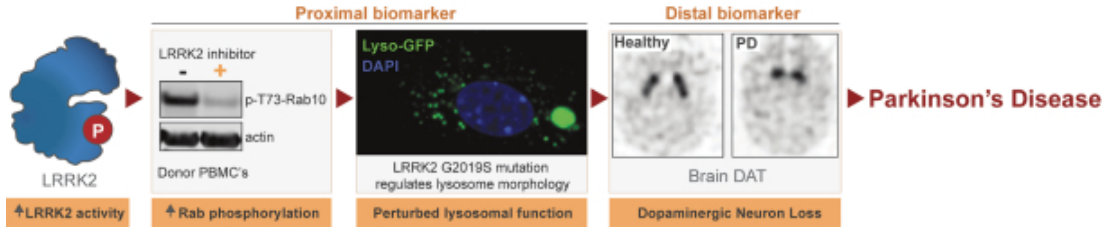


Figure 8: Example of strategic approach to biomarker generation for biomarkers of LRRK2 target engagement (i.e., Rab phosphorylation), pathway modulation (i.e., lyososmal function) and disease modification (i.e. brain DAT imaging) to build evidence of relevant biologic activity that will impact clinical outcomes.

Approach to Patient Selection

In the past, the diagnosis of neurodegenerative diseases has generally relied on clinical diagnosis, without direct confirmation of pathology. This approach is inherently prone to errors, including misdiagnosis. The lack of pathology-confirming biomarkers has led to the enrollment of patients in clinical trials for neurodegenerative diseases who were very unlikely to respond to treatment, including patients who in fact did not have the disease being studied.

Our focus on degenogenes and the underlying biology of genetic pathways enables a patient selection approach. This approach is much more precise compared to relying only on a clinical diagnosis. For example, genotyping for LRRK2 patients is a strategy for a Parkinson's disease patient selection strategy. Alzheimer's disease is likely a heterogenous disease with different biology contributing to common downstream effects, including amyloid deposition in the brain. In Alzheimer's disease, understanding the biology of patient subsets defined by APOE4 genetic status as well as inflammatory biomarkers highlighted by Genome Wide Association Studies, provides hypotheses for development of novel biomarkers that can identify the subset of patients most likely to benefit from a particular therapeutic approach.

By utilizing biomarkers and genetic information, we can better target and select the best patient population for our clinical trials and product candidates.

Our Portfolio

As described above, our portfolio currently comprises six core programs and five seed programs. In addition, we continually evaluate additional targets for inclusion as seed programs, while we seek to maintain a rigorous process of prioritization and resource allocation to maintain an optimal balance

between aggressively advancing lead programs and ensuring replenishment of the portfolio. We discuss our six core programs in further detail below.

Lysosomal Function Pathway Programs

LRRK2 Inhibitor Program

The two most advanced product candidates are potent, selective and brain penetrant small molecule LRRK2 inhibitor product candidates for Parkinson's disease. DNL201 is currently in a Phase 1 clinical trial and DNL151 has completed IND-enabling preclinical studies and we plan to file an IND or CTA in the fourth quarter of 2017.

Therapeutic Rationale

Lysosomal dysfunction is a central pathology of Parkinson's disease. Genetic mutations in several proteins associated with Parkinson's disease, including LRRK2, GBA and aSyn, disrupt normal lysosomal function and contribute to the formation of Lewy bodies, which are intracellular aggregates containing aSyn proteins, and neurodegeneration (Figure 9). LRRK2 regulates lysosomal function by phosphorylating Rab proteins, which control intracellular lysosomal trafficking (Figure 10). Mutations in the LRRK2 gene that cause Parkinson's disease increase both LRRK2 kinase activity and the phosphorylation of Rab proteins. Excessive phosphorylation of Rab proteins alters Rab localization and disrupts normal lysosomal movement and maturation. Inhibition of LRRK2 kinase activity with a LRRK2 kinase inhibitor reduces Rab phosphorylation and restores normal lysosomal morphology.

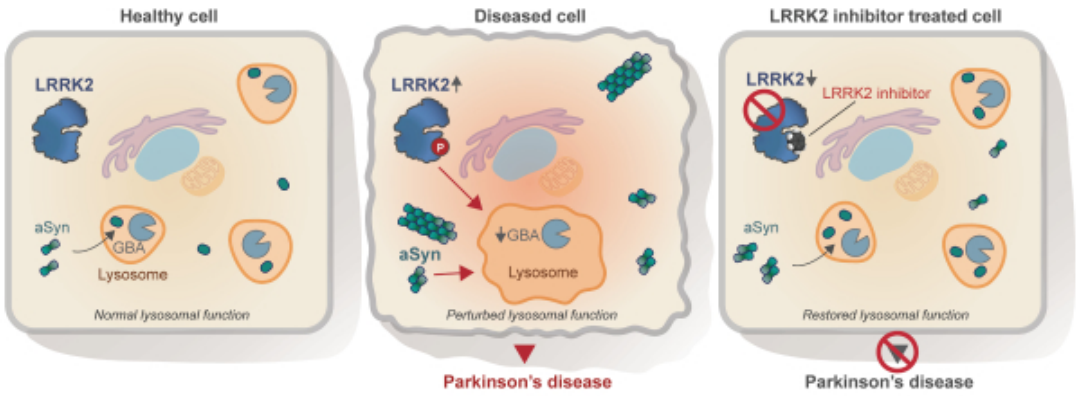


Figure 9: LRRK2 acts in healthy cells to maintain normal lysosomal function. Excessive LRRK2 activation or expression reduces lysosomal function and contributes to the progression of Parkinson's disease. Lysosomal dysfunction and Parkinson's disease can also be caused by high levels of aSyn and by loss of function of GBA. LRRK2 inhibition can restore normal lysosomal function and reduce toxicity in Parkinson's disease models.

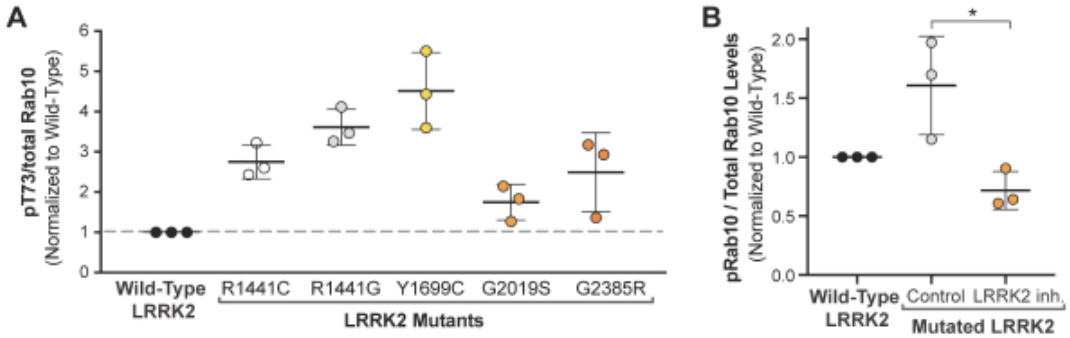


Figure 10. Phosphorylated Rabs are a novel marker of LRRK2 activity. Multiple distinct LRRK2 mutations result in elevated phosphorylation of the downstream marker Rab10 (A), while inhibition of LRRK2 is sufficient to decrease Rab10 phosphorylation (B). * indicates p<0.05.

Inhibition of LRRK2 kinase activity has been shown to be beneficial in several cellular and *in vivo* models. The most common LRRK2 mutation, G2019S, is a point mutation that results in increased kinase activity, abnormal lysosomal biology and an increased risk of Parkinson's disease. LRRK2 G2019S expression in cells from transgenic mice or other cell lines reduces the lysosomal capacity of the cell, leading to decreased lysosomal function. These defects are dependent on LRRK2 kinase activity, and treatment with DNL201 rescues the observed lysosomal phenotype (Figure 11). LRRK2 G2019S expression in neurons leads to a similar lysosomal phenotype and also results in reduced neurite outgrowth, an effect that can be rescued with LRRK2 kinase inhibition.

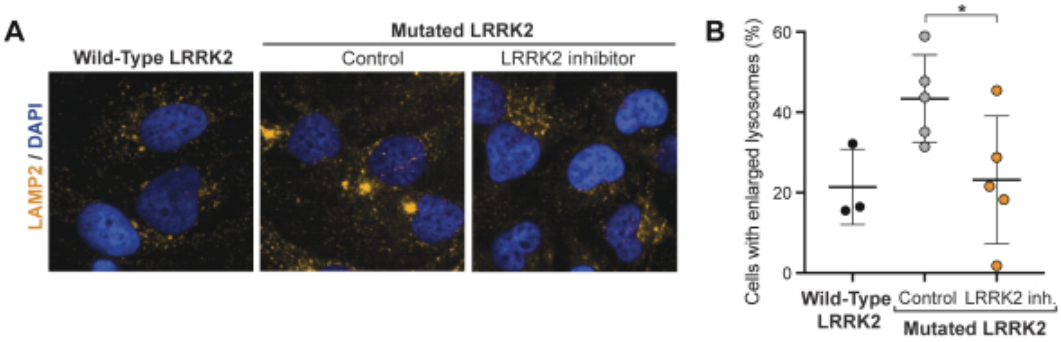


Figure 11: Effect of LRRK2 mutations on lysosomes. Cells expressing LRRK2 with the G2019S mutation display clusters of enlarged and dysfunctional lysosomes that are not present in cells expressing normal (WT) LRRK2. The presence of these abnormal lysosomes can be reversed through treatment with LRRK2 kinase inhibitors (A). Lysosomes can be visualized via LAMP2 (orange) while DAPI (blue) labels nuclei. A quantification of this experiment is shown in (B). * indicates p<0.05.

Patients with Parkinson's disease often have high levels of activated immune cells and inflammatory markers in blood and CSF. LRRK2 is highly expressed in glia and other immune cells, and LRRK2 kinase inhibition or knockout of the LRRK2 gene protects animals in inflammatory disease models, including rhabdomyolysis kidney injury, exposure to the bacterial toxin lipopolysaccharide, and experimental autoimmune uveitis. These findings suggest that LRRK2 inhibition may reduce the deleterious inflammatory responses associated with Parkinson's disease.

Mutations in the aSyn gene and aSyn overexpression may cause certain forms of familial Parkinson's disease, and aSyn oligomers are thought to accelerate neurodegeneration. *In vitro* and *in*

vivo models that employ aSyn oligomers to cause inflammation and cellular and lysosomal dysfunction are commonly used as preclinical models of Parkinson's disease. Microglia from mice that do not express LRRK2 absorb and degrade aSyn more effectively than wild-type mouse microglia. In most cell and mouse aSyn models, reducing LRRK2 kinase activity or expression protects animals from neurodegeneration and excessive inflammation. These findings provide further support for inhibition of LRRK2 activity as a therapeutic strategy to treat Parkinson's disease.

Patient Population

Mutations in the LRRK2 gene are the most frequent cause of familial Parkinson's disease and, in addition, are present in 1-2% of patients with sporadic Parkinson's disease in the United States. In total, we estimate that LRRK2 mutations account for approximately 2% to 3%, or 20,000 to 30,000, of one million total Parkinson's disease patients in the United States. The most common LRRK2 mutation, G2019S, is a point mutation that results in increased kinase activity and abnormal lysosomal biology. In addition to G2019S, six other pathogenic LRRK2 mutations resulting in increased LRRK2 expression or function have been strongly linked to Parkinson's disease.

While mutations that increase LRRK2 kinase activity provide the most direct link to the therapeutic rationale, other genetic drivers of Parkinson's disease, such as mutations in GBA and aSyn, are also associated with lysosomal dysfunction, which may be addressed through LRRK2 inhibition.

Furthermore, patients with idiopathic Parkinson's disease, i.e. patients with a clinical diagnosis of Parkinson's disease without a known genetic cause, typically also show signs of lysosomal dysfunction. Thus, as lysosomal dysfunction is a central pathology in patients with and without known genetic drivers of disease, inhibition of LRRK2 may be a therapeutically beneficial approach for all forms of Parkinson's disease (Figure 12).

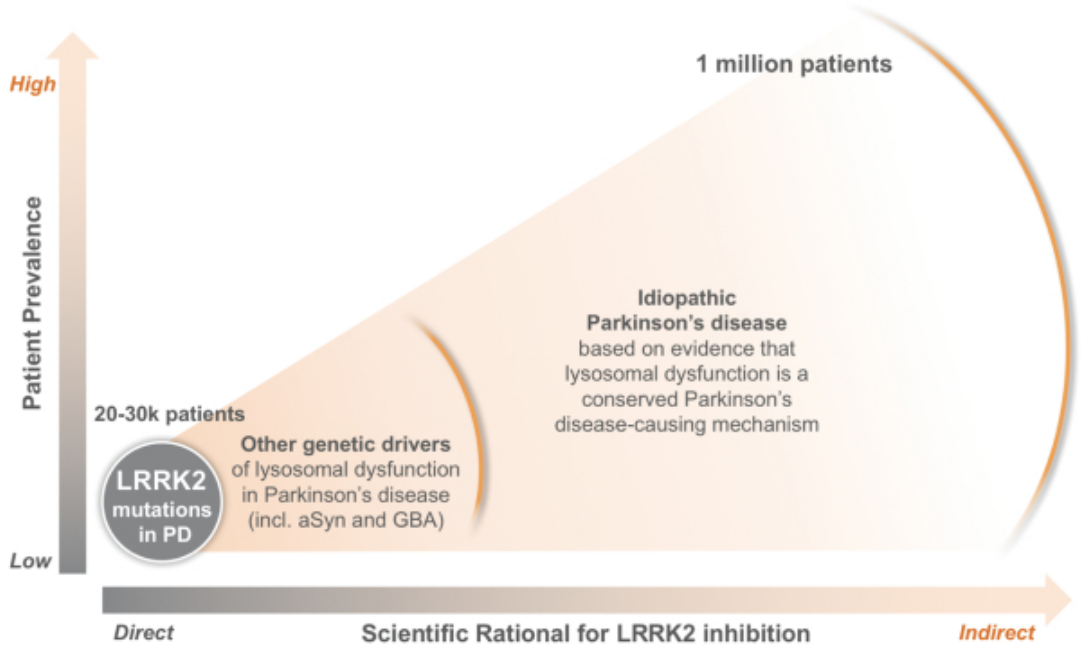


Figure 12: Target Parkinson's disease patient populations for LRRK2 inhibitor. (Figure not to scale)

Pharmacological Properties and Brain Exposure

We have a broad portfolio of potent, selective and brain penetrant LRRK2 inhibitors with attractive pharmacological properties. Our lead product candidates, DNL201 and DNL151, are selective, orally available, brain-penetrant, reversible small molecule inhibitors of LRRK2. The pharmacology of both product candidates has been investigated in a broad range of biochemical and cell-based *in vitro* assays, and both product candidates have been shown to inhibit LRRK2 activity with low nanomolar potency in human blood cells.

We have completed extensive preclinical PK and PK/PD evaluations of DNL201 and DNL151. Based on these data and preclinical modeling of clearance, the expected human half-life is compatible with BID (twice daily) dosing and QD (once daily) dosing for DNL201 and DNL151, respectively. Comparable unbound plasma and CSF exposures were observed in rodents and monkey, demonstrating that the compounds are brain penetrant and can achieve meaningful and sustained brain exposures as shown in a representative dataset for DNL201 (Figure 13). PD was characterized using a marker of LRRK2 kinase activity, phosphorylation of LRRK2 kinase at Serine 935, or pS935. Inhibition of pS935 in PBMCs is comparable to inhibition of pS935 in the brain after 28 days of dosing of DNL201 in monkey, demonstrating that peripheral blood inhibition of pS935 can be used to predict inhibition of pS935 in the brain. In toxicology studies in rodent and monkey, administration of DNL151 and DNL201 consistently resulted in dose-dependent inhibition of LRRK2 activity in peripheral tissues and in brain as measured by a reduction of pS935 LRRK2 levels.

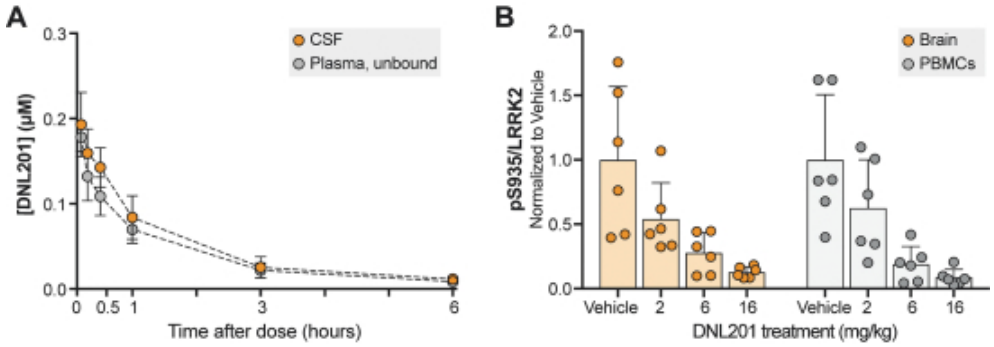


Figure 13. Exposure of DNL201 in monkey CSF and plasma (unbound) and activity of DNL201 in brain and PBMCs. DNL201 concentrations in monkey plasma (unbound) and CSF following intravenous administration of DNL201 demonstrate comparable plasma unbound and CSF exposures (A). Comparable pS935 inhibition in PBMCs and brain is observed in monkey 24 hours after the last dose is given (B).

The preclinical safety profiles of DNL201 and DNL151 have been characterized in a comprehensive battery of non-GLP and GLP safety pharmacology and single dose and repeat dose *in vivo* toxicology evaluations in rat and monkey. These PK, PK/PD and preclinical safety data indicate that both molecules can achieve significant levels of inhibition of LRRK2 kinase activity in the brain at dose levels that can be evaluated in clinical trials.

The definitive 28-day GLP toxicity studies for both DNL201 and DNL151 were conducted in monkey and rat. For these studies, the monkey was selected as the non-rodent species in order to fully characterize previously reported data showing that multiple structurally distinct LRRK2 inhibitors cause pharmacologically-driven lung histology changes. A target-related kidney finding has also been previously reported in rodents dosed with LRRK2 inhibitors and in rodent transgenic models. These

findings consist of accumulation of lipid membranes of lysosomal organelles (lamellar bodies) in cells in the lung and vacuolization (droplets) in the kidney, also a lysosomal phenotype. In summary, these histologic changes related to loss of function or inhibition of LRRK2 kinase did not impact life span in these animal models or have obvious functional effects. Mice that lack LRRK2 protein (LRRK2 knockout mice) live a normal life span with no obvious pulmonary or renal function abnormalities despite accumulation of lamellar bodies in the lung and droplets in the kidney. In a Michael J. Fox Foundation, or MJFF, sponsored study, three distinct LRRK2 kinase inhibitors produced a mild accumulation of the previously described lamellar bodies in the lung. After 15 days of dosing, there were no functionally significant alterations in any pulmonary function endpoint examined, including lung diffusion capacity, lung compliance, and forced vital capacity. In addition, after cessation of dosing, the findings were fully reversible. The conclusion of this MJFF sponsored study was that the morphological changes observed in the lungs of LRRK2 kinase inhibitor treated monkeys may not prevent the clinical evaluation of the therapeutic potential of LRRK2 kinase inhibitors in Parkinson's disease. We have further characterized the cellular effects of LRRK2 kinase inhibitors and believe that the histological changes seen with LRRK2 inhibition in kidney and lung are due to direct effects on lysosomal morphology that are related to the therapeutic potential of LRRK2 inhibition in treatment of Parkinson's disease. In a cellular model of Parkinson's disease, a LRRK2 G2019S cell line model, cellular abnormalities due to defects in lysosomal function are characterized by morphologic abnormalities including a reduced number of lysosomes and abnormally large lysosomes. With inhibition of LRRK2 in this cellular model, the altered lysosomal morphology can be corrected, and with full inhibition, increased lysosomal number and area is observed with accumulation of lamellar bodies similar to the changes seen in rodent models lacking LRRK2 function and in monkeys dosed with LRRK2 inhibitors.

In the 28-day GLP toxicity studies for DNL201 in rats and monkeys, no adverse findings were observed at doses with exposure multiples >9-fold higher than the predicted maximum concentration, or Cmax, at therapeutic dose levels. In both rats and monkeys, findings were determined to be reversible following a 28-day treatment free period. On-target histological changes of vacuolation in rat kidney and lamellar body accumulation in monkey lung with DNL201 dosing were observed as expected. In prior pilot toxicity studies for DNL201, which were designed to define the maximum tolerated dose of DNL201 in rat, severe clinical signs were observed at high doses where the observed exposure is well in excess of that required for therapeutic efficacy (e.g. Cmax is ^{3}20-fold higher than the predicted Cmax at therapeutic dose levels). These severe clinical signs included labored breathing and severe hypoactivity. Results from an investigative preclinical cardiovascular study performed by us in rats supports that these severe clinical signs are caused by a monitorable cardiovascular mechanism characterized by a mild drop in blood pressure and increased heart rate after the first and second dose in all animals studied, followed by more profound drops in blood pressure associated with severe clinical signs after the third dose in a subset of rats. In this study, the rats recovered from the clinical signs after cessation of dosing.

Based on these studies, the FDA approved the Phase 1 clinical trial for DNL201, but imposed an exposure cap on the trial (an exposure cap is considered a partial clinical hold). We are nonetheless able to dose to an exposure that we believe will be sufficient to inhibit LRRK2 50% on average over the dosing period. We have also implemented routine and frequent assessments of heart rate, blood pressure, and ECGs in this study to monitor for translatability of the preclinical findings to this clinical study. The U.S. Food and Drug Administration, or FDA, may re-evaluate the exposure cap for this study, and may potentially raise it, based on the safety and tolerability data generated by the study as it progresses as well as the data supporting the monitorability of the effects of the study (Figure 14).

For DNL151, in the 28-day GLP toxicity studies, no adverse findings were observed at doses with exposure multiples >11-fold higher than the predicted Cmax at therapeutic dose levels in both monkey and rat. All findings were determined to be non-adverse and reversible following a 28-day treatment free period. In pilot toxicity studies severe clinical signs were observed at Cmax ^{3} 18 fold and ^{3} 49 fold

above the predicted Cmax at therapeutic dose levels in monkey and rat, respectively. These severe clinical signs include signs consistent with cardiovascular effects, and signs consistent with effects on the central nervous system, including tremors, pupillary changes, and decreased activity. Based on the findings, we plan to proactively propose an interim exposure cap based on the severe clinical signs seen in the most sensitive species (monkey) in the Phase 1 clinical trial protocol. Similar to DNL201, we believe that with the proposed exposure cap we can achieve exposures that inhibit LRRK2 at least 50% on average over the dosing period. We plan to use the clinical data from this study, if favorable, to support the revaluation of this proposed initial exposure cap.

Based on our robust biomarker assay capabilities to monitor target engagement and assess the exposures desired to reach our target engagement goals, the preclinical safety data support that both molecules can achieve significant levels of inhibition of LRRK2 kinase activity in the brain at dose levels that can be evaluated in clinical studies under the exposure caps.

Biomarker-Driven Development

We are using genetic, biochemical and imaging biomarkers to support evidence of target engagement, pathway engagement of biologic function relevant to Parkinson's disease (e.g., lysosomal biology) and effect on dopaminergic neurons as well as patient selection.

We have developed a validated assay that measures pS935 phosphorylation as a marker of LRRK2 kinase activity to demonstrate target engagement. We are also developing techniques to further investigate the impact of LRRK2 inhibition on lysosomal function or inflammation in clinical studies, including methods to assess levels of phosphorylated Rab proteins.

Brain imaging techniques have been developed to measure deficits in dopaminergic transmission, which is closely associated with the decrease of dopaminergic neurons, a hallmark of Parkinson's disease. These techniques should allow us to monitor the potential beneficial effect of our LRRK2 product candidates on neurological function.

We are initiating efforts to recruit a targeted patient population with disease causing LRRK2 mutations including G2019S, R1441C, R1441G, I2020T and Y1699C. These mutations can be easily identified with a blood test.

Development Plan

In June 2017, we initiated a randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in healthy young and healthy elderly subjects for DNL201 (Figure 14). The study aims to investigate the safety and tolerability of single and multiple oral doses of DNL201 and characterize the PK and PD of DNL201 in plasma and CSF. Target engagement is being assessed in blood (PBMCs) using the pS935 biomarker and extrapolated to estimate target engagement in the brain. As an exploratory endpoint, candidate biomarkers in CSF are also being evaluated. The target engagement goal for the LRRK2 clinical development program is to achieve at least 50% average target inhibition over the dosing interval in order to normalize LRRK2 kinase activity. This target engagement goal is based on data indicating that LRRK2 activity in Parkinson's patients is estimated to be almost twice that than healthy individuals.

In the ongoing Phase 1 clinical trial in healthy volunteers, dose escalation up to single doses of 60 mg was found to be safe and well tolerated. At this dose, >50% average target inhibition was measured using the pS935 LRRK2 biomarker in PMBCs and the mean CSF/unbound plasma concentration ratio was 0.99 demonstrating that DNL201 is distributed extensively into CSF, a measure

of brain drug exposure. We believe these data support advancement into the multiple dose portion of the study to evaluate doses where the projected exposures are below the FDA exposure cap, but are sufficient to achieve a 50% average inhibition of LRRK2 kinase activity. Based on clinical safety data as well as investigative preclinical toxicology data supporting monitorability of these findings, we believe review of the data with the FDA may allow additional dose escalation to achieve higher levels of target inhibition.

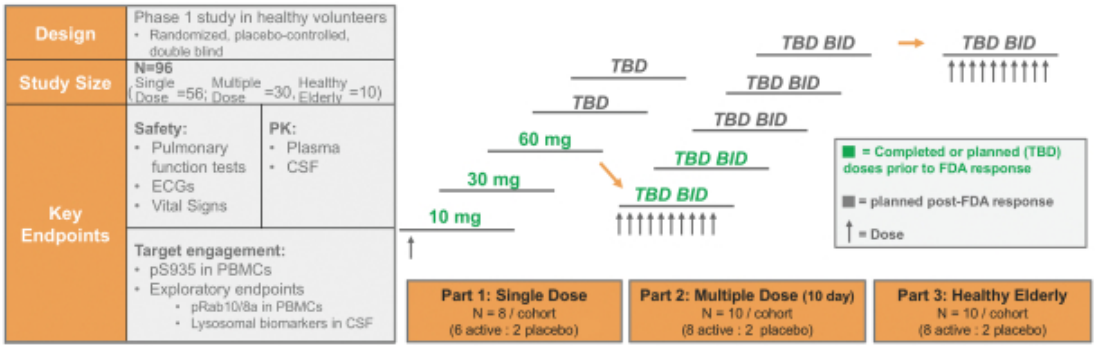


Figure 14. Overview of DNL201 Phase 1 clinical trial in healthy volunteers.

After completion of the ongoing Phase 1 clinical trial in healthy volunteers for DNL201 and the future Phase 1 clinical trial for DNL151, we plan to progress one of DNL201 or DNL151 into a 28-day Phase 1b double-blind, placebo-controlled safety, PK and biomarker study in LRRK2 mutation-carrying Parkinson's disease patients. The primary objectives of this trial will be to evaluate safety, PK and PD of such candidate in LRRK2 patients to identify the lead optimal dose(s) to study in potential future Phase 2 and Phase 3 clinical trials.

ATV:aSyn Program

Our ATV:aSyn program targets aSyn, a protein that has been identified as genetically linked to Parkinson's disease. We have developed high affinity antibodies for aSyn and are currently characterizing molecules in order to select a lead to couple with our proprietary ATV platform. We expect to file an IND or CTA for this program in 2020.

Therapeutic Rationale

aSyn is a protein in the brain linked to the development of Parkinson's disease. Lysosomal dysfunction in neurons can contribute to aSyn aggregation. This in turn leads to neuronal degeneration and results in the formation of Lewy bodies, the defining neuropathological characteristic of Parkinson's disease. Certain genetic mutations in aSyn and overexpression of the gene encoding aSyn have been identified as a cause of familial Parkinson's disease while a common polymorphism in this gene increases the risk for Parkinson's disease. Examination of human brains has revealed that aSyn pathology spreads spatially during the course of the disease, while animal model data demonstrate that this spread can be blocked with anti-aSyn antibodies (Figure 15).

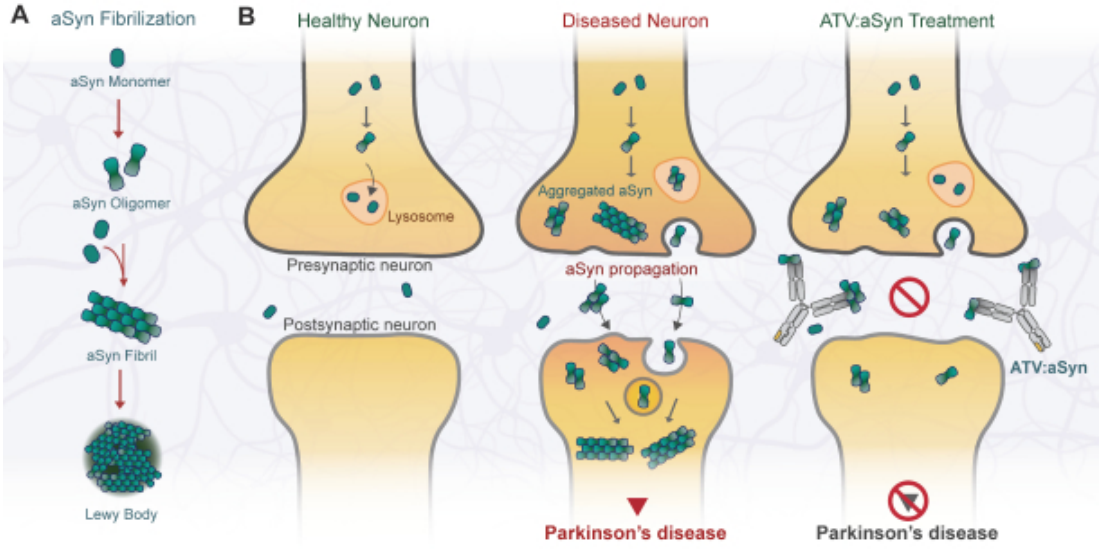


Figure 15: The aSyn protein is present in healthy neurons but can become misfolded and aggregated into oligomers, fibrils, and Lewy body pathology in Parkinson's disease (A). In diseased neurons, misfolded or oligomeric aSyn that can be transmitted from one cell to another, resulting in spreading of aSyn pathology throughout the brain. ATV:aSyn antibodies are designed to block this spread through neutralizing extracellular aSyn (B).

We are developing ATV:aSyn for the treatment of Parkinson's disease. While at least one of our competitors has advanced an anti-aSyn antibody into early-stage clinical studies, we believe that ATV:aSyn will be differentiated from competitors by achieving higher brain concentrations through our ATV technology and higher affinity binding to the multiple forms of aSyn. We believe that this combination may result in superior target engagement leading to a higher probability of demonstrating efficacy in patients with Parkinson's disease.

Pharmacological Properties and Brain Exposure

We have identified a panel of anti-aSyn antibodies with different binding properties that may have best-in-class potential based on high affinity binding, distinct epitopes and excellent selectivity. We have designated three of these antibodies, anti-aSyn1, anti-aSyn2, and anti-aSyn3, as leads for further characterization. The aSyn present in the brains of Parkinson's disease patients can be found in monomer, soluble oligomer or insoluble fibril forms of aSyn. Anti-aSyn1 and anti-aSyn2 display low nanomolar affinity to all forms of aSyn while anti-aSyn3 shows picomolar binding that is specific to aSyn oligomers, which have been hypothesized to represent a key toxic species in Parkinson's disease.

We determined that PK profiles for our lead anti-aSyn antibodies were comparable to a control antibody in mice, indicating there are no incremental exposure liabilities with these molecules. Target engagement for anti-aSyn1 and anti-aSyn2 was then demonstrated in both brain and blood using mice expressing the human form of aSyn. Both lead antibodies also demonstrated superior aSyn binding in CSF from Parkinson's disease patients as compared to benchmark anti-aSyn antibodies comparable to competitor antibodies currently in clinical development. This experiment establishes that both anti-aSyn1 and anti-aSyn2 bind to biologically relevant human aSyn.

We plan to test our three lead anti-aSyn product candidates for their ability to block aSyn spreading in the brains of animal models. Our product candidate that demonstrates the most favorable

profile of target engagement and efficacy will be selected for combination with our ATV platform as our first ATV:aSyn clinical candidate for IND-enabling studies. We plan to test the ability of our humanized ATV:aSyn to bind aSyn in the brain and prevent spreading of pathology using human TfR knock-in mice, as well as other experimental models.

Biomarker-Driven Development

We are focused on enabling our ATV:aSyn program via establishment of clinically translatable biomarkers of target engagement and pathway modulation. In preclinical models, we will measure levels of total aSyn and aSyn bound to antibody in the interstitial fluid of the brain, CSF and plasma to determine the level of target engagement required to block the spreading of aSyn. We plan to use these results to develop a model to identify target exposures in human required to achieve target goals for free and antibody bound aSyn in plasma and CSF that block the spread of aSyn in disease. In later stage trials, we plan to measure disease progression using imaging biomarkers (e.g. DAT imaging). We also plan to initiate work on an aSyn PET probe that would allow the extent of aSyn pathology in patient brains to be directly measured. If successful, PET imaging will be integrated into both preclinical and clinical studies to measure drug activity as well as to select patients for clinical trials.

Development Plan

Our ATV:aSyn program is currently in preclinical development, and we plan to file an IND or CTA application in 2020. Parkinson's disease will be the primary indication for this program. For our clinical studies, we plan to evaluate patients in the early stages of disease that have not yet been treated with dopaminergic replacement or dopamine agonist therapy in order to evaluate effects on function in Parkinson's disease patients. This stage of disease will also capture individuals prior to the broad spread of aSyn pathology and maximize our ability to modify the disease trajectory. Following proof of concept in Parkinson's disease, patients with other synucleinopathies, such as dementia with Lewy bodies, or DLB, and multiple system atrophy, or MSA, may also benefit and could be explored.

ETV:IDS Enzyme Replacement Therapy Program

We are developing ETV:IDS as a treatment for the lysosomal storage disorder MPS II. ETV:IDS is an IDS fusion protein that has been designed to have increased brain exposure. Lead ETV:IDS proteins are currently in preclinical development, and we plan to file an IND or CTA in the first half of 2019.

Therapeutic Rationale

Mucopolysaccharidosis II, or MPS II, also known as Hunter Syndrome, is an X-linked recessive genetic LSD caused by a single gene defect leading to a deficiency in the enzyme IDS. IDS is essential for the breakdown of the glycosaminoglycans, or GAGs, heparan and dermatan sulfate, and its deficiency results in a toxic accumulation of these GAGs and perturbed lysosomal function (Figure 16). Clinical features of MPS II include an enlarged spleen and liver, hearing loss, respiratory tract and cardiac dysfunction, and skeletal abnormalities. Approximately two-thirds of patients suffer from the neuropathic form of the disease, which is characterized by intellectual disability and a progressive cognitive decline that emerges between three and five years of age.

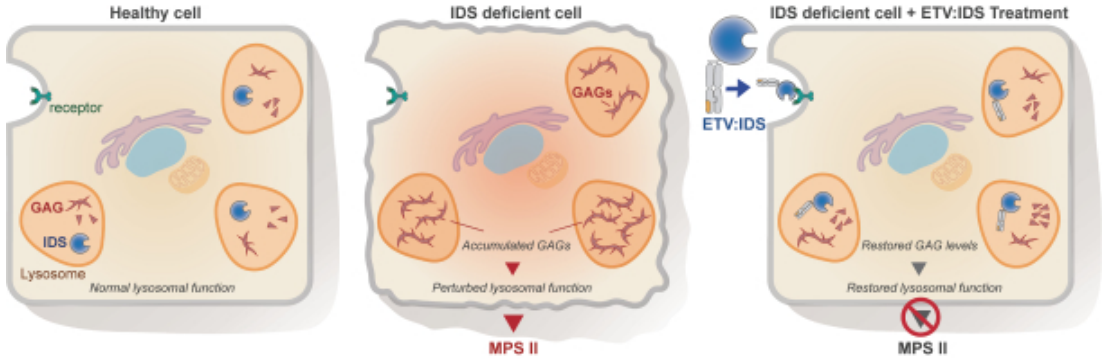


Figure 16: Lack of the lysosomal enzyme IDS results in GAG accumulation leading to lysosomal dysfunction and MPS II (Hunter Syndrome), which is characterized by a range of symptoms including neuronal degeneration. Treatment with ETV:IDS should promote GAG processing and rescue neurons from degeneration.

According to the MPS Society, MPS II affects between 1 in 100,000 to 1 in 150,000 males which would imply between 1,000 and 1,600 males in the United States are afflicted with MPS II based on current population estimates.

MPS II is currently treated with intravenous infusions of recombinant IDS protein. While these treatments can normalize spleen and liver size and improve walking ability, they do not efficiently distribute to the brain and, therefore, cannot address the neurological manifestations of the disease. There is a demonstrated need for therapies that effectively cross the BBB so as to treat both neurological and peripheral manifestations of MPS II and other LSDs.

Pharmacological Properties and Brain Exposure

We are developing therapeutic fusion proteins that effectively cross the BBB and diffuse to critical peripheral tissues. Our ETV platform fuses an engineered Fc, which includes a TfR binding site to improve brain uptake, with an enzyme. We have successfully generated active ETV:IDS fusion proteins that retain binding to TfR and reduce accumulation of GAGs in IDS knockout cells at sub-nanomolar concentrations (Figure 17). Our lead ETV:IDS product candidate has a long half-life and significant tissue distribution in wild-type mice. We are currently studying the tissue distribution and efficacy of ETV:IDS fusion proteins *in vivo* using both IDS knockout mice and a proprietary IDS deficient, human TfR knock-in mouse model. These studies are enabled by proprietary methodologies that we have developed to monitor the PK profile of intact ETV:IDS fusion proteins in these animals.

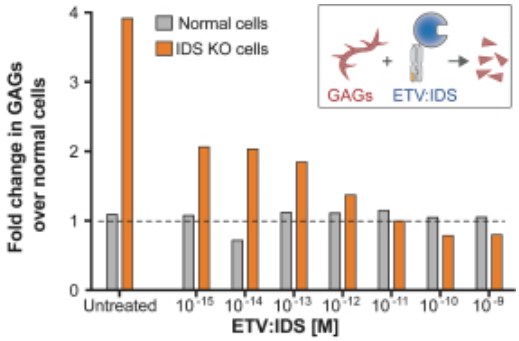


Figure 17: Measurement of ETV:IDS activity. Treatment of cells lacking the IDS enzyme (IDS KO cells) with the ETV:IDS construct is sufficient to result in a dose dependent decrease in the levels of heparan and dermatan sulfate levels but does not have an effect on GAG levels in normal cells. Based on this dose response study, ETV:IDS is estimated to have picomolar cellular potency.

Biomarker-Driven Development

Studies have demonstrated accumulation of GAGs in plasma and urine of MPS II patients as well as elevated levels of GAGs in CSF of both attenuated and neuronopathic MPS II patients. GAG levels have emerged as an accepted biomarker of therapeutic efficacy for treatment of MPS II and related LSDs based on positive correlations between the reduction of urine GAG levels and clinical endpoints following administration of approved therapy for MPS II. Because approved MPS II therapies are not able to cross the BBB, CSF GAG levels remain elevated in MPS II patients who are undergoing approved MPS II therapies.

We have developed a highly sensitive assay to assess levels of heparan and dermatan sulfate accumulation *in vivo* that will allow us to quantitatively investigate the PD effect of our product candidate in preclinical studies and clinical trials. This assay has shown that IDS deficiency leads to the accumulation of GAGs heparan and dermatan sulfate in tissues and fluids of IDS knock-out mice.

Development Plan

We plan to file an IND or CTA for our lead ETV:IDS product candidate in early 2019. We plan to study such product candidate in a Phase 1/2 12-week multiple-ascending dose study in MPS II patients, either in addition to IDS replacement therapy or in patients that have ceased administration of this therapy. We believe that the assessment of changes in CSF GAG levels in all patients, as well as the exploration of systemic effects such as reduction in urine and plasma GAG levels in patients not receiving IDS replacement therapy, will enable rapid confirmation of both distribution of ETV:IDS to the brain and the efficacy of our product candidates in brain and peripheral tissues.

Glial Biology Pathway Programs

RIPK1 Inhibitor Program

The most advanced product candidate in our RIPK1 inhibitor program, DNL747, is a potent, selective and brain penetrant small molecule RIPK1 inhibitor product candidate for Alzheimer's disease and ALS. DNL747 is in IND-enabling preclinical studies and we plan to submit an IND or CTA in early 2018.

Therapeutic Rationale

Aberrant glial biology characterized by neuro-immune dysfunction is a cardinal feature of the pathology of many chronic neurodegenerative diseases including Alzheimer's disease and ALS. Recent GWAS have identified that a large proportion of the genetic risk for late-onset Alzheimer's disease can be explained by genes that are expressed in microglia, the resident immune cells of the brain, implicating microglia as an important effector of neurodegeneration. Mutations in two distinct genes that cause familial ALS, Optineurin, or OPTN, and Tank Binding Kinase, or TBK, can result in increased levels of RIPK1 activity in microglia.

RIPK1 is highly expressed by microglia and levels of RIPK1 activity are increased in chronic neurodegenerative disease. RIPK1 activation in microglia results in production of a number of pro-inflammatory cytokines that can cause tissue damage. Stimulation of RIPK1 signaling in cultured microglia results in production of cytokines and other pro-inflammatory factors, including Ccl2 (MCP-1), IL-1b, and IL-6, while treatment with RIPK1 inhibitors attenuates the induction of these factors (Figure 18). In Alzheimer's disease patients carrying the APOE4 allele, which is a prevalent genetic risk factor for Alzheimer's disease, common polymorphisms in IL-6R result in earlier onset of disease, demonstrating the potential importance of RIPK1 dependent IL-6 signaling pathways. Together, these data suggest increased RIPK1 function in microglia contributes to Alzheimer's disease, ALS and potentially other neurodegenerative diseases.

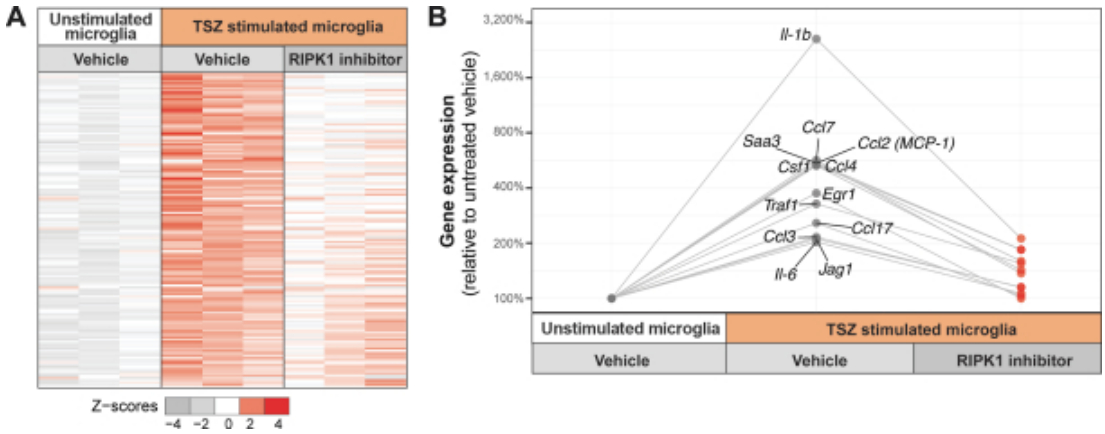


Figure 18: Production of pro-inflammatory cytokines in microglia is RIPK1 dependent. Stimulation of microglia with a TNF cocktail (TSZ) results in induction of many genes, and the majority of these changes are reversed after treatment with a RIPK1 inhibitor (A). Many of the top upregulated genes represent pro-inflammatory cytokines and chemokines such as IL-1b, IL-6 and Ccl2 (MCP-1). The up-regulation in all of these genes is reversed upon RIPK1 inhibitor treatment as shown in (B).

RIPK1 function is best characterized as being downstream of the receptor TNFR1. Specifically, the activation of RIPK1 downstream of TNFa signaling is likely a major component of the RIPK1-dependent neuro-immune phenotype observed in the context of chronic neurodegenerative disease (Figure 19). Brain penetrant inhibitors of RIPK1 therefore represent an attractive approach to targeting the TNF pathway, a highly validated biologic target in human disease, which we believe has not been adequately tested in the brain due to poor brain penetration of large molecule therapeutics, which are widely used for peripheral inflammatory disease. In addition, an oral, brain penetrant RIPK1 inhibitor can provide a more selective method to modulate TNF signaling through the pro-inflammatory TNFR1 receptor as compared to the non-selective anti-TNF antibodies that effect signaling through TNFR2, which is important for myelination of nerves, as well as TNFR1.

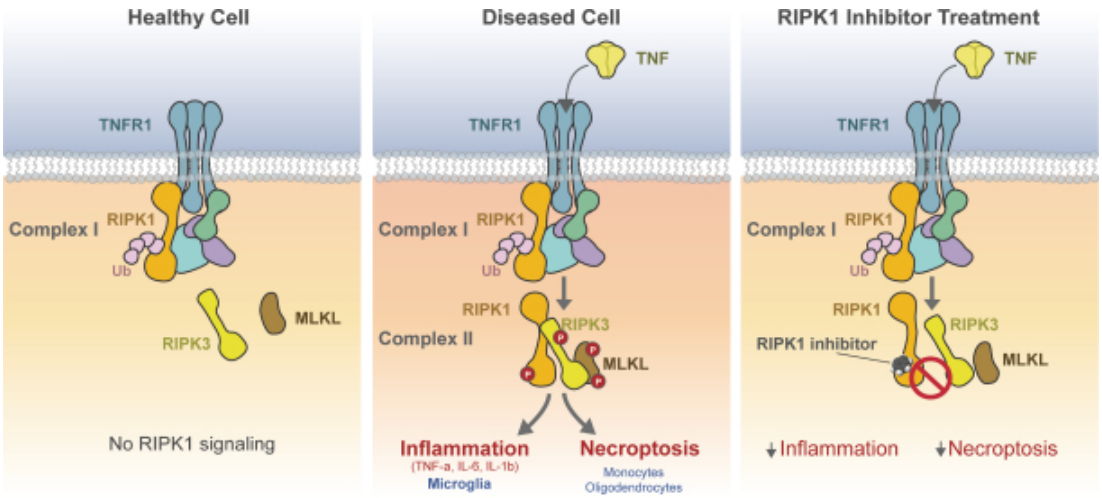


Figure 19: The RIPK1 signaling pathway displays minimal activity in health cells. Stimulation of TNFR1 in disease can lead to activation of RIPK1 kinase activity and generates a pro-inflammatory response in microglia and cell death via necroptosis in other cell types including monocytes and oligodendrocytes. Inhibition of RIPK1 activity with a small molecule is sufficient to block both the production of pro-inflammatory cytokines and necroptosis.

In addition to the role of RIPK1 in neuro-immune function, the RIPK1 pathway is also a central regulator of necroptosis, a form of programmed cell death. The role of RIPK1 in necroptosis of neurons has been implicated in Alzheimer's disease, providing another potential pathway where inhibition may be beneficial in disease.

We anticipate that an oral therapy targeting neuro-immune dysfunction could be used as either a monotherapy for treatment of Alzheimer's disease or in combination with therapeutics that target other mechanisms such as tau and amyloid. Although delaying the progression of Alzheimer's disease may be most effective by targeting early stage disease (prodromal and mild Alzheimer's disease populations), we anticipate that a RIPK1 inhibitor would also have benefit in later stage Alzheimer's disease (mild to moderate Alzheimer's disease), where microglial pathology is pervasive.

Genetic risk factors identify subpopulations of the disease that may differentially respond to therapies. The neuro-immune cascade downstream of RIPK1 and the genetics of Alzheimer's disease provide candidate biomarkers for selection of a neuroinflammatory subpopulation of Alzheimer's disease that may be more responsive to a therapy targeting microglial dysfunction. These risk factors include biomarkers of neuro-immune dysfunction, such as soluble TREM2, RIPK1 dependent inflammatory cytokines in the CSF (e.g. MCP-1, IL-1b, and IL-6), and genetic risks identified by GWAS, such as the IL-6R polymorphism.

According to estimates from the Alzheimer's Association, 5.5 million people in the United States suffer from Alzheimer's disease. Approximately 4.9 million of these people have prodromal, mild and moderate Alzheimer's disease. We estimate that patients who represent a neuroinflammatory subpopulation as described above make up approximately 30% to 50% of the total patient population.

A similar approach to patient selection may be applied to ALS. According to estimates from the ALS Association, there are more than 20,000 ALS patients in the United States. Although OPTN mutations are found in only a small fraction of patients, postmortem analysis of CNS tissue reveals microglial activation and an inflammatory profile in nearly all ALS patients.

Pharmacological Properties and Brain Exposure

We have a broad portfolio of potent, selective and brain penetrant RIPK1 inhibitors with attractive pharmacological properties. The lead candidate, DNL747, is a potent, selective, orally available, brain penetrant small molecule inhibitor of RIPK1. The pharmacology of the lead has been investigated in a broad range of primary and secondary biochemical assays, cell-based *in vitro* assays, and in animals. *In vitro* studies demonstrate that DNL747 is highly selective against kinase and receptor panels. Treatment of primary human microglia with DNL747 is able to inhibit RIPK1 kinase activity and reduce the production of cytokines (Figure 20).

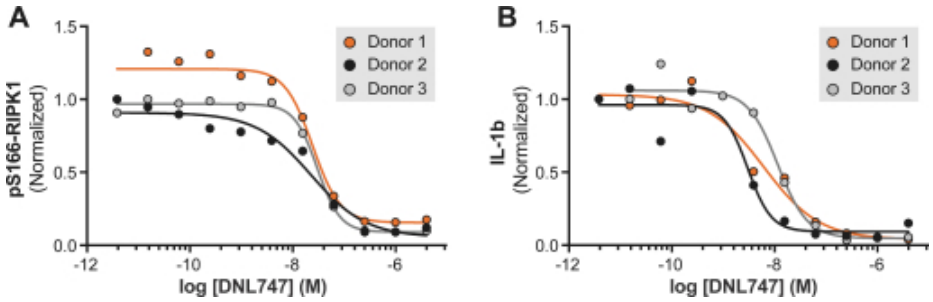


Figure 20: DNL747 demonstrates potent activity in human primary cells. Treatment of primary human microglia with DN747 results in a dose dependent reduction in p-RIPK1 (A) and IL-1b production (B).

Treatment with RIPK1 inhibitor tool compounds, including compounds we have generated, have neuro-immune modulatory effects in animal models. In animal models of Alzheimer's disease and ALS, an increase in RIPK1 is correlated with microglial activation (Figure 21). Inhibition of RIPK1 kinase activity reduces key signatures of microglial activation and reduces levels of cytokines in the brain including soluble TREM2, IL-6 and total RIPK1 (Figure 22). Long-term treatment of Alzheimer's disease or ALS in animal models with RIPK1 inhibitor tool compounds has been demonstrated to result in reduced neuro-immune dysfunction, attenuated neurodegeneration and improved function, as described in a recent publication in the journal *Science* by our collaborator Junying Yuan at Harvard University.

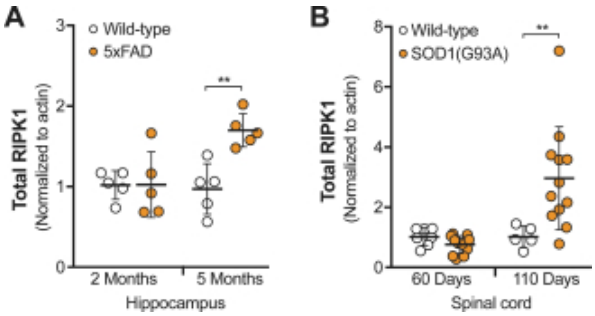


Figure 21: RIPK1 is elevated in neurodegenerative disease models. An age dependent increase in RIPK1 that correlates with microglia activation can be seen in the 5XFAD model of Alzheimer's disease (A) and the SOD1 model of ALS (B). ** indicates p<0.01

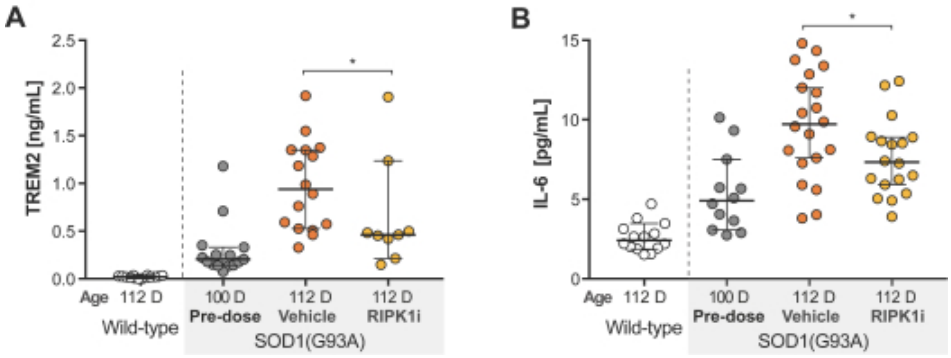


Figure 22: Short term treatment with a RIPK1 inhibitor reduces neuro-inflammatory microglial markers in neurodegenerative disease models. The SOD1 model of ALS displays elevated levels of sTREM2 and IL-6 as compared to wild type control mice at 100 days that further increases at 112 days as the disease progresses. Treatment of SOD1 mice with a RIPK1 inhibitor from 100 days of age to 112 days of age results in reduced levels of sTREM2 (A) and IL-6 (B) in the spinal cord to near the 100 day pre-dose levels. * indicates p<0.05.

We have completed extensive preclinical PK and PD studies with DNL747 in multiple species. Preclinical modeling of clearance predicts a human half-life compatible with twice daily dosing. PD has been characterized using a marker of RIPK1 activity, phosphorylation of RIPK1 at Serine 166, or pS166. This biomarker has been characterized in *in vitro* assays in human and monkey PBMCs and has been demonstrated to be robustly reduced by RIPK1 inhibitors.

DNL747 is currently being tested in comprehensive GLP toxicity studies, including 28-day repeat-dose studies in rat and monkey and safety pharmacology studies. DNL747 was well tolerated in pilot 7-day repeat-dose toxicity studies up to high doses and exposures. Exposures were 20- to 100-fold higher than the exposures at predicted therapeutic dose levels to achieve IC90 coverage at trough. No concerns were identified in *in vitro* safety screening for genotoxicity, cardiovascular ion channel inhibition, and hepatotoxicity assessments. DNL747 has been well tolerated to date in the ongoing 28-day GLP repeat-dose toxicity studies.

Biomarker-Driven Development

We have generated a number of assays to measure target engagement and pathway modulation for our RIPK1 program in order to facilitate and increase the probability of success of clinical development. To directly measure the level of RIPK1 activity, we have developed an assay to measure autophosphorylation of RIPK1 at pS166. This assay will enable quantitative measurement of target engagement in the blood of patients following a single dose or multiple doses of our RIPK1 inhibitor in Phase 1 clinical trials. Based on this information, we expect to be able to select the appropriate dose levels for later stage trials.

To measure the effect of RIPK1 on the production of pro-inflammatory cytokines by microglia, we have identified candidate pathway biomarkers of RIPK1 activity, including RIPK1 dependent cytokines, such as TNFa, IL-1b and IL-6, which are elevated in brains of patients with Alzheimer's disease. We will first use these assays to directly measure these cytokines in the CSF of subjects in a Phase 1 healthy volunteer trial to begin to determine a relationship between drug exposure and reduction of basal levels of inflammation in the brain. We then plan to use the same assays to determine the effect of RIPK1 inhibition on reduction of inflammatory cytokines in Alzheimer's disease patients and ALS patients in a small Phase 2a clinical trial. In addition to development of fluid biomarker assays, we have also invested in the development of a novel PET tracer related to a mitochondrial protein that is a biomarker of glial biology dysfunction. We are currently running a translocator protein, or TSPO,

imaging study, which is a PET study in ALS patients to determine the test-retest reliability of this imaging biomarker and its utility as a direct and non-invasive measure of neuro-immune dysfunction.

In order to examine the effect of RIPK1 inhibition on the progression of neurodegeneration, we are also assessing the effect of RIPK1 inhibition in preclinical models for the effect on neurofilament (axon support) levels in blood plasma and CSF. It has recently been reported that the loss of neurons in many neurodegenerative conditions increases the levels of the protein neurofilament in both the CSF and plasma of patients. We believe that a relatively small, short clinical trial focusing on a biomarker-like neurofilament could demonstrate that a product candidate can reduce neurodegenerative processes and, therefore, build confidence in the clinical benefit of the product candidate in a larger pivotal trial.

GWAS genetic data have identified a polymorphism in the IL-6 receptor in a subset of Alzheimer's disease patients that may be a useful biomarker for selection of patients expected to benefit from RIPK1 inhibition. This common genetic variant is associated with a more prevalent neuroinflammatory phenotype in an APOE4 carrier subpopulation of Alzheimer's disease patients. As increased levels of IL-6 results from increased activity of the RIPK1 signaling pathway, patients with this IL-6 receptor mutation are expected to be more likely to respond to treatment with a RIPK1 inhibitor.

Development Plan

Pending the results from our IND-enabling preclinical studies, we plan to submit an IND or CTA for DNL747 in early 2018 and initiate a Phase 1 clinical trial in healthy volunteers in the first half of 2018. The Phase 1 study is expected to be randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in healthy young and elderly subjects to investigate the safety and tolerability of single and multiple oral doses of DNL747 and characterize the PK and PD of DNL747 in plasma and CSF. Target engagement will be assessed in PBMCs using the pS166 biomarker and extrapolated to estimate target engagement in brain. As an exploratory endpoint, candidate inflammatory biomarkers in the CSF are also being evaluated. We anticipate the target engagement goal for the RIPK1 clinical development program will be to achieve 70% to 90% target inhibition at trough concentrations in order to maximize inhibition of the RIPK1 pathway to enable testing of a broad range of doses in future clinical studies in patients. As an extension to our Phase 1 clinical trial design, we also plan to enroll a cohort of Alzheimer's disease patients to assess PK, safety and target engagement in this population. This will provide key insight to guide dose selection for subsequent patient trials and the identification of potential biomarker and clinical endpoints.

After completion of the Phase 1 trial in healthy volunteers, we plan to proceed to two Phase 2a studies evaluating biomarker endpoints in ALS and Alzheimer's disease. The primary objectives of these patient studies is expected to be to evaluate safety, PK and PD of DNL747 in Alzheimer's disease and ALS patients and identify evidence of central pathway engagement. We are currently evaluating endpoints to be used in these studies including CSF cytokines and TSPO imaging to demonstrate relevant effects on inflammatory cytokines and microglial function.

Back-up and Other Compounds

As part of our parallel development strategy, we have also developed a number of structurally diverse backup RIPK1 inhibitor molecules that are currently being characterized. Upon completion, we expect to be able to advance these candidates to the IND or CTA filing stage in 2019.

In August 2016, we filed a CTA for an earlier RIPK1 inhibitor compound, DNL104, and initiated a single center, randomized, double blind, placebo-controlled, dose escalating Phase 1 study in the Netherlands. Thirty-six subjects received a single dose of DNL104 and 16 subjects received multiple

doses of DNL104. This study provided evidence of peripheral and CSF drug exposure and pathway inhibition by measurement of pRIPK1 in blood, and identified candidate RIPK1 dependent cytokines that change in human CSF. DNL104 was well tolerated during the dosing interval and there were no CNS related safety signals. However, three out of 16 active-treated subjects who received multiple dose developed liver test abnormalities of 2.5x to 5x above normal levels of liver enzyme activity. Based on both preclinical and clinical data, we believe that these findings are off-target liabilities that are molecule specific to the DNL104 molecule and not a result of RIPK1 inhibition. This conclusion resulted in a decision to discontinue DNL104 and advance the structurally distinct molecule DNL747, which we predict to have a superior PK profile and low risk for liver toxicity.

ATV:TREM2 Program

ATV: TREM2 is a therapeutic candidate designed to rescue microglial function in Alzheimer's disease through modulating the activity of a genetically validated target. We have developed high affinity antibodies for TREM2 and are currently characterizing molecules in order to select a lead to couple with our proprietary ATV platform. We plan to file an IND or CTA for this program in 2020.

Therapeutic Rationale

A major component of Alzheimer's disease pathology is the presence of neuro-immune dysfunction. Microglia, the resident immune cells of the brain, show signs of activation and release of toxic cytokines in patients with Alzheimer's disease. Recent human genetic studies have identified single nucleotide polymorphism in a number of microglia specific genes that contribute to Alzheimer's disease, which strongly implicates glial function as a contributor to disease risk. TREM2 is a cell surface receptor expressed exclusively by microglia in the brain which regulates multiple processes including survival, migration, phagocytosis, and cytokine release. In 2013, a rare variant of TREM2 was found to be associated with a three-fold higher risk of Alzheimer's disease onset, which strongly implicates TREM2 as a functional contributor to disease progression.

The TREM2 mutations identified in patients with Alzheimer's disease results in loss of normal TREM2 function. Mouse models of Alzheimer's disease display more severe phenotypes in the absence of TREM2, including more diffuse amyloid plaques and increased synaptic loss. Conversely, data from our microglial assays demonstrate that increasing TREM2 signaling can improve microglial survival and function, indicating that activating TREM2 has a beneficial effect on this cell type (Figure 23). Based on this combination of genetic and functional data, we hypothesize that positive modulation of TREM2 activity will improve microglia function and slow the progression of Alzheimer's disease.

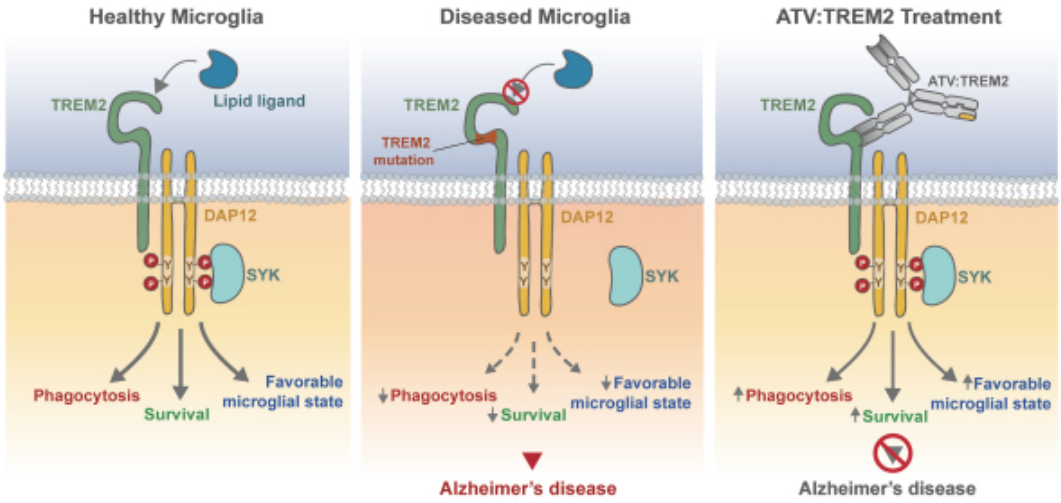


Figure 23: TREM2 is a cell surface receptor expressed on microglia. Activation of the TREM2 signaling pathway in healthy microglia leads to improved survival and promotes a favorable microglial state. TREM2 mutations result in reduced signaling and attenuated microglia function, while treatment with ATV:TREM2 is able to improve survival and boost microglial function.

We believe that patients with a specific neuroinflammatory signature as a result of glial dysfunction may particularly benefit from therapeutics targeting positive modulation of TREM2. These patients could be identified through a combination of genetic, CSF and imaging biomarkers. This population could be expanded to encompass all prodromal to mild and moderate Alzheimer's disease patients based on a demonstration of pathway modulation in the clinic.

Pharmacological Properties and Brain Exposure

We have generated multiple classes of anti-TREM2 antibodies with affinities less than 10nM. By using an array of functional assays, we have demonstrated that these antibodies have diverse functional effects, including several that show agonism and positive allosteric modulation (Figure 24). We are currently testing these antibodies in human microglia to determine which mechanism of action results in the desired effect on TREM2-mediated microglial function. We plan to then progress our lead antibody with the optimal affinity and activity profile to *in vivo* studies.

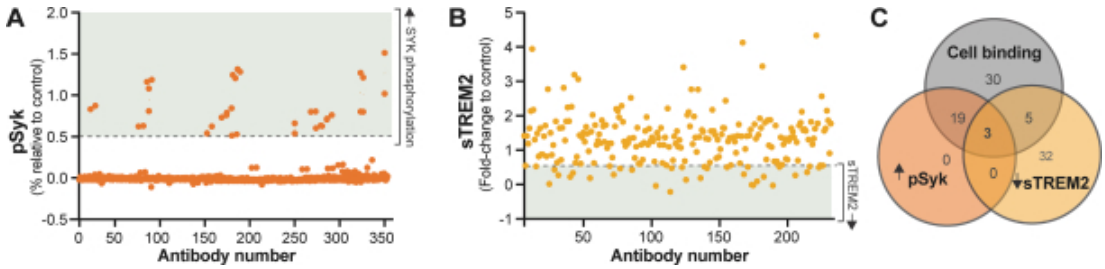


Figure 24: Profiling of anti-TREM2 antibodies. Antibodies were profiled for their ability to induce TREM2 signaling and measured by pSyk (A) and for their effect on shedding of soluble TREM2 (sTREM2) from the cell surface (B). Anti-TREM2 antibodies were identified with various combinations of activities. This includes 57 antibodies that bound TREM2 on the surface of cells (Cell binding), of which 19 increased Syk phosphorylation (pSyk), 5 lowered soluble TREM2 levels (sTREM2), and 3 antibodies displayed both of these activities (C).

We will evaluate the lead TREM2 antibodies *in vivo* for target engagement and disease-relevant efficacy in animal models of Alzheimer's disease. We will then progress the most promising of the lead TREM2 antibodies as a potential clinical candidate to be humanized and coupled with our ATV platform, ATV:TREM2, in order to improve brain uptake and enable target engagement in clinical studies.

Biomarker-Driven Development

The development of ATV:TREM2 is expected to be facilitated by a number of biomarkers to measure target engagement, pathway modulation and impact on disease progression. Upon cleavage of the extracellular domain of TREM2, a soluble form of TREM2, sTREM2, is released from the cell surface. sTREM2 is detectable in CSF. We have focused on anti-TREM2 antibodies that modulate the levels of sTREM2, enabling sTREM2 to be used as a biomarker of target engagement both in preclinical models and Phase 1 clinical trials. We intend to correlate TREM2 levels with downstream functional endpoints using preclinical models, allowing measurement of sTREM2 levels in a Phase 1 clinical trial to confirm target engagement and increase the probability of success.

The ability of ATV:TREM2 to modulate microglial function in preclinical models will be measured through histology and examination of microglial gene expression. These endpoints will be correlated to readouts that can be measured in clinical studies such TSPO-PET imaging and cytokine levels in CSF. As part of clinical trials, we plan to examine these endpoints both pre-dose and following treatment to assess microglia activation state.

Development Plan

The primary indication for ATV:TREM2 is Alzheimer's disease. The development of ATV:TREM2 will be facilitated by a number of biomarkers to measure target engagement, pathway modulation and an impact on disease progression. Our focus on anti-TREM2 antibodies that modulate levels of sTREM2, a soluble form of TREM2, will enable sTREM2 to be used as a biomarker of target engagement both in preclinical models and Phase 1 clinical trials. sTREM2 is released from the cell surface upon cleavage of the extracellular domain of TREM2 and is detectable in CSF. In preclinical models dosed with ATV: TREM2, sTREM2 levels will be correlated with the ability of ATV:TREM2 to modulate microglial function as assessed through histology and examination of microglial gene expression. Understanding the relationship between changes in sTREM2 and microglial function, will enable assessment of both target engagement and a biologically relevant effect of ATV:TREM2 dosing in Phase 1 clinical trials. Early stage clinical studies will also assess candidate biomarkers to identify patients that are most likely to benefit from a TREM2 mediated approach. Examples of these candidate

biomarkers include CSF sTREM2 and TSPO-PET, two biomarkers that are elevated in patients with Alzheimer's disease. These examples may be used as both a patient selection biomarker to identify patients with pathologic neuro-immune function and as a measure of TREM2 pathway modulation.

These endpoints will be correlated to readouts that can be measured in clinical studies such TSPO-PET imaging and cytokine levels in CSF. As part of clinical trials, we plan to examine these endpoints both pre-dose and following treatment to assess microglia activation state. We plan to file an IND or CTA for this program in 2020.

Cellular Homeostasis Pathway Program

ATV: BACE1/Tau Program

ATV: BACE1/Tau is a bispecific program targeting the production of amyloid beta, or Abeta, and the spreading of Tau, the two key pathological processes of Alzheimer's disease. We have developed high affinity antibodies for BACE1 and Tau and are currently optimizing them before combining them into a single therapeutic agent using our proprietary ATV platform. We plan to file an IND or CTA in 2020.

Therapeutic Rationale

Alzheimer's disease pathology is characterized by the presence of amyloid plaques and neurofibrillary tangles. The pathologies arise as a consequence of protein aggregation, a form of disrupted cellular homeostasis, eventually leading to neuronal degeneration. Amyloid plaques are comprised of Abeta, an extracellular fragment of amyloid precursor protein, or APP, which is generated by cleavage of APP by BACE1 and gamma secretase. Mutations in amyloid precursor protein, or APP, processing components that increase Abeta levels are sufficient to cause early onset Alzheimer's disease. Conversely, mutations in APP that reduce BACE1 cleavage may protect individuals from Alzheimer's disease. These genetic links demonstrate the central role of the amyloid pathway in Alzheimer's disease, and are particularly supportive of BACE1 inhibition as a therapeutic approach (Figure 25).

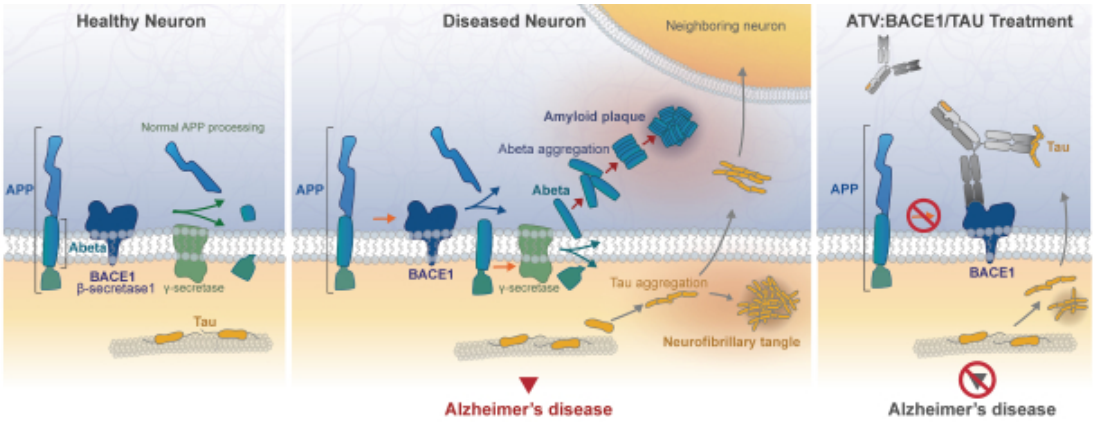


Figure 25: Abeta is generated through sequential cleavage of APP by beta-secretase 1 (BACE1) and gamma secretase to generate Abeta. In Alzheimer's disease, Abeta aggregates to form oligomers and amyloid plaques. Tau is present in healthy neurons but can misfold and aggregate in disease to form either neurofibrillary tangles or Tau oligomers that can spread from one cell to another in disease. ATV:BACE1/Tau blocks both of these Alzheimer's disease pathologies through inhibiting cleavage of APP by BACE1 and sequestering extracellular Tau to prevent its spread.

Tau is believed to regulate microtubule stability in neurons, but it can also aggregate to form neurofibrillary tangles, or NFTs, present in many neurodegenerative diseases, including Alzheimer's

disease. Detailed examination of Alzheimer's disease patients' brains has revealed that Tau pathology spreads spatially during the course of the disease. This spreading of Tau pathology is correlated with cognitive decline. Tau antibodies are currently in clinical development based on animal model data demonstrating that they are capable of blocking the spread of Tau pathology.

Preclinical data also show amyloid pathology accelerates Tau pathological spreading, which is consistent with findings in Alzheimer's disease patients that show Tau pathology progresses later as compared to amyloid plaques. Therefore, our approach of targeting both pathologies with a bispecific antibody may also have synergistic activity. The target patient population for our ATV:BACE1/Tau clinical studies is patients with early-stage Alzheimer's disease and confirmed Abeta pathology as measured by amyloid PET imaging.

Pharmacological Properties and Brain Exposure

We have discovered lead anti-BACE1 and anti-Tau antibodies that have been humanized and are now undergoing optimization processes designed to further improve affinity and cellular potency. Our anti-BACE1 lead displays less than 10nM cellular potency for inhibition of Abeta production (Figure 26). Anti-BACE1 antibodies have demonstrated improved selectivity as compared to small molecule approaches currently in clinical development by sparing inhibition of BACE2, which has the potential to lead to a superior safety profile following chronic dosing. When coupled to our ATV platform, anti-BACE1 antibodies have been shown to reduce Abeta levels in the brain by approximately 55% in a human TfR mouse model.

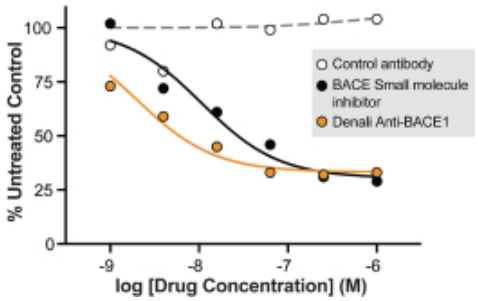


Figure 26: Activity of Anti-BACE1 antibody. Our anti-BACE1 antibody shows comparable ability to inhibit Abeta production by cells as compared to a benchmark small molecule BACE inhibitor.

Our lead anti-Tau antibody recognizes all forms of Tau present in the brains of Alzheimer's disease patients and has high affinity. It demonstrates superior target engagement in animal models as compared to our benchmark antibodies which are similar to certain antibodies that third parties currently have in clinical development, even without being coupled to our ATV platform (Figure 27). We believe the epitope recognized by our Tau antibody is advantageous relative to binding sites of benchmark antibodies as it would recognize truncated forms of Tau not recognized by antibodies directed against N-terminal or C-terminal epitopes. We have conducted proof of concept studies with anti-BACE1/Tau bi-specific antibodies that demonstrate both arms retain full functionality when combined into a single molecule.

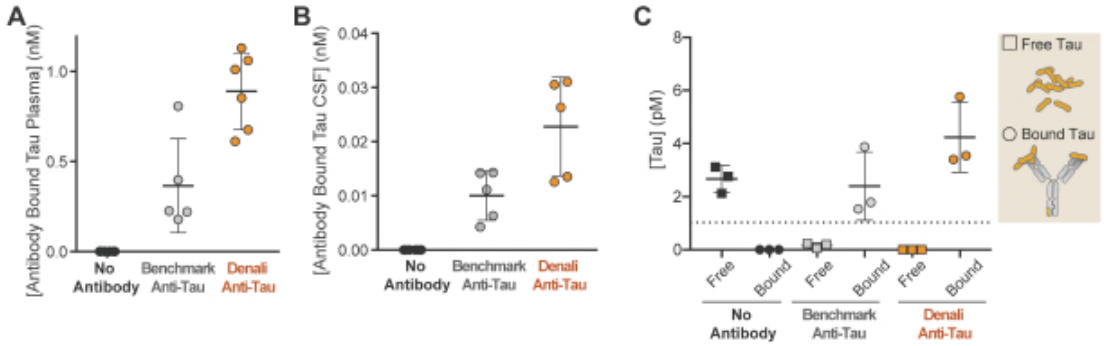


Figure 27. Our lead anti-Tau antibody displays target engagement that is superior to benchmark antibodies. The amount of antibody bound Tau in either plasma (A) or CSF (B) following a single dose of either our lead anti-Tau or a Benchmark control anti-Tau. Our lead anti-Tau also recognizes all extracellular Tau present in CSF from an Alzheimer's patient (C).

We believe our ATV:BACE1/Tau program may be the first therapeutic to target both hallmark Alzheimer's disease pathologies as a single therapeutic agent and has the potential for synergistic activity, restoring protein homeostasis with regards to the two most common Alzheimer's disease pathologies. To directly demonstrate the efficacy of the ATV:BACE1/Tau molecule, we are developing a proprietary mouse model by crossing our human TfR knock-in mouse with an established genetic model of Tau pathology. These preclinical efficacy studies are planned for 2018, and are expected to enable the examination of brain exposure and Abeta levels in the brain, and assess the effect on spreading of Tau pathology.

Biomarker-Driven Development

We plan to use validated genetic, biochemical and imaging biomarkers to support patient selection, evidence of target engagement and functional efficacy for our ATV:BACE1/Tau program. These include assays for measurement of CSF Abeta and Tau, as well as Abeta and Tau PET imaging tracers. The acute measurement of Abeta after BACE1 inhibition can be utilized to confirm ATV:BACE1/Tau uptake and target engagement, thus validating our ATV platform for BBB uptake in humans in Phase 1 clinical testing.

In preclinical models, brain levels of Abeta are reduced following a single dose of a BACE1 antibody coupled to the ATV platform (Figure 26), while dosing Tau antibodies led to increased levels of Tau bound to antibody in plasma and CSF. These two readouts can be translated to human testing by measuring CSF levels as a direct measure of target engagement for an ATV:BACE1/Tau molecule. Preclinical studies will be conducted to measure CSF levels of Abeta and Tau in animal models and correlated to effects on amyloid and Tau pathology following chronic dosing. These data and established CSF biomarkers are expected to enable effective testing of ATV:BACE1/Tau in humans.

Development Plan

Our Phase 1 clinical trials will be designed to evaluate the safety and pharmacology of ATV:BACE1/Tau and evaluate target engagement in both healthy volunteers and Alzheimer's disease patients. In this study and in later stage clinical trials, we plan to measure the activity of ATV:BACE1/Tau through CSF Abeta measurement, confirming BACE1 inhibition. In later stage clinical studies we plan to use Tau PET imaging to ascertain whether ATV:BACE1/Tau is able to prevent the spread of Tau pathology. Our target patient population is patients with prodromal and mild Alzheimer's disease and confirmed Abeta pathology as measured by amyloid PET imaging. We estimate this patient population to be approximately 3.4 million in the United States.

The results from this Phase 1 study with ATV:BACE1/Tau will provide information on the overall safety and pharmacologic profile of our ATV platform.

Back-up and Other Compounds

We are also pursuing ATV:Tau bivalent as an alternative approach to ATV:BACE1/Tau. This molecule will have the added advantage of two antibody arms engaging tau, resulting in potentially higher affinity target engagement, combined with ATV to improve brain exposure. This approach is attractive as local target concentrations of Tau in the synapse may be high. A decision to advance ATV:Tau will be based on establishing superior target engagement biomarker data in animal model CSF and human CSF as compared to known competitor molecules. We plan to file an IND or CTA in 2020.

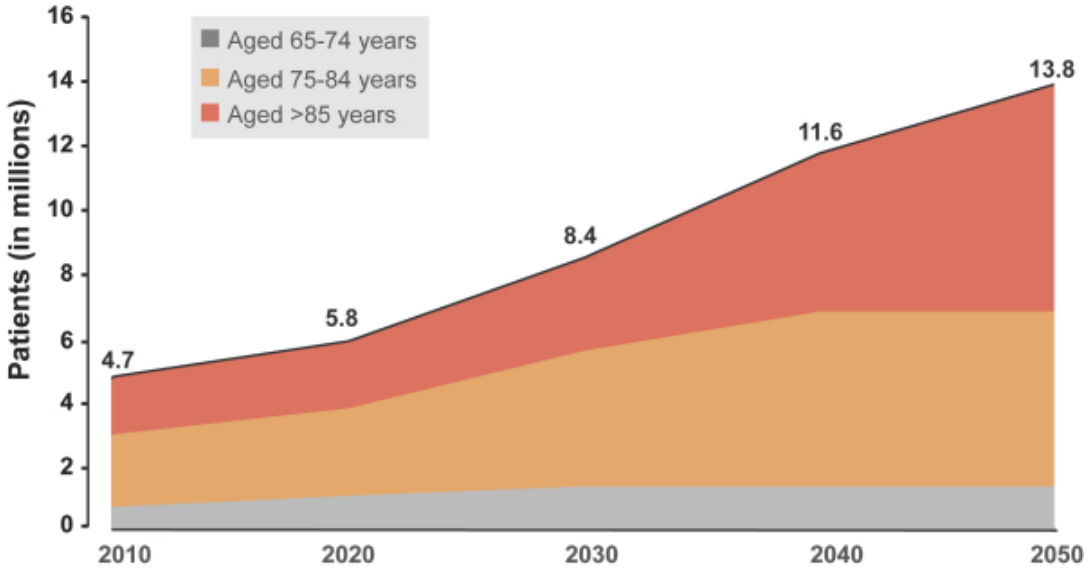
Neurodegeneration: A Significant Unmet Medical Need

Neurodegeneration is one of the largest unmet medical needs of our time, with a rapidly growing patient population. The risk of most neurodegenerative diseases increases with age, but people of all ages can also be affected due to genetic and/or environmental factors. Neurodegenerative diseases are generally progressive in nature and result in the degeneration and/or death of neurons in the brain that result in cognitive decline, functional impairment and eventually death. Alzheimer's and Parkinson's diseases represent the largest among the neurodegenerative diseases.

There are few effective therapeutic options available for patients with Alzheimer's disease, Parkinson's disease, ALS and other neurodegenerative diseases.

Alzheimer's Disease

Alzheimer's disease is a progressive form of dementia that impacts cognitive and motor function in those with the disease. Alzheimer's disease is likely a heterogenous disease driven by genetic risk and environmental factors with common pathology of amyloid deposition in the brain. It is estimated by the World Health Organization to represent between 60% to 70% of all cases of dementia. Alzheimer's disease is the sixth leading cause of death in the United States. As the disease progresses, patients lose the ability to carry out basic daily tasks and eventually to respond to their environment. According to estimates from the Alzheimer's Association, 5.5 million people in the United States suffer from Alzheimer's disease, and patient prevalence is expected to increase to 13.8 million people by 2050.



Source: Alzheimer's Association
Figure 28: Projected number of people in the United States with Alzheimer's disease.

The cost of care to society is massive. The direct costs to American society of caring for those with Alzheimer's disease and other dementias will total an estimated $259 billion in 2017, and is projected to increase to $1.1 trillion by 2050, according to the Alzheimer's Association.

The two classes of drugs approved for the treatment of Alzheimer's disease dementia are cholinesterase inhibitors (donepezil, galantamine, rivastigmine and tacrine) and NMDA receptor antagonists (memantine). These therapeutic products do not modify or alter the progression of the underlying disease and provide only modest efficacy in treating the symptoms of Alzheimer's disease. Namenda (memantine), the most recent FDA-approved new therapeutic product for Alzheimer's disease, was approved in the United States in 2003.

Parkinson's Disease

Parkinson's disease is the second most common neurodegenerative disease of adult onset, behind only Alzheimer's disease. Parkinson's disease is a chronic and progressive movement disorder. According to the Parkinson's Disease Foundation, as many as one million people in the United States today suffer from Parkinson's disease, with approximately 60,000 Americans diagnosed with Parkinson's disease each year.

Lysosomal dysfunction is a central pathology of Parkinson's disease. Certain genetic mutations affecting lysosomal dysfunction, such as LRRK2, aSyn and GBA mutations, are linked to Parkinson's disease. In addition, clinical diagnosis of Parkinson's disease without a known cause is called idiopathic Parkinson's disease and represents the majority of known cases.

For Parkinson's disease, most therapeutic products approved for treatment of the motor symptoms of the disease are related to levodopa and other dopamine agonists. While some existing products provide meaningful symptomatic relief, they have significant side effect risks, fail to address the progression of the disease, and over time gradually lose their effectiveness in treating the symptoms of the disease.

Other Rare Neurodegenerative Diseases

There are many types of rare neurodegenerative diseases, including ALS and LSDs, among others. ALS is a severe and fast progressing neurodegenerative disease. The incidence rate of ALS in the United States is approximately 2 in 100,000 people, with more than 20,000 people in the United States currently suffering from ALS, according to estimates from the ALS Association. The life expectancy of a patient with ALS averages two to five years after diagnosis. By 2040, the projected number of ALS cases in the United States is expected to increase to approximately 30,000.

LSDs are a group of approximately 50 inherited metabolic diseases that are characterized by an abnormal build-up of various toxic materials in the body's cells. LSDs are usually triggered when a particular enzyme is missing or exists in too small an amount to enable the complete breakdown of macromolecules. Each LSD is characterized by the nature of the substances that accumulate and their effects on the body. As a group, LSDs have an estimated frequency of about one in every 5,000 live births. Some of the most common LSDs are Gaucher disease, Fabry disease, and MPS II (Hunter syndrome). Other rare neurodegenerative indications include Huntington's disease, frontotemporal dementia and spinal muscular atrophy, among others.

Manufacturing

We believe it is important to our business and success to have a reliable, high-quality preclinical and clinical drug supply. As we mature as a company and approach commercial stage operations, securing reliable high-quality commercial drug supply will be critical.

We do not currently own or operate facilities for product manufacturing, storage, distribution or testing.

We rely on third-party contract manufacturers, or CMOs, to manufacture and supply our preclinical and clinical materials to be used during the development of our product candidates. We have established relationships with several CMOs.

We currently do not need commercial manufacturing capacity. When and if this becomes relevant, we intend to evaluate both third-party manufacturers as well as building out internal capabilities and capacity. We may choose one or both options, or a combination of the two.

Commercialization Plan

We do not currently have any approved drugs and we do not expect to have any approved drugs in the near term. Therefore, we have no sales, marketing or commercial product distribution capabilities and have no experience as a company in marketing drugs.

When and if any of our product candidates are approved for commercialization, we intend to develop a commercialization infrastructure for those products in the United States and potentially in certain other key markets. We may also rely on partnerships to provide commercialization infrastructure, including sales and marketing and commercial distribution.

Competition

The biotechnology and pharmaceutical industries, including in the neurodegenerative disease field, are characterized by rapidly advancing technologies, strong competition and an emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental

agencies and public and private research institutions. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, method of administration, cost, level of promotional activity and intellectual property protection.

Our product candidates will compete with current therapies approved for the treatment of neurodegenerative diseases, which to date have been primarily targeted at treating the symptoms of such diseases rather than halting or slowing the progression of the disease. However, in addition to such currently approved therapies, we believe that our product candidates, if approved, may also compete with other potential therapies intended to halt or slow the progression of neurodegenerative disease that are being developed by a number of companies and institutions, including but not limited to:

- *Alzheimer's Disease*: Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Biogen, Eli Lilly, Eisai, GlaxoSmithKline, Merck and Roche (including Genentech, its wholly owned subsidiary), and are in various stages of clinical trials.
- *Parkinson's Disease*: Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including Prothena, Roche, Sage Therapeutics and Sanofi, and are in various stages of clinical trials.
- *ALS:* Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies and academic institutions, including Cytokinetics and Mallinckrodt, and are in various stages of clinical trials.
- *Lysosomal Storage Diseases*: The currently approved treatments for LSDs are enzyme based therapies. Potentially disease modifying therapeutics are being developed by several large and specialty pharmaceutical and biotechnology companies, including ArmaGen, BioMarin, JCR Pharmaceuticals, Sanofi, Shire and Ultragenyx, and are in various stages of clinical trials.

In addition, there are companies that are developing technologies that would compete directly with our technologies, including:

- *Blood-Brain Barrier Technology*: There are several large and specialty pharmaceutical and biotechnology companies developing BBB delivery technologies that utilize RMT, including AbbVie, biOasis Technologies, ArmaGen, JCR Pharmaceuticals and Roche (including Genentech, its wholly owned subsidiary), among others.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, novel biological discoveries and BBB platform technology, including new targets and applications, and other inventions that are important to our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and licensing opportunities to develop and maintain our proprietary position.

For our product candidates, we generally pursue patent protection covering compositions of matter, methods of use and manufacture. For example, our most advanced product candidate in the LRRK2 program, DNL201, is covered by an issued composition of matter patent in the United States and several other countries. Furthermore, we own and have filed patent applications in the United States that are directed to the composition of matter of certain antibodies and small molecule product candidates that we intend to develop, as well as the Fc domain portion of our BBB platform technology

that binds to TfR. However, given that the development of our technology and product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our technology and product candidates is also at an early stage. We do not own or in-license any issued patents in the United States directed to the composition of matter of any of the antibodies or enzymes that we have thus far developed using our BBB platform technology, or issued patents in the United States directed to the composition of the Fc domain portion of our BBB platform technology that binds to TfR, or issued patents in the United States directed to the composition of the specific product candidates being developed in our RIPK1, TREM2, aSyn or IDS core programs. As further described below, we have filed or intend to file patent applications on these and other aspects of our technology and product candidates, and as we continue the development of our product candidates, we intend to identify additional means of obtaining patent protection that would potentially enhance commercial success, including protection for additional methods of use, formulation or manufacture.

ATV Programs

For our ATV programs, we license multiple patent families from F-star directed to, among other things, modifying immunoglobulin non-CDR loops to create antigen binding sites. These licensed patent families include approximately four issued U.S. patents and five pending U.S. non-provisional patent applications, and over 180 issued foreign patents and over 10 pending foreign patent applications. The issued patents in the earliest of these families are expected to expire in 2026, not including any patent term adjustments and any patent term extensions.

Furthermore, we own two pending U.S. provisional applications directed to the composition and sequences of our TfR-binding ATVs. Any future U.S. and foreign patents that may issue from these patent families (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions. We do not own or in-license any issued U.S. patents that are directed to the composition of matter of our ATV programs.

ATV: BACE1/Tau

In addition, we license one patent family from VIB that is directed to, among other things, our anti-BACE1 antibody to be used with our BBB platform technology licensed from F-star. This licensed family includes one issued U.S. patent and one pending U.S. non-provisional patent application; and approximately 16 issued foreign patents and three pending foreign patent applications. The issued patents in this family are expected to expire in 2030, excluding any patent term adjustments and any patent term extensions. We own one pending U.S. provisional application directed to, among other things, our anti-Tau antibody to be used with our BBB platform technology licensed from F-star. Any future U.S. and foreign patents that may issue from this patent family (assuming the necessary non-provisional patent applications are timely filed and all other applicable requirements are satisfied) would be expected to expire in 2038, excluding any patent term adjustments and any patent term extensions.

LRRK2

We license multiple patent families from Genentech directed to, among other things, our LRRK2 program, including DNL201, DNL151 and other related compounds. These licensed patent families include approximately 10 granted U.S. patents, and approximately 105 granted foreign patents and 67 pending foreign patent applications. The issued patents in these licensed families are expected to expire in 2031, excluding any patent term adjustments and any patent term extensions.

DNL201

We license a patent family from Genentech directed to, among other things, DNL201, which includes one issued U.S. patent, and approximately five granted foreign patents and six pending

foreign patent applications. The issued U.S. patent claims the composition of matter of DNL201 and is expected to expire in 2031, excluding any patent term adjustments and any patent term extensions.

DNL151

We own one patent family directed to DNL151, which includes one pending U.S. non-provisional patent application, one pending patent cooperation treaty, or PCT, application and two pending foreign patent applications. Future U.S. and foreign patents issued from this patent family are expected to expire in 2037, excluding any patent term adjustments and any patent term extensions. In addition, we license five foreign granted patents and one allowed European patent application from Genentech related to the DNL151 compound class. We do not own or in-license any issued U.S. patents covering the composition of matter of DNL151.

RIPK1

For our most advanced RIPK1 product candidate, DNL747, we own a patent family directed to the composition of matter of DNL747, which includes one pending U.S. non-provisional patent application, one PCT application and two pending foreign patent applications. Future U.S. and foreign patents issued from this patent family are expected to expire in 2037, excluding any patent term adjustments and any patent term extensions.

We cannot guarantee that our owned and licensed pending patent applications, or any patent applications that we may in the future file or license from third parties, will result in the issuance of patents. We also cannot predict the scope of claims that may be allowed or enforced in our patents. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and product candidates. For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information and continuing technological innovation to develop and maintain our

competitive position. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment with us or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or our failure to obtain a license to proprietary rights required to develop or commercialize our future products may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention. For more information, see "Risk Factors—Risks Related to Our Intellectual Property."

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA, the Public Health Service Act, or PHSA, and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of

government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Any future product candidates must be approved by the FDA through either a New Drug Application, or NDA, or a Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to the FDA of an NDA or BLA;
- A determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the filing for review;
- Satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- Potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The data required to support an NDA or BLA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including Good Laboratory Practices, or GLP, regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or BLA. The FDA will accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase I clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase II clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase III clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its

intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA or BLA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

NDA/BLA Review Process

Following completion of the clinical trials, data are analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA or BLA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA or BLA must be obtained before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to the

FDA's fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as an NDA or BLA, is $2,380,100. PDUFA also imposes an annual product fee for human drugs and biologics (approximately $97,750) and an annual establishment fee (approximately $580,000) on facilities used to manufacture prescription drugs and biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs or BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs and BLAs before it accepts them for filing, and may request additional information rather than accepting the NDA or BLA for filing. The FDA must make a decision on accepting an NDA or BLA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months, from the filing date, in which to complete its initial review of a new molecular-entity NDA or original BLA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA or original BLA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA or BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA or BLA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA or BLA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs and biologics that meet certain criteria. Specifically, new drugs and biologics are eligible for fast track designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA or BLA approval, but ideally no later than the pre-NDA or pre-BLA meeting.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug or biologic shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions, as it deems necessary to assure safe use of the product.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as

fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process.

Abbreviated Licensure Pathway of Biological Products as Biosimilar or Interchangeable

The Patient Protection and Affordable Care Act, or PPACA, or Affordable Care Act, or ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products shown to be highly similar to an FDA-licensed reference biological product. The BPCIA attempts to minimize duplicative testing, and thereby lower development costs and increase patient access to affordable treatments. An application for licensure of a biosimilar product must include information demonstrating biosimilarity based upon the following, unless the FDA determines otherwise:

- analytical studies demonstrating that the proposed biosimilar product is highly similar to the approved product notwithstanding minor differences in clinically inactive components;
- animal studies (including the assessment of toxicity); and
- a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) sufficient to demonstrate safety, purity and potency in one or more conditions for which the reference product is licensed and intended to be used.

In addition, an application must include information demonstrating that:

- the proposed biosimilar product and reference product utilize the same mechanism of action for the condition(s) of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism(s) of action are known for the reference product;
- the condition or conditions of use prescribed, recommended, or suggested in the labeling for the proposed biosimilar product have been previously approved for the reference product;
- the route of administration, the dosage form, and the strength of the proposed biosimilar product are the same as those for the reference product; and
- the facility in which the biological product is manufactured, processed, packed or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Biosimilarity means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. In addition, the law provides for a designation of “interchangeability” between the reference and biosimilar products, whereby the biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product. The higher standard of interchangeability must be demonstrated by information sufficient to show that:

- the proposed product is biosimilar to the reference product;
- the proposed product is expected to produce the same clinical result as the reference product in any given patient; and
- for a product that is administered more than once to an individual, the risk to the patient in terms of safety or diminished efficacy of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch.

FDA approval is required before a biosimilar may be marketed in the United States. However, complexities associated with the large and intricate structures of biological products and the process by which such products are manufactured pose significant hurdles to the FDA's implementation of the law that are still being worked out by the FDA. For example, the FDA has discretion over the kind and amount of scientific evidence—laboratory, preclinical and/or clinical—required to demonstrate biosimilarity to a licensed biological product.

The FDA intends to consider the totality of the evidence, provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a stepwise approach in the development of their biosimilar products. Biosimilar product applications thus may not be required to duplicate the entirety of preclinical and clinical testing used to establish the underlying safety and effectiveness of the reference product. However, the FDA may refuse to approve a biosimilar application if there is insufficient information to show that the active ingredients are the same or to demonstrate that any impurities or differences in active ingredients do not affect the safety, purity or potency of the biosimilar product. In addition, as with BLAs, biosimilar product applications will not be approved unless the product is manufactured in facilities designed to assure and preserve the biological product's safety, purity and potency.

The submission of a biosimilar application does not guarantee that the FDA will accept the application for filing and review, as the FDA may refuse to accept applications that it finds are insufficiently complete. The FDA will treat a biosimilar application or supplement as incomplete if, among other reasons, any applicable user fees assessed under the Biosimilar User Fee Act of 2012 have not been paid. In addition, the FDA may accept an application for filing but deny approval on the basis that the sponsor has not demonstrated biosimilarity, in which case the sponsor may choose to conduct further analytical, preclinical or clinical studies and submit a BLA for licensure as a new biological product.

The timing of final FDA approval of a biosimilar for commercial distribution depends on a variety of factors, including whether the manufacturer of the branded product is entitled to one or more statutory exclusivity periods, during which time the FDA is prohibited from approving any products that are biosimilar to the branded product. The FDA cannot approve a biosimilar application for twelve years from the date of first licensure of the reference product. Additionally, a biosimilar product sponsor may not submit an application for four years from the date of first licensure of the reference product. A reference product may also be entitled to exclusivity under other statutory provisions. For example, a reference product designated for a rare disease or condition (an "orphan drug") may be entitled to seven years of exclusivity, in which case no product that is biosimilar to the reference product may be approved until either the end of the twelve-year period provided under the biosimilarity statute or the end of the seven-year orphan drug exclusivity period, whichever occurs later. In certain circumstances, a regulatory exclusivity period can extend beyond the life of a patent, and thus block biosimilarity applications from being approved on or after the patent expiration date. In addition, the FDA may under certain circumstances extend the exclusivity period for the reference product by an additional six months if the FDA requests, and the manufacturer undertakes, studies on the effect of its product in children, a so-called pediatric extension.

The first biological product determined to be interchangeable with a branded product for any condition of use is also entitled to a period of exclusivity, during which time the FDA may not determine that another product is interchangeable with the reference product for any condition of use. This exclusivity period extends until the earlier of: (1) one year after the first commercial marketing of the first interchangeable product; (2) 18 months after resolution of a patent infringement against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; (3) 42 months after approval of the first interchangeable product, if a patent infringement suit

against the applicant that submitted the application for the first interchangeable product is still ongoing; or (4) 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse experiences, and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the

Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs also must comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Affordable Care Act. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of biologic and pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review

process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of a NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

European Union Drug Development

As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Affordable Care Act contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The Affordable Care Act made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The Affordable Care Act also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. The Centers for Medicare & Medicaid Services, or CMS, have proposed to expand Medicaid rebate liability to the territories of the United States as well.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of

the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. As of 2010, the Affordable Care Act expanded the types of entities eligible to receive discounted 340B pricing, although, under the current state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs. In addition, as 340B drug prices are determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Licenses and Collaborations

F-star License and Collaboration Agreement

Overview

In August 2016, we entered into a license and collaboration agreement with F-star Gamma Limited, F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology Limited, or, collectively, F-star. The goal of the collaboration is the development of certain constant Fc-domains of an antibody with non-native antigen binding activity, or Fcabs, to enhance delivery of therapeutics across the BBB into the brain. The collaboration leverages F-star's modular antibody technology and our expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the F-star collaboration agreement, we can nominate up to three Fcab targets, or Accepted Fcab Targets, within the first three years of the date of the collaboration agreement; and

we have selected TfR as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, we can nominate up to eight Fab targets, or Accepted Fab Targets, which are targets bound by the variable domains of an antibody or other therapeutic modalities, or Fabs. Under the F-star collaboration agreement, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Fcab directed to an Accepted Fcab Target, which we refer to as a Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action until the expiration of our buy-out option, as described below. In addition, we are obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans.

Financial Obligations

We paid F-star Gamma an upfront fee of $5.5 million, which includes the selection of the first Accepted Fcab Target, TfR, under the collaboration. We are obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target we select, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. We are also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Buy-Out Option

In connection with the entry into the F-star collaboration agreement, we also purchased an option for an upfront option fee of $0.5 million, which we refer to as the buy-out-option, to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement. We must elect whether to exercise our buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by us of a notice that we are progressing an Fcab identified from our library that binds to an Accepted Fcab Target. In addition, if we exercise the buy-out option, we will become an owner of certain intellectual property owned by F-star Gamma (by way of our ownership of F-star Gamma) and we will become a direct licensee of certain intellectual property of F-star Biotechnology (by way of our assumption of F-star Gamma's license agreement with F-star Biotechnology). If we exercise the buy-out option we will be obligated to make initial exercise payments under the buy-out option agreement and F-star Gamma's license agreement with F-star Biotechnology ranging from, in the aggregate, approximately $18.0 million to $50.0 million, plus a payment under the buy-out option agreement of the estimated net cash of F-star Gamma at the time of such exercise. In addition, we will be required under the buy-out option agreement and F-star Gamma's license agreement with F-star Biotechnology to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by us or solely by F-star or jointly by us and F-star and the timing of our exercise of the buy-out option. Following exercise of the buy-out option, we will not be required to make any further milestone or royalty payments under the F-star collaboration agreement.

If we exercise the buy-out option, then F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology will continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action.

If we do not exercise the buy-out option prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until our rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target. In addition, in the event that we do not exercise the buy-out option prior to expiration of the buy-out option period, we have granted F-star Gamma a non-exclusive, royalty-free, irrevocable, perpetual, sublicensable license under our background and program intellectual property and any joint program intellectual property, to exploit any Fcab (other than one identified solely by us) against an Accepted Fcab Target and/or any antibody to the extent containing such Fcab (other than an Fcab identified solely by us or jointly with F-star), but excluding any rights to any Fabs and Accepted Fab Targets. If we elect not to exercise the buy-out option, we continue to have the option to obtain certain exclusive licenses as we describe further below.

License Option

With respect to each Accepted Fab Target, we have the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that we or F-star identify, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target, as described above. Under each such license, we will be obligated to use commercially reasonable efforts to develop and commercialize the applicable licensed product in certain major market countries. If we do not exercise such a license option or otherwise elect to terminate it, such license option will generally expire upon the dosing of the fifth patient dosed in the first Phase 1 trial of the relevant antibody that binds to the applicable Accepted Fab Target.

Each time we exercise the license option described above, we will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Our royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country, and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to us an Fcab that meets pre-defined criteria. We have the right to credit a certain amount of royalty payments that we pay to third parties with respect to certain licensed products against our royalty obligation to F-star Gamma but such credit cannot reduce our royalty obligation to F-star Gamma by more than fifty percent.

Other Rights

In addition to the buy-out option and option to obtain certain exclusive licenses described above, F-star Gamma and F-star Biotechnology granted us non-exclusive licenses under certain intellectual property to conduct technology development to discover and develop Fcabs. We also received a non-exclusive license under certain of F-star Biotechnology's platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the blood brain barrier, subject to certain specified restrictions.

F-star retains the right to use its intellectual property, including any intellectual property that we and F-star jointly own pursuant to the terms of the collaboration agreement, outside the scope of the

licenses granted to us. In addition, we granted F-star Biotechnology a non-exclusive, irrevocable, perpetual, sublicensable license under certain of our intellectual property to develop and commercialize certain of F-star's platform technology, subject to certain exclusivity obligations and the licenses granted to us under the collaboration agreement. Further, we are obligated to assign to F-star certain patents and know-how that we generate under the collaboration agreement related to F-star's platform technology or certain Fcabs identified solely by F-star.

Termination

Unless earlier terminated, the F-star collaboration agreement will remain in effect until all of our royalty and milestone payment obligations to F-star Gamma expire. Either party may terminate the F-star collaboration agreement if the other party materially breaches the collaboration agreement, subject to specified notice and cure provisions, or for the other party's bankruptcy or insolvency. In addition, F-star Gamma may terminate the F-star collaboration agreement if we challenge any of the patent rights licensed to us by F-star. We are able to terminate the F-star collaboration agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days' prior written notice to F-star.

Upon any termination by us for convenience or by F-star Gamma for our material uncured breach or insolvency, in each case either in whole or on an Accepted Fcab Target-by-Accepted Fcab Target or an Accepted Fab Target-by-Accepted Fab Target basis, among other things, the rights granted to us under the F-star collaboration agreement will terminate. Further, upon any such termination, if we have not exercised the buy-out option, (i) we must grant F-star Gamma certain non-exclusive, irrevocable and perpetual licenses under certain intellectual property owned by us arising out of the collaboration agreement to exploit certain antibodies that do not contain our proprietary Fabs or Fcabs identified solely by us, and (ii) F-star will no longer be restricted from developing and commercializing licensed products with respect to any terminated Accepted Fcab Target and/or Accepted Fab Target, as applicable.

Genentech Exclusive License Agreement

In June 2016, we entered into an exclusive license agreement with Genentech. The agreement gives us access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress our in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted us (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. We are obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

Our financial obligations under the agreement with Genentech included an upfront payment of $8.5 million and a technology transfer fee of $1.5 million. In addition, we may owe Genentech milestone payments upon the achievement of certain development, regulatory and commercial milestones, up to a maximum of $315.0 million in the aggregate. In addition, we are obligated to pay royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by us, (ii) the date a compound was first discovered, derived or optimized by us, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level

of annual net sales of the relevant licensed product. We also have the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, but such credit cannot reduce our royalty obligation to Genentech by more than fifty percent. Our royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country or (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country. If one of our licensed products incorporates a compound provided to us by Genentech, has orphan drug exclusivity, and is not covered by a valid claim of a licensed patent, we must pay royalties on net sales of such licensed products on a country-by-country and licensed product-by-licensed product basis until such orphan drug exclusivity in such country expires, but our obligation to pay these royalties may be eliminated or reduced if there is a clinically superior product marketed in such country.

Unless earlier terminated, our agreement with Genentech will continue in effect until all of our royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, we will retain our licenses under the intellectual property Genentech licensed to us on a non-exclusive, royalty-free basis. Genentech may terminate the agreement if we challenge any of the patent rights licensed to us by Genentech, or if we materially breach the agreement, subject to specified notice and cure provisions, or enter into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for our material breach, bankruptcy or insolvency after we have made a milestone payment to Genentech, then we are obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of our patents, know-how and regulatory filings directed to Genentech-provided compounds. We do not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

Scientific Advisory Board

We have assembled a highly qualified scientific advisory board comprised of advisors who have, collectively, deep expertise in neurodegenerative diseases, genomics, protein engineering, drug development and drug discovery as well as translational medicine. Our scientists work in collaboration with these advisors to identify new disease targets, develop a biomarker strategy, enhance our BBB platform technology and accelerate discovery and development.

Name	Affiliated Entity
Marc Tessier-Lavigne, Ph.D. (Chair)	Stanford University
Scott Biller, Ph.D.	Agios Pharmaceuticals
Alison Goate, DPhil	Mount Sinai
David Holtzman, M.D.	Washington University in St. Louis
Leonard Petrucelli, Ph.D.	Mayo Clinic
Eric Reiman, M.D.	Banner Alzheimer's Institute
Lee Rubin, Ph.D.	Harvard University
Kevan Shokat, Ph.D.	University of California San Francisco
Scott Small, M.D.	Columbia University
Huda Zoghbi, M.D.	Baylor University

Employees

As of June 30, 2017, we had approximately 120 employees, all of whom were full-time and around 100 of whom were engaged in research and development activities. Approximately two-thirds of our employees hold Ph.D. or M.D. degrees. Substantially all of our employees are located in South San Francisco, California. None of our employees are represented by a labor union or covered under a collective bargaining agreement.

Facilities

Our corporate headquarters are located in South San Francisco, California, where we lease approximately 38,000 square feet of office, research and development, engineering and laboratory space pursuant to a lease agreement which commenced on August 1, 2016 and expires on July 31, 2024, with an option to extend for 5 years. This facility houses all our personnel. We believe that our existing facilities are adequate for our near-term needs, but expect to need additional space as we grow. We believe that suitable additional or alternative space would be available as required in the future on commercially reasonable terms.

Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of our executive officers and directors as of August 18, 2017:

Name	Age	Position
Executive Officers:		
Ryan J. Watts, Ph.D.	41	President, Chief Executive Officer and Director
Alexander O. Schuth, M.D.	44	Chief Operating Officer and Secretary
Steve E. Krognes	49	Chief Financial Officer and Treasurer
Carole Ho, M.D.	44	Chief Medical Officer
Non-Employee Directors:		
Vicki Sato, Ph.D.	69	Chairperson of our Board of Directors
Douglas Cole, M.D.	57	Director
Jay Flatley	64	Director
Robert Nelsen	54	Director
David Schenkein, M.D.	60	Director
Marc Tessier-Lavigne, Ph.D.	57	Director

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the corporate governance and nominating committee

Executive Officers

Ryan J. Watts, Ph.D. is one of our Co-Founders and has served as a member of our board of directors since March 2015 and as our President and Chief Executive Officer since August 2015. From March 2015 to August 2015, Dr. Watts acted as our interim President, Chief Scientific Officer and Head of Research and Development. Dr. Watts co-founded and joined Denali from Genentech, a biotechnology company, where he held various research and leadership roles of increasing responsibility between 2004 and 2015; from 2013 to February 2015, Dr. Watts served as Director of the Department of Neuroscience; from 2010 to 2013, Dr. Watts served as Associate Director of the Department of Neuroscience; and from 2004 to 2010, Dr. Watts led or served on numerous research and early development teams. In addition, Dr. Watts led Genentech's BBB team between 2009 and 2015, and he served as Chair of the Joint Research Committee with AC Immune between 2006 and 2010 (program currently in Phase 3) and between 2012 and 2014 (program currently in Phase 1). Dr. Watts received his Ph.D. in Biological Sciences from Stanford University and his B.S. in Biology from the University of Utah. Dr. Watts has authored and co-authored more than 60 scientific papers and has been an invited peer reviewer in numerous publications including Cell, Nature Biotechnology, Nature Medicine, Neuron, Science and Science Translational Medicine.

We believe Dr. Watts is qualified to serve on our board of directors because of the perspective and experience he provides as one of our founders and as our President and Chief Executive Officer, as well as his broad experience within the pharmaceutical industry, particularly in the area of neuroscience and drug discovery and development.

Alexander O. Schuth, M.D. is one of our Co-Founders and has served as our Chief Operating Officer since March 2015 and as Secretary since June 2015. Dr. Schuth co-founded and joined Denali from Genentech, where he held various roles of increasing responsibility between 2005 and 2015; from September 2014 to March 2015, Dr. Schuth served as Head of Technology Innovation and Diagnostics

Partnering; from March 2010 to September 2014, Dr. Schuth served as Head of Neuroscience Partnering; from January 2007 to March 2010, Dr. Schuth worked in the business development team; and from August 2005 to January 2007, Dr. Schuth worked as an R&D finance manager. At Genentech, Dr. Schuth led a product development team from preclinical to clinical development. From January 2001 to May 2003, he served as Investment Banking Associate in the equity capital markets group at Merrill Lynch in London. He currently serves on the board of directors of Molecular Health, a privately held biopharmaceutical company. Dr. Schuth received his M.B.A. from The Wharton School of the University of Pennsylvania and his M.D. from the Charite Medical School at the Humboldt University in Berlin, Germany.

Steve E. Krognes has served as our Chief Financial Officer since October 2015 and Treasurer since November 2015. Mr. Krognes joined Denali from Genentech, where he served as Chief Financial Officer and a member of the Executive Committee from April 2009 to September 2015. Mr. Krognes also oversaw Genentech's Site Services organization between 2011 and 2015, and Genentech's IT organization between 2009 and 2011. He chaired the Genentech Access to Care Foundation between 2009 and 2015. From January 2004 to April 2009, Mr. Krognes served as Head of Mergers & Acquisitions and a member of the Finance Executive Committee at Roche, a Swiss biotechnology company. From July 2002 to December 2003, Mr. Krognes served as Director of M&A at Danske Bank based in Norway. From April 2000 to June 2002, he served as a Venture Capitalist with Pylonia Ventures, a Swedish venture investments company. Prior to that, Mr. Krognes worked as a consultant at McKinsey and an investment banker at Goldman Sachs, based in London and Boston. Mr. Krognes currently serves as a member of the boards of directors of Corvus Pharmaceuticals, a biopharmaceutical company, RLS Global, a Swedish life science company, and the California Academy of Sciences, a private scientific and educational institution. Mr. Krognes served as a board member of the California Life Science Association between 2010 and 2015. He received his M.B.A. from Harvard Business School and his B.S. in Economics from The Wharton School of the University of Pennsylvania.

Carole Ho, M.D. has served as our Chief Medical Officer and Head of Development since June 2015. Dr. Ho joined Denali from Genentech, where she held various roles of increasing responsibility between 2007 and 2015; from October 2014 to June 2015, Dr. Ho served as Vice President, Non-Oncology Early Clinical Development; from April 2011 to October 2014, Dr. Ho served as Senior Group Medical Director, Early Clinical Development; from June 2009 to April 2011, Dr. Ho served as Group Medical Director Global Product Development (Inflammation); and from October 2007 to June 2009, Dr. Ho served as Medical Director, Early Clinical Development. From November 2006 to October 2007, Dr. Ho served as Associate Medical Director at Johnson & Johnson, a health care products company. From June 2002 to November 2006, she was an instructor in the Department of Neurology and Neurological Sciences at Stanford University. Dr. Ho received her M.D. from Cornell University and her B.S. in Biochemical Sciences from Harvard College. Dr. Ho held a Medical Licensure from the American Board of Neurology and Psychiatry between 2004-2014, and has been a member of the American Academy of Neurology since 2002.

Non-Employee Directors

Vicki Sato, *Ph.D.* has served as a member of our board of directors since April 2015 and as Chairperson of our board of directors since August 2016. From September 2006 until July 2017, Dr. Sato served as a professor of management practice at Harvard Business School. From July 2005 until October 2015, she was also a professor in the Department of Molecular and Cell Biology at Harvard University. From September 2000 to May 2005, Dr. Sato served as the President of Vertex Pharmaceuticals, a pharmaceutical company. From 1992 until 2000, she served as the Chief Scientific Officer and Senior Vice President of Research and Development of Vertex Pharmaceuticals. Dr. Sato joined Vertex Pharmaceuticals in 1992, after serving as Vice President of Research at Biogen, a

biotechnology company. Dr. Sato serves on the boards of directors of Bristol Myers Squibb, Syros Pharmaceuticals and BorgWarner. She previously served on the board of directors of PerkinElmer until April 2017. Dr. Sato received her A.M. and Ph.D. degrees from Harvard University and her A.B. in Biology from Radcliffe College.

We believe Dr. Sato is qualified to serve on our board of directors because of her extensive industry experience and leadership experience as a senior executive and director of several life sciences companies.

Douglas Cole, *M.D.* has served as a member of our board of directors since May 2015. Dr. Cole joined Flagship Pioneering, which conceives, creates, resources and develops first-in-category life sciences companies, in 2001, and is currently Managing Partner, where he has focused on life science investments. He currently serves on the board of directors of Editas Medicine, a public biotechnology company, and serves on the board of directors of a number of private companies. Previously, Dr. Cole served on the boards of directors of Agios Pharmaceuticals, Receptos, AVEO Pharmaceuticals, Tetraphase Pharmaceuticals and Concert Pharmaceuticals. Dr. Cole received his M.D. from the University of Pennsylvania School of Medicine and his B.A. in English from Dartmouth College.

We believe Dr. Cole is qualified to serve on our board of directors because of his substantial experience as a venture capital investor in emerging life sciences companies, as well as his experience serving on the boards of directors for several life sciences companies.

Jay Flatley has served as a member of our board of directors since April 2015. Since July 2016, Mr. Flatley has served as the Executive Chairman of the board of directors of Illumina, a public company focused on sequencing- and array-based solutions for genetic analysis. From January 2016 to July 2016, he served as Illumina's Chairman and has served as a member of its board of directors since October 1999. From December 2013 to July 2016, Mr. Flatley served as the Chief Executive Officer of Illumina and as the President and Chief Executive Officer from October 1999 to December 2013. Prior to joining Illumina, Mr. Flatley was Co-founder, President, Chief Executive Officer, and a director of Molecular Dynamics, a life sciences company focused on genetic discovery and analysis, from July 1994 until its sale to Amersham Pharmacia Biotech in September 1998. Mr. Flatley is an advisory board member for U.C. San Diego's Moore Cancer Center and serves on the board of directors at Coherent, a photonics manufacturing company. Mr. Flatley received his B.S. and M.S. in Industrial Engineering from Stanford University and his B.A. in Economics from Claremont McKenna College.

We believe Mr. Flatley is qualified to serve on our board of directors because of his extensive leadership experience and industry knowledge.

Robert Nelsen has served as a member of our board of directors since May 2015. Mr. Nelsen has served as a Co-founder and Managing Director of ARCH Venture Partners, a venture capital firm focused on early-stage technology companies, or its affiliated entities, since 1986. Mr. Nelsen is a director of Juno Therapeutics, Sienna Biopharmaceuticals and Syros Pharmaceuticals, along with certain private companies. Previously, Mr. Nelsen served on the boards of directors of Agios Pharmaceuticals, KYTHERA Biopharmaceuticals, Adolor Corporation, Illumina, Fate Therapeutics, deCODE genetics, NeurogesX, Bellerophon Therapeutics, Sage Therapeutics and Caliper Life Sciences. He also previously served as trustee of Fred Hutchinson Cancer Research Center. Mr. Nelsen received his M.B.A. from the University of Chicago and his B.S. degrees in Economics and Biology from the University of Puget Sound.

We believe Mr. Nelsen is qualified to serve on our board of directors because of his experience as a venture capitalist building and serving on the boards of directors of many public and private emerging companies, including biotechnology companies.

David Schenkein, *M.D.* has served as a member of our board of directors since April 2015. Since August 2009, Dr. Schenkein has served as President and Chief Executive Officer of Agios Pharmaceuticals, a pharmaceuticals company. From April 2006 to July 2009, Dr. Schenkein served as a Senior Vice President of Oncology Development at Genentech. Dr. Schenkein currently serves on the boards of directors of Agios Pharmaceuticals and bluebird bio. Previously, Dr. Schenkein served on the board of directors of Foundation Medicine. He also currently serves as an adjunct attending physician in hematology at Tufts Medical Center. Dr. Schenkein received his M.D. from the State University of New York Upstate Medical School and his B.A. in Chemistry from Wesleyan University.

We believe that Dr. Schenkein is qualified to serve on our board of directors because of his extensive background in the biotechnology industry and leadership experience as a senior executive and director of biotechnology companies.

Marc Tessier-Lavigne, *Ph.D.* is one of our Co-Founders and has served as a member of our board of directors since March 2015. From March 2015 to August 2016, Dr. Tessier-Lavigne served as the Chairman of our board of directors. Since September 2016, Dr. Tessier-Lavigne has served as President of Stanford University. From March 2011 to September 2016, he served as President of the Rockefeller University, as well as professor and head of the Laboratory of Brain Development and Repair. From September 2003 to March 2011, Dr. Tessier-Lavigne served in positions of increasing responsibility at Genentech, where in 2009 he was named Executive Vice President for Research and Chief Scientific Officer. He currently serves on the board of directors of Regeneron Pharmaceuticals. Previously, he served on the boards of directors of Pfizer, Juno Therapeutics and Agios Pharmaceuticals. Dr. Tessier-Lavigne received his Ph.D. in Neurophysiology from University College London, his B.A. in Philosophy and Physiology from Oxford University and his B.Sc. in Physics from McGill University. He conducted postdoctoral work at the MRC Developmental Neurobiology Unit in London and at Columbia University.

We believe Dr. Tessier-Lavigne is qualified to serve on our board of directors because of his pioneering research, scientific knowledge, service on boards of directors of public companies in the life sciences industry and leadership in the biotechnology industry.

Board of Directors Composition

Our board of directors currently consists of seven members. After the completion of this offering, the number of directors will be fixed by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors will be divided among the three classes as follows:

- the Class I directors will be , and their terms will expire at the annual meeting of stockholders to be held in 2018;
- the Class II directors will be , and their terms will expire at the annual meeting of stockholders to be held in 2019; and
- the Class III directors will be , and their terms will expire at the annual meeting of stockholders to be held in 2020.

At each annual meeting of stockholders, upon the expiration of the term of a class of directors, the successor to each such director in the class will be elected to serve from the time of election and qualification until the third annual meeting following his or her election and until his or her successor is duly elected and qualified, in accordance with our amended and restated certificate of incorporation. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of our directors.

This classification of our board of directors may have the effect of delaying or preventing changes in control of our company.

Director Independence

Upon the completion of this offering, we anticipate that our common stock will be listed on , or . Under the rules of , independent directors must comprise a majority of a listed company's board of directors within one year of the completion of its initial public offering. In addition, the rules of require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Audit committee members and compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Exchange Act. Under the rules of , a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered to be independent for purposes of Rule 10A-3 and under the rules of , a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board of directors committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of , the board of directors must affirmatively determine that the member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director; and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that , representing of our seven directors, do not have relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of .

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and

circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled “Certain Relationships and Related Party Transactions.” There are no family relationships among any of our directors or executive officers.

Board of Directors Leadership Structure

Our board of directors is currently chaired by Dr. Sato. As a general policy, our board of directors believes that separation of the positions of Chairperson and Chief Executive Officer reinforces the independence of our board of directors from management, creates an environment that encourages objective oversight of management’s performance and enhances the effectiveness of our board of directors as a whole. As such, Dr. Watts serves as our President and Chief Executive Officer while Dr. Sato serves as the Chairperson of our board of directors but is not an officer. We expect and intend the positions of Chairperson of our board of directors and Chief Executive Officer to continue to be held by two separate individuals in the future.

Board of Directors Committees

Our board of directors has an audit committee, a compensation committee and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below.

Audit Committee

The members of our audit committee are , and . is the chairman of our audit committee. is our audit committee financial expert, as that term is defined under the SEC rules implementing SOX Section 407, and possesses financial sophistication, as defined under the rules of . Our audit committee oversees our corporate accounting and financial reporting process and assists our board of directors in monitoring our financial systems. Our audit committee will also:

- select and hire the independent registered public accounting firm to audit our financial statements;
- help to ensure the independence and performance of the independent registered public accounting firm;
- approve audit and non-audit services and fees;
- review financial statements and discuss with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews and the reports and certifications regarding internal controls over financial reporting and disclosure controls;
- prepare the audit committee report that the SEC requires to be included in our annual proxy statement;
- review reports and communications from the independent registered public accounting firm;
- review the adequacy and effectiveness of our internal controls and disclosure controls and procedure;
- review our policies on risk assessment and risk management;
- review related party transactions; and
- establish and oversee procedures for the receipt, retention and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of .

Compensation Committee

The members of our compensation committee are , and . is the chairman of our compensation committee. Our compensation committee oversees our compensation policies, plans and benefits programs. The compensation committee will also:

- oversee our overall compensation philosophy and compensation policies, plans and benefit programs;
- review and approve or recommend to our board of directors for approval compensation for our executive officers and directors;
- prepare the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administer our equity compensation plans.

Our compensation committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of .

Corporate Governance and Nominating Committee

The members of our corporate governance and nominating committee are , and . is the chairman of our corporate governance and nominating committee. Our corporate governance and nominating committee oversees and assists our board of directors in reviewing and recommending nominees for election as directors. Specifically, the corporate governance and nominating committee will:

- identify, evaluate and make recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- consider and make recommendations to our board of directors regarding the composition of our board of directors and its committees;
- review developments in corporate governance practices;
- evaluate the adequacy of our corporate governance practices and reporting; and
- evaluate the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee will operate under a written charter, to be effective prior to the completion of this offering, which will satisfy the applicable rules of the SEC and the listing standards of .

Director Compensation

To date, none of our non-employee directors has received any cash compensation for serving on our board of directors, other than Mr. Flatley and Drs. Sato, Schenkein and Tessier-Lavigne, who each earn $30,000 annually, paid on a quarterly basis, for service as a member of our board of directors. From time to time, we have granted stock options or issued restricted stock to those non-employee directors who are also not affiliated with our venture fund investors for their service on our board of directors, and such grants were made in April 2015 to Mr. Flatley and Drs. Sato and Schenkein. An

additional grant was made to Dr. Sato for her service as the Chairperson of our board of directors in August 2016. We do reimburse our directors for expenses associated with attending meetings of our board of directors and its committees. Following the completion of this offering, we expect to implement an annual cash and equity compensation program for our non-employee directors.

The following table presents the total compensation each of our non-employee directors received during the year ended December 31, 2016. Other than as set forth in the table, we did not pay any compensation, make any equity awards or non-equity awards to or pay any other compensation to any of our non-employee directors in 2016.

	Fees Earned or Paid in Cash ($)	Option Awards ($) (1)	Total ($)
Vicki Sato, Ph.D. (2)	15,000	148,095	163,095
Douglas Cole, M.D.	—	—	—
Jay Flatley (3)	15,000	—	15,000
Stephen Knight, M.D. (4)	—	—	—
Robert Nelsen	—	—	—
David Schenkein, M.D. (5)	15,000	—	15,000
Marc Tessier-Lavigne, Ph.D. (6)	15,000	—	15,000
Stacie Weninger, Ph.D. (7)	—	—	—

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with Financial Accounting Standard Board Accounting Standards Codification Topic 718, or ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the directors upon vesting of the applicable awards.

(2) Dr. Sato is paid a quarterly cash retainer of $7,500 for her service on our board of directors. As of December 31, 2016, Dr. Sato held an option to purchase 150,000 shares of our common stock. One-third of the shares subject to the option vest on August 23, 2017, and two-thirds of the remaining shares vest annually thereafter, subject to continued service through each such vesting date. As of December 31, 2016, Dr. Sato held 300,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(3) Mr. Flatley is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Mr. Flatley held 300,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(4) Dr. Knight resigned as a member of our board of directors on August 11, 2017.

(5) Dr. Schenkein is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Dr. Schenkein held 300,000 restricted shares of our common stock. One-fourth of the shares subject to the restricted stock award vested on April 17, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(6) Dr. Tessier-Lavigne is paid a quarterly cash retainer of $7,500 for his service on our board of directors. As of December 31, 2016, Dr. Tessier-Lavigne held an aggregate of 12,456,172 restricted shares of our common stock. Of the total number of shares, 10,937,500 shares are subject to a restricted stock agreement whereby one-fourth of the shares vested on March 12, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date. Of the total number of shares, 1,518,672 shares are subject to a restricted stock agreement whereby one-fourth of the shares vested on March 24,

2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service through each such vesting date.

(7) Dr. Weninger resigned as a member of our board of directors on August 11, 2017.

Directors who are also our employees receive no additional compensation for their service as directors. During 2016, Dr. Watts was our only employee director. See the section titled “Executive Compensation” for additional information about Dr. Watts’ compensation.

Compensation Committee Interlocks and Inside Participation

None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board of directors committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following the completion of this offering, the code of business conduct and ethics will be available on our website at www.denalitherapeutics.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions or our directors on our website identified above. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws, each to be effective upon the completion of this offering, will provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director’s duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director’s duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director’s responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into an indemnification agreement with each member of our board of directors and each of our officers. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism, or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

EXECUTIVE COMPENSATION

Our named executive officers for 2016, which consist of our principal executive officer and the next three most highly compensated executive officers, are:

- Ryan J. Watts, Ph.D., our President and Chief Executive Officer;
- Alexander O. Schuth, M.D., our Chief Operating Officer and Secretary;
- Steve E. Krognes, our Chief Financial Officer and Treasurer; and
- Carole Ho, M.D., our Chief Medical Officer.

Summary Compensation Table

The following table sets forth information regarding the compensation of our named executive officers for the year ended December 31, 2016.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($) (1)	Total ($)
Ryan J. Watts, Ph.D. *President and Chief Executive Officer*	2016	$450,000	$157,500(2)	$ —	$ 607,500
Alexander O. Schuth, M.D. *Chief Operating Officer and Secretary*	2016	$350,000	$122,500(2)	$ —	$ 472,500
Steve E. Krognes *Chief Financial Officer and Treasurer*	2016	$425,000	$398,750(3)	$ —	$ 823,750
Carole Ho, M.D. *Chief Medical Officer*	2016	$395,000	$138,250(2)	$495,600	$1,028,850

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

(2) The amount reported represents a bonus based upon the achievement of company objectives for the year ended December 31, 2016, which was paid in January 2017.

(3) The amount reported represents (i) the portion of the sign-on bonus from 2015 of $250,000, which was earned in October 2016 pursuant to the terms of Mr. Krognes' employment agreement and (ii) a bonus of $148,750 based upon the achievement of company objectives for the year ended December 31, 2016, which was paid in January 2017. Had Mr. Krognes' employment been terminated by us for cause or by Mr. Krognes other than for good reason, in each case before October 1, 2016, he would have been required to repay the signing bonuses paid to him, including the $250,000 that was paid to him upon the commencement of his employment with us on October 1, 2015.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2016:

		Option Awards					Stock Awards	
Name	Grant Date (1)	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity incentive awards: number of securities underlying unexercised unearned options (#)	Option Exercise Price ($) (2)	Option Expiration Date	Number of Shares of Stock That Have Not Vested (#)	Market Value of Shares of Stock That Have Not Vested ($) (3)
Ryan J. Watts, Ph.D.	03/13/2015	—	—	—	—	—	5,332,032(4)	7,038,283
	08/21/2015	—	—	4,982,469(5)	0.17	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	740,353(4)	977,266
Alexander O. Schuth, M.D.	03/13/2015	—	—	—	—	—	1,831,984(6)	2,418,219
	08/21/2015	—	—	996,494(5)	0.17	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	254,387(6)	335,791
Steve E. Krognes	11/20/2015	—	—	500,000(5)	0.17	11/19/2025	—	—
	11/20/2015	—	—	—	—	—	1,416,667(7)	1,870,001
Carole Ho, M.D.	08/21/2015	—	—	500,000(5)	0.17	8/20/2025	—	—
	08/21/2015	—	—	—	—	—	625,000(8)	825,000
	07/02/2016	—	500,000(9)	—	1.32	7/01/2026	—	—

(1) Each of the outstanding options to purchase shares of our common stock was granted pursuant to our 2015 Plan.
(2) This column represents the fair market value of a share of our common stock on the date of grant, as determined by our board of directors or its authorized committee.
(3) Because our common stock was not traded on a public market on December 31, 2016, the market value has been calculated based on an estimated per-share common stock value of $1.32 per share as of December 31, 2016.
(4) One-fourth of the total number of shares subject to each restricted stock grant vested on February 23, 2016, and one thirty-sixth of the remaining shares subject to each restricted stock grant is scheduled to vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of the shares subject to the restricted stock grants shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the award agreement, provided, however, that each such award shall be immediately vested in full if on or after the consummation of the change of control but on or prior to the first anniversary date of such consummation, Dr. Watts' employment with us is terminated without cause by us or by Dr. Watts for good reason, subject to Dr. Watts' execution of a release of claims in our favor.
(5) The shares subject to the option will vest upon certain performance goals being met as follows, in each case subject to the named executive officer's continued service to us: (a) 50% of the shares subject to the option vest upon (i) the date on which the reported closing price of our common stock on NASDAQ or the New York Stock Exchange (or other national securities exchange) has, for 90 consecutive trading days, equaled or exceeded $10.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization), with the first day of the 90-day measurement period no earlier than the date that is 180 days after our initial public offering for our common stock, or (ii) the date on which we close a change of control (as defined in the named executive officer's employment offer letter agreement) transaction in which the stockholders receive consideration equal to no less than $10.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization) in exchange for the sale of their capital stock and (b) 50% of the shares subject to the option vest upon (i) the date on which the reported closing price of our common stock on NASDAQ or the New York Stock Exchange (or other national securities

exchange) has, for 90 consecutive trading days, equaled or exceeded $20.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization), with the first day of the 90-day measurement period no earlier than the date that is 180 days after our initial public offering for our common stock, or (ii) the date on which we close a change of control transaction in which the stockholders receive consideration equal to no less than $20.00 per share (subject to adjustments for any stock split, reverse stock split or certain other changes in capitalization) in exchange for the sale of their capital stock.

(6) The shares subject to each restricted stock grant will vest as follows, in each case subject to Dr. Schuth's continued service to us: (a) 54.54% of the total number of shares subject to each restricted stock grant, or Tranche 1, vested as to one-fourth of the original number of Tranche 1 shares on March 17, 2016, and then as to 1/36 of the remaining number of shares of Tranche 1 each month thereafter and (b) 45.46% of the total number of shares subject to each restricted stock grant, or Tranche 2, shall vest on March 17, 2018. In the event of a change of control, the vesting of the shares subject to each restricted stock grant shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the award agreement, provided, however, that each such award shall be immediately vested in full if on or after the consummation of the change of control but on or prior to the first anniversary date of such consummation, Dr. Schuth's employment with us is terminated without cause by us or by Dr. Schuth for good reason, subject to Dr. Schuth's execution of a release of claims in our favor.

(7) The shares were acquired pursuant to an early exercise provision and remain subject to our repurchase right in accordance with the vesting schedule of the options. One-fourth of the total number of shares subject to the option vested on October 1, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or after the consummation of the change of control but on or prior to the first anniversary date of such consummation, Mr. Krognes' employment with us is terminated without cause by us or by Mr. Krognes for good reason, subject to Mr. Krognes' execution of a release of claims in our favor.

(8) The shares were acquired pursuant to an early exercise provision and remain subject to our repurchase right in accordance with the vesting schedule of the options. One-fourth of the total number of shares subject to the option vested on June 19, 2016, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested and exercisable. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or after the consummation of the change of control but on or prior to the first anniversary date of such consummation, Dr. Ho's employment with us is terminated without cause by us or by Dr. Ho for good reason, subject to Dr. Ho's execution of a release of claims in our favor.

(9) One-fourth of the total number of shares subject to the option vested on July 2, 2017, and one thirty-sixth of the remaining shares vest monthly thereafter, subject to continued service to us through each such vesting date. In the event of a change of control, the vesting of these shares shall be accelerated in part so that the number of shares, if any, that would otherwise have first become vested in the period between the date of change of control and the date on which all but the unvested shares that would have vested in the final 12 months of the vesting period shall have first become vested shall immediately become vested and exercisable. The remaining number of shares representing the last 12 months of vesting shall continue to vest in accordance with the original vesting schedule within the next 12 months set forth in the equity award agreement, provided however that the shares shall be immediately vested in full if on or after the

consummation of the change of control but on or prior to the first anniversary date of such consummation, Dr. Ho's employment with us is terminated without cause by us or by Dr. Ho for good reason, subject to Dr. Ho's execution of a release of claims in our favor.

Non-Equity Incentive Plan Compensation

Each of our named executive officers was awarded a discretionary annual cash bonus for 2016 based on attainment of corporate objectives for 2016. The 2016 target bonus amounts for each named executive officer (35% of base salary for each named executive officer), along with a target bonus pool equal to 100% of all employees' target bonuses, and the related 2016 corporate objectives, were recommended by the compensation committee of our board of directors to our board of directors in mid-2015 and approved by our board of directors in November 2015. The corporate objectives were comprised of key short-term and long-term goals of one or more facets of our business relating to research and development, hiring goals, finance, corporate development and operations. At the same time, our board of directors determined that if at least 70% of the corporate objectives were achieved by the end of the 2016 calendar year, the bonus pool would be funded at 100%.

In November 2016, the compensation committee of our board of directors reviewed the progress against the applicable 2016 corporate objectives, determined that 73% of the performance objectives had been met to such date and recommended that our board of directors fully fund the cash bonus pool at 100% of target levels. After taking into consideration these recommendations and our board of directors' own review, our board of directors approved the full 2016 bonus pool funding, and the payment of 100% of target bonuses to our named executive officers from such pool, subject to each such officer's continued employment through the bonus payment date. Each of our named executive officers received 100% of his or her target bonus amount in January 2017. Following the end of 2016, management assessed the full year achievement against the 2016 corporate goals, and determined that 76% of such goals had ultimately been achieved. The amounts in the Summary Compensation Table under the column "Non-Equity Incentive Plan Compensation" are based on the bonuses awarded under the above-described 2016 bonus program.

Employment Arrangements with Our Named Executive Officers

Ryan J. Watts, Ph.D.

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Dr. Watts, our President and Chief Executive Officer. The confirmatory employment letter will have no specific term and will provide for at-will employment. Dr. Watts' current annual base salary is $504,250 and Dr. Watts is considered annually for a target bonus of 55% of his annual base salary, subject to the terms and conditions of a bonus plan approved by our board of directors.

Alexander O. Schuth, M.D.

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Dr. Schuth, our Chief Operating Officer and Secretary. The confirmatory employment letter will have no specific term and will provide for at-will employment. Dr. Schuth's current annual base salary is $380,250 and Dr. Schuth is considered annually for a target bonus of 40% of his annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors.

Steve E. Krognes

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Mr. Krognes, our Chief Financial Officer and Treasurer. The confirmatory

employment letter will have no specific term and will provide for at-will employment. Mr. Krognes' current annual base salary is $437,750 and Mr. Krognes is considered annually for a target bonus of 40% of his annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors. In addition, Mr. Krognes was awarded a one-time signing bonus of $500,000. Had Mr. Krognes' employment been terminated by us for cause or by Mr. Krognes other than for good reason, in each case before October 1, 2016, he would have been required to repay the signing bonus paid to him.

Carole Ho, M.D.

We currently expect that, prior to the completion of this offering, we will enter into a confirmatory employment letter with Dr. Ho, our Chief Medical Officer. The confirmatory employment letter will have no specific term and will provide for at-will employment. Dr. Ho's current annual base salary is $406,850 and Dr. Ho is considered annually for a target bonus of 40% of her annual base salary, subject to the terms of the applicable bonus plan developed by our chief executive officer and approved by our board of directors. In addition, Dr. Ho was awarded a one-time signing bonus of $199,033. Had Dr. Ho's employment been terminated by us for cause or by Dr. Ho other than for good reason, in each case before June 25, 2016, she would have been required to repay the signing bonus paid to her.

Potential Payments upon Termination or Change of Control

We currently expect that, prior to the completion of this offering, we will adopt arrangements for our executive officers, including our named executive officers, that provide for payments and benefits on termination or change of control, which arrangements may be included in the anticipated confirmatory offer letters or separate plans or agreements.

Employee Benefit and Stock Plans

2017 Equity Incentive Plan

Prior to the completion of this offering, our board of directors intends to adopt, and we expect our stockholders will approve, our 2017 Plan. We expect that our 2017 Plan will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. Our 2017 Plan will provide for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to our employees, directors and consultants and our parent and subsidiary corporations' employees and consultants.

Authorized Shares. A total of shares of our common stock will be reserved for issuance pursuant to our 2017 Plan. In addition, the shares reserved for issuance under our 2017 Plan also will include (a) those shares reserved but unissued under our 2015 Plan as of immediately prior to the termination of the 2015 Plan, and (b) shares subject to awards under our 2015 Plan that, on or after the termination of the 2015 Plan, expire or terminate and shares previously issued pursuant to our 2015 Plan, as applicable, that, on or after the termination of the 2015 Plan, are forfeited or repurchased by us (provided that the maximum number of shares that may be added to our 2017 Plan pursuant to (a) and (b) is shares). The number of shares available for issuance under our 2017 Plan will also include an annual increase on the first day of each fiscal year beginning on January 1, 2018, equal to the least of:

- shares;

- percent (%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as our board of directors may determine.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2017 Plan. With respect to stock appreciation rights, only the net shares actually issued will cease to be available under the 2017 Plan and all remaining shares under stock appreciation rights will remain available for future grant or sale under the 2017 Plan. Shares that have actually been issued under the 2017 Plan under any award will not be returned to the 2017 Plan; provided, however, that if shares issued pursuant to awards of restricted stock, restricted stock units, performance shares or performance units are repurchased or forfeited, such shares will become available for future grant under the 2017 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under the 2017 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in a reduction in the number of shares available for issuance under the 2017 Plan.

Plan Administration. Our board of directors or one or more committees appointed by our board of directors will administer our 2017 Plan. The compensation committee of our board of directors is expected to administer our 2017 Plan. In the case of awards intended to qualify as ‘‘performance-based compensation’’ within the meaning of Section 162(m) of the Code, the committee will consist of two or more ‘‘outside directors’’ within the meaning of Section 162(m) of the Code. In addition, if we determine it is desirable to qualify transactions under our 2017 Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2017 Plan, the administrator has the power to administer our 2017 Plan and make all determinations deemed necessary or advisable for administering the 2017 Plan, including but not limited to, the power to determine the fair market value of our common stock, select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2017 Plan, determine the terms and conditions of awards (including, but not limited to, the exercise price, the times or times at which the awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions, and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of our 2017 Plan and awards granted under it, to prescribe, amend and rescind rules relating to our 2017 Plan, including creating sub-plans, and to modify or amend each award, including but not limited to the discretionary authority to extend the post-termination exercisability period of awards (provided that no option or stock appreciation right will be extended past its original maximum term), and to allow a participant to defer the receipt of payment of cash or the delivery of shares that would otherwise be due to such participant under an award). The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type which may have a higher or lower exercise price and/or different terms, awards of a different type and/or cash, or by which the exercise price of an outstanding award is increased or reduced. The administrator’s decisions, interpretations and other actions are final and binding on all participants.

Stock Options. Stock options may be granted under our 2017 Plan. The exercise price of options granted under our 2017 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an option may not exceed ten years. With respect to any participant who

owns more than 10% of the voting power of all classes of our outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the option will remain exercisable for 12 months. In all other cases, in the absence of a specified time in an award agreement, the option will remain exercisable for three months following the termination of service. An option may not be exercised later than the expiration of its term. Subject to the provisions of our 2017 Plan, the administrator determines the other terms of options.

Stock Appreciation Rights. Stock appreciation rights may be granted under our 2017 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding ten years. After the termination of service of an employee, director or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation rights agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the stock appreciation rights will remain exercisable for 12 months. In all other cases, in the absence of a specified time in an award agreement, the stock appreciation rights will remain exercisable for three months following the termination of service. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2017 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Stock. Restricted stock may be granted under our 2017 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director or consultant and, subject to the provisions of our 2017 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions to vesting it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us); provided, however, that the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture.

RSUs. RSUs may be granted under our 2017 Plan. RSUs are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2017 Plan, the administrator determines the terms and conditions of RSUs, including the vesting criteria and the form and timing of payment. The administrator may set vesting criteria based upon the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. Notwithstanding the foregoing, the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance Units and Performance Shares. Performance units and performance shares may be granted under our 2017 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance goals established by the administrator are achieved or the awards otherwise vest. The administrator will establish performance objectives or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number and/or the value of performance units and performance shares to be paid out to participants. The administrator may set performance objectives based on the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance criteria or other vesting provisions for such performance units or performance shares. Performance units shall have an initial dollar value established by the administrator on or prior to the grant date. Performance shares shall have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay earned performance units or performance shares in the form of cash, in shares or in some combination thereof.

Outside Directors. Our 2017 Plan provides that all outside (non-employee) directors will be eligible to receive all types of awards (except for incentive stock options) under our 2017 Plan. Prior to the completion of this offering, we intend to implement a formal policy pursuant to which our outside directors will be eligible to receive equity awards under our 2017 Plan. In order to provide a maximum limit on the awards that can be made to our outside directors, our 2017 Plan provides that in any given fiscal year, an outside director will not be granted awards having a grant-date fair value greater than $, but this limit is increased to $ in connection with his or her initial service (in each case, excluding awards granted to him or her as a consultant or employee). The grant-date fair values will be determined according to GAAP. The maximum limits do not reflect the intended size of any potential grants or a commitment to make grants to our outside directors under our 2017 Plan in the future.

Non-Transferability of Awards. Unless the administrator provides otherwise, our 2017 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. If the administrator makes an award transferrable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Certain Adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2017 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2017 Plan and/or the number, class and price of shares covered by each outstanding award and the numerical share limits set forth in our 2017 Plan.

Dissolution or Liquidation. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and all awards will terminate immediately prior to the consummation of such proposed transaction.

Merger or Change in Control. Our 2017 Plan provides that in the event of a merger or change in control, as defined under our 2017 Plan, each outstanding award will be treated as the administrator determines, without a participant's consent. The administrator is not required to treat all awards, all awards held by a participant or all awards of the same type, similarly.

In the event that a successor corporation or its parent or subsidiary does not assume or substitute an equivalent award for any outstanding award, then such award will fully vest, all restrictions on such award will lapse, all performance goals or other vesting criteria applicable to such award will be deemed achieved at 100% of target levels and such award will become fully exercisable, if applicable,

for a specified period prior to the transaction, unless specifically provided for otherwise under the applicable award agreement or other written agreement with the participant. The award will then terminate upon the expiration of the specified period of time. If an option or stock appreciation right is not assumed or substituted, the administrator will notify the participant in writing or electronically that such option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right will terminate upon the expiration of such period.

If an outside director's awards are assumed or substituted for in a merger or change in control and the service of such outside director is terminated on or following a change in control, other than pursuant to a voluntary resignation, his or her options and stock appreciation rights, if any, will vest fully and become immediately exercisable, all restrictions on his or her restricted stock and restricted stock units will lapse and all performance goals or other vesting requirements for his or her performance shares and units will be deemed achieved at 100% of target levels and all other terms and conditions met.

Amendment; Termination. The administrator has the authority to amend, suspend or terminate our 2017 Plan provided such action does not impair the existing rights of any participant. Our 2017 Plan automatically will terminate in 2027, unless we terminate it sooner.

2017 Employee Stock Purchase Plan

Prior to the effectiveness of this offering, our board of directors intends to adopt, and we expect our stockholders will approve, our ESPP. Our ESPP will be effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. We believe that allowing our employees to participate in our ESPP provides them with a further incentive towards ensuring our success and accomplishing our corporate goals.

Authorized Shares. A total of shares of our common stock will be available for sale under our ESPP. The number of shares of our common stock that will be available for sale under our ESPP also includes an annual increase on the first day of each fiscal year beginning on January 1, 2018, equal to the least of:

- shares;
- percent (%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or
- such other amount as the administrator may determine.

Plan Administration. Our board of directors, or a committee appointed by our board of directors will administer our ESPP, and have full but non-exclusive authority to interpret the terms of our ESPP and determine eligibility to participate, subject to the conditions of our ESPP, as described below. We expect our compensation committee to administer our ESPP. The administrator will have full and exclusive discretionary authority to construe, interpret and apply the terms of the ESPP, to delegate ministerial duties to any of our employees, to designate separate offerings under the ESPP, to designate our subsidiaries and affiliates as participating in the ESPP, to determine eligibility, to adjudicate all disputed claims filed under the ESPP and to establish procedures that it deems necessary or advisable for the administration of the ESPP, including, but not limited to, adopting such procedures, sub-plans and appendices to the enrollment agreement as are necessary or appropriate to permit participation in the ESPP by employees who are foreign nationals or employed outside the U.S. The administrator's findings, decisions and determinations are final and binding on all participants to the full extent permitted by law.

Eligibility. Generally, all of our employees will be eligible to participate if they are customarily employed by us, or any participating subsidiary, for at least 20 hours per week and more than five months in any calendar year. The administrator, in its discretion, may, prior to an enrollment date for all options granted on such enrollment date in an offering, determine that an employee who (i) has not completed at least two years of service (or a lesser period of time determined by the administrator) since his or her last hire date, (ii) customarily works not more than 20 hours per week (or a lesser period of time determined by the administrator), (iii) customarily works not more than five months per calendar year (or a lesser period of time determined by the administrator), (iv) is a highly compensated employee within the meaning of Section 414(q) of the Code or (v) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to disclosure requirements under Section 16(a) of the Exchange Act, is or is not eligible to participate in such offering period.

However, an employee may not be granted rights to purchase shares of our common stock under our ESPP if such employee:

- immediately after the grant would own capital stock possessing 5% or more of the total combined voting power or value of all classes of our capital stock; or
- hold rights to purchase shares of our common stock under all of our employee stock purchase plans that accrue at a rate that exceeds $25,000 worth of shares of our common stock for each calendar year.

Offering Periods. Our ESPP includes a component that allows us to make offerings intended to qualify under Section 423 of the Code and a component that allows us to make offerings not intended to qualify under Section 423 of the Code to designated companies, as described in our ESPP. Our ESPP provides for -month offering periods. The offering periods are scheduled to start on the first trading day on or after and of each year, except for the first offering period, which will commence on the first trading day on or after the effective date of the registration statement of which this prospectus forms a part and will end on the first trading day on or after . Each offering period will include purchase periods, which will be the approximately -month period commencing with one exercise date and ending with the next exercise date; provided, however, that the first exercise date under the ESPP will be the first trading day on or after .

Contributions. Our ESPP permits participants to purchase shares of our common stock through contributions (in the form of payroll deductions or otherwise to the extent permitted by the administrator) of up to % of their eligible compensation. A participant may purchase a maximum of shares of our common stock during a purchase period.

Exercise of Purchase Right. Amounts contributed and accumulated by the participant are used to purchase shares of our common stock at the end of each -month purchase period. The purchase price of the shares will be % of the lower of the fair market value of our common stock on the first trading day of each offering period or on the exercise date. If the fair market value of our common stock on the exercise date is less than the fair market value on the first trading day of the offering period, participants will be withdrawn from the current offering period following their purchase of shares of our common stock on the purchase date and will be automatically re-enrolled in a new offering period. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of our common stock. Participation ends automatically upon termination of employment with us.

Non-Transferability. A participant may not transfer rights granted under our ESPP. If our compensation committee permits the transfer of rights, it may only be done by will, the laws of descent and distribution or as otherwise provided under our ESPP.

Merger or Change in Control. Our ESPP provides that in the event of a merger or change in control, as defined under our ESPP, a successor corporation may assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute for the outstanding purchase right, the offering period then in progress will be shortened, and a new exercise date will be set that will be before the date of the proposed merger or change in control. The administrator will notify each participant that the exercise date has been changed and that the participant's option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

Amendment; Termination. The administrator has the authority to amend, suspend or terminate our ESPP, except that, subject to certain exceptions described in our ESPP, no such action may adversely affect any outstanding rights to purchase shares of our common stock under our ESPP. Our ESPP automatically will terminate in 2037, unless we terminate it sooner.

2015 Stock Incentive Plan

On April 21, 2015, our board of directors adopted and our stockholders approved our 2015 Plan. The 2015 Plan has been amended from time to time to increase the aggregate number of shares of our common stock reserved for issuance under the 2015 Plan, and was most recently amended on November 11, 2016, which amendment was approved by our stockholders on December 12, 2016. The 2015 Plan permits the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and the employees of any parent and subsidiary corporation or other entities the employees of which are eligible to receive incentive stock options under the Code, and for the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards to our employees, officers, directors, consultants and advisors or any parent or subsidiary of ours. It is expected that as of one business day prior to the effectiveness of the registration statement of the registration statement of which this prospectus forms a part, the 2015 Plan will be terminated and we will not grant any additional awards under the 2015 Plan thereafter. However, the 2015 Plan will continue to govern the terms and conditions of the outstanding awards previously granted thereunder.

Authorized Shares. The maximum aggregate number of shares issuable under the 2015 Plan was 33,300,000 shares of our common stock. As of June 30, 2017, options to purchase 23,816,215 shares of our common stock were outstanding under the 2015 Plan, 2,266,667 shares of restricted stock were outstanding under the 2015 Plan, no shares subject to stock appreciation rights were outstanding under the 2015 Plan, no restricted stock units were outstanding under the 2015 Plan and no other stock-based awards were outstanding under the 2015 Plan.

Plan Administration. Our board of directors or a committee or subcommittee delegated by our board of directors administers the 2015 Plan. Subject to the provisions of the 2015 Plan, the administrator has the authority to grant awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the 2015 Plan as it deems advisable, including to establish one or more sub-plans for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The administrator may amend or terminate any outstanding award, including substituting an award for another award of the same or a different type, changing the date of exercise or realization and converting an incentive stock option into a nonstatutory stock option, although the affected participant's consent will be required unless the administrator determines that the action does not materially adversely affect the participant's rights under the 2015 Plan, or the change is permitted under the adjustment, merger or Reorganization Event provisions of the 2015 Plan. The administrator may also amend any outstanding award granted under the 2015 Plan to provide an exercise price per share that is lower than the then-current exercise price per share of the outstanding award, and may cancel any outstanding award (whether or not granted under the 2015 Plan) and grant new, substitute

awards under the 2015 Plan covering the same or a different number of shares and having an exercise price per share that is lower than the then-current exercise price per share of the cancelled award. The administrator may correct any defect, supply any omission or reconcile any inconsistency in the 2015 Plan or award in the manner and to the extent it deems expedient to carry the 2015 Plan into effect and is the sole and final judge of such expediency. All decisions by the administrator are made in the administrator's sole discretion and are final and binding on all persons having or claiming any interest in the 2015 Plan or in any award.

Stock Options. Stock options may be granted under our 2015 Plan. The exercise price of options granted under our 2015 Plan must at least be equal to 100% of the fair market value of our common stock on the date of grant. The term of a stock option may not exceed 10 years. The administrator will determine the methods of payment of the exercise price of an option, which may include cash or check, owned shares, a broker-assisted cashless exercise, "net exercise," a promissory note, as well as other types of consideration permitted by applicable law.

If a participant's service terminates other than for cause or the participant's death or disability, the participant may exercise his or her option within at least 30 days of termination or such longer period as reflected in the individual award agreement. If a participant's service terminates due to the participant's death or disability, the participant may exercise his or her option within at least six months of termination or such longer period as reflected in the individual award agreement. However, in no event may an option be exercised later than the expiration of its term. Subject to the provisions of the 2015 Plan, the administrator determines the other terms of options.

Stock Appreciation Rights. Stock appreciation rights may be granted under our 2015 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding 10 years. After the termination of service of an employee, director or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation right agreement. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2015 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share measurement price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted Stock. Restricted stock may be granted under our 2015 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director or consultant and, subject to the provisions of our 2015 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever conditions for lapse of the restriction on the shares it determines to be appropriate. Unless otherwise provided in the applicable award agreement, any dividends declared and paid by us with respect to shares of restricted stock will be paid to the participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Shares of restricted stock as to which the restrictions have not lapsed are subject to our right of repurchase or forfeiture.

Restricted Stock Units. Restricted stock units may be granted under our 2015 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2015 Plan, the administrator will determine the terms and conditions of restricted stock units, including the vesting criteria and the form and timing of payment. The administrator, in its sole discretion, may pay earned restricted stock units in the form of

cash, in shares or in some combination thereof. Participants who receive restricted stock units have no voting rights with respect to the restricted stock units. The award agreement for restricted stock units may provide participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of our common stock, which may be settled in cash and/or shares, and may be subject to the same restrictions on transfer and forfeitability as the restricted stock units to which they relate, as may be provided in the award agreement.

Other Stock-Based Awards. Other stock based awards may be granted under our 2015 Plan. Other stock-based awards are also available as a form of payment in the settlement of other awards granted under our 2015 Plan or as payment in lieu of compensation to which a participant is otherwise entitled. Other stock-based awards may be paid in shares of our common stock or cash, as determined by the administrator. Subject to the provisions of the 2015 Plan, the administrator determines the terms and conditions of other stock-based awards granted under the 2015 Plan.

Non-Transferability of Awards. Our 2015 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her lifetime. However, awards that are not subject to Section 409A of the Code may be transferred to family members through gifts or (other than incentive stock options) domestic relations orders, or to an executor or guardian upon the death of a participant.

Certain Adjustments. In the event of certain changes in our capitalization, the administrator will adjust the number and class of shares that may be delivered under the 2015 Plan and/or the number, class, price, repurchase price and other per-share-related provisions, as applicable, of shares covered by, each outstanding award.

Merger or Reorganization Event. The 2015 Plan provides that in the event of a merger or other Reorganization Event, as defined under the 2015 Plan, each outstanding award, except restricted stock, will be treated as the administrator determines, including, without limitation, that awards shall be assumed or substituted, that, upon written notice to a participant; that awards will terminate immediately prior to the consummation of the transaction; that awards will become fully exercisable or restrictions applicable to the award will lapse in whole or in part upon the transaction; or, upon a Reorganization Event under which the holders of shares of common stock will receive a cash payment for each share surrendered in the Reorganization Event, that awards will be terminated in exchange for a cash payment equal to the number of shares subject to the award multiplied by the acquisition price minus the exercise, measurement, or purchase price of the award. In addition, in the event of a Reorganization Event that is a liquidation or dissolution, the administrator may provide that awards will be converted into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement, or purchase price thereof and applicable tax withholdings). Certain additional restrictions apply to restricted stock units to which Section 409A of the Code apply. On a Reorganization Event, our repurchase rights with respect to restricted stock will inure to the benefit of the successor and shall, unless the administrator determines otherwise, apply to the property into which the shares are converted. In the event of our proposed liquidation or dissolution, restrictions on restricted stock then outstanding will be automatically deemed satisfied.

Amendment, Termination. The administrator has the authority to amend the 2015 Plan, provided that if at any time the approval of our stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to incentive stock options, our board of directors may not effect such modification or amendment without such approval. As noted above our 2015 Plan will terminate in connection with our adoption of our 2017 Plan and no further awards will be granted thereunder. All outstanding awards will continue to be governed by their existing terms.

Executive Incentive Compensation Plan

Prior to the effectiveness of this offering, our board of directors intends to adopt our Executive Incentive Compensation Plan, or our Incentive Compensation Plan. Our Incentive Compensation Plan will allow our compensation committee to provide incentive awards, generally payable in cash, to employees selected by our compensation committee, including our named executive officers, based upon performance goals established by our compensation committee.

Under our Incentive Compensation Plan, our compensation committee determines the performance goals applicable to any award, which goals may include, without limitation, . The performance goals may differ from participant to participant and from award to award.

Our compensation committee will administer our Incentive Compensation Plan. The administrator of our Incentive Compensation Plan may, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, and/or increase, reduce or eliminate the amount allocated to the bonus pool for a particular performance period. The actual award may be below, at or above a participant's target award, in the discretion of the administrator. The administrator may determine the amount of any reduction on the basis of such factors as it deems relevant, and it is not required to establish any allocation or weighting with respect to the factors it considers.

Actual awards will be paid in cash (or its equivalent) only after they are earned, which usually requires continued employment through the date the actual award is paid. The compensation committee reserves the right to settle an actual award with a grant of an equity award under our then-current equity compensation plan, which equity award may have such terms and conditions, including vesting, as the compensation committee determines. Payment of awards occurs as soon as administratively practicable after they are earned, but no later than the dates set forth in our Incentive Compensation Plan.

Our board of directors and our compensation committee will have the authority to amend, alter, suspend or terminate our Incentive Compensation Plan, provided such action does not impair the existing rights of any participant with respect to any earned awards.

401(k) Plan

We maintain a 401(k) retirement savings plan for the benefit of our employees, including our named executive officers, who satisfy certain eligibility requirements. Under the 401(k) plan, eligible employees may elect to defer a portion of their compensation, within the limits prescribed by the Code, on a pre-tax or after-tax (Roth) basis through contributions to the 401(k) plan. The 401(k) plan authorizes employer safe harbor contributions. The 401(k) plan is intended to qualify under Sections 401(a) and 501(a) of the Code. As a tax-qualified retirement plan, pre-tax contributions to the 401(k) plan and earnings on those pre-tax contributions are not taxable to the employees until distributed from the 401(k) plan, and earnings on Roth contributions are not taxable when distributed from the 401(k) plan.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

In addition to the compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections titled “Management” and “Executive Compensation,” and the registration rights described in the section titled “Description of Capital Stock—Registration Rights,” the following is a description of each transaction since January 1, 2014 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeded or exceeds $120,000; and
- any of our directors, executive officers or holders of more than 5% of our outstanding capital stock, or any immediate family member of, or person sharing the household with, any of these individuals or entities, had or will have a direct or indirect material interest.

Sales of Securities

Common stock

From March 2015 through August 2015, we sold an aggregate of 11,263,154 shares of our common stock at a purchase price of $0.01 per share, for an aggregate purchase price of $112,632, to six accredited investors and we issued an aggregate of 13,356,172 shares of our common stock at $0.01 to $0.17 per share, with an aggregate fair market value of $376,549, to four of our directors, each an accredited investor, in exchange for services to us. The following table summarizes purchases of our common stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Common Stock	Total Purchase Price
5% Stockholders:			
AKDL, L.P.		1,250,000	$ 12,500
ARCH Venture Fund VIII, L.P.	Robert Nelsen	1,250,000	$ 12,500
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	1,250,000	$ 12,500
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (1)	Stephen Knight, M.D.; Stacie Weninger, Ph.D. (2)	7,249,996	$ 72,500
Directors and Executive Officers:			
Marc Tessier-Lavigne, Ph.D.		12,456,172	$ 367,550
Vicki Sato, Ph.D.		300,000	$ 3,000
Jay Flatley		300,000	$ 3,000
David Schenkein, M.D.		300,000	$ 3,000

(1) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(2) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series A-1 Convertible Preferred Stock

In May 2015, we issued and sold an aggregate of 39,108,223 shares of our Series A-1 convertible preferred stock at a purchase price of $1.00 per share, for aggregate proceeds of $39,108,223, to a

total of 30 accredited investors, including: ARCH Venture Fund VIII, L.P., Flagship Ventures Fund V, L.P., F-Prime Capital Partners Healthcare Fund IV L.P., Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited, AKDL, L.P., Dr. Sato, Dr. Tessier-Lavigne and The Flatley Family Trust.

In July 2015, we issued and sold an aggregate of 9,683,334 shares of our Series A-1 convertible preferred stock at a purchase price of $1.00 per share, for aggregate proceeds of $9,683,334, to a total of 11 accredited investors, including Dr. Schenkein.

In January 2016, we issued and sold an aggregate of 47,000,000 shares of our Series A-1 convertible preferred stock at a purchase price of $1.00 per share, for aggregate proceeds of $47,000,000, to a total of nine accredited investors, including: ARCH Venture Fund VIII, L.P., Flagship Ventures Fund V, L.P., F-Prime Capital Partners Healthcare Fund IV L.P., Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited, AKDL, L.P. and Steve E. Krognes.

In June 2016, we issued and sold an aggregate of 88,666,177 shares of our Series A-1 convertible preferred stock at a purchase price of $1.00 per share, for aggregate proceeds of $88,666,177, to a total of eight accredited investors. The following table summarizes purchases of our Series A-1 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series A-1 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
AKDL, L.P.		58,000,000	$ 58,000,000
ARCH Venture Fund VIII, L.P.	Robert Nelsen	40,275,000	$ 40,275,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	33,300,000	$ 33,300,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (1)	Stephen Knight, M.D.; Stacie Weninger, Ph.D. (5)	24,300,000	$ 24,300,000
Executive Officers and Directors:			
Steve E. Krognes (2)		2,000,000	$ 2,000,000
Vicki Sato, Ph.D.		250,000	$ 250,000
Jay Flatley (3)		1,000,000	$ 1,000,000
David Schenkein, M.D. (4)		1,000,000	$ 1,000,000
Marc Tessier-Lavigne, Ph.D.		100,000	$ 100,000

(1) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(2) Consists of 2,000,000 shares of Series A-1 convertible preferred stock held of record by The Steve Edward Krognes Revocable Trust, for which Mr. Krognes serves as trustee.

(3) Consists of 1,000,000 shares of Series A-1 convertible preferred stock held by The Flatley Family Trust, for which Mr. Flatley serves as trustee.

(4) Consists of (a) 464,046 shares of Series A-1 convertible preferred stock held by the David P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as trustee, (b) 35,954 shares of Series A-1 convertible preferred stock held by the David P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as trustee, (c) 464,046 shares of Series A-1 convertible preferred stock held by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust and (d) 35,954 shares of Series A-1 convertible preferred stock held by the Amy P. Schenkein 2004 Revocable Trust. Dr. Schenkein shares voting and dispositive power over the shares held by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust and the Amy P. Schenkein 2004 Revocable Trust.

(5) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series A-2 Convertible Preferred Stock

In June 2016, we issued and sold an aggregate of 17,446,133 shares of our Series A-2 convertible preferred stock at a purchase price of $2.00 per share, for aggregate proceeds of $34,892,266, to a total of 15 accredited investors. The following table summarizes purchases of our Series A-2 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series A-2 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
AKDL, L.P.		10,000,000	$ 20,000,000
ARCH Venture Fund VIII, L.P.	Robert Nelsen	1,500,000	$ 3,000,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	500,000	$ 1,000,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (1)	Stephen Knight, M.D.; Stacie Weninger, Ph.D. (2)	500,000	$ 1,000,000

(1) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are F-Prime Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).
(2) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Series B-1 Convertible Preferred Stock

In June 2016, we issued and sold an aggregate of 30,585,000 shares of our Series B-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $122,340,000, to a total of 17 accredited investors, including: ARCH Venture Fund VIII, L.P., Flagship Ventures Fund V, L.P., F-Prime Capital Partners Healthcare Fund IV L.P., Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited and AKDL, L.P.

In August 2016, we issued and sold an aggregate of 1,912,500 shares of our Series B-1 convertible preferred stock at a purchase price of $4.00 per share, for aggregate proceeds of $7,650,000, to a total of 10 accredited investors. The following table summarizes purchases of our Series B-1 convertible preferred stock by related persons:

Stockholder	Affiliated Director(s) or Officer(s)	Shares of Series B-1 Convertible Preferred Stock	Total Purchase Price
5% Stockholders:			
AKDL, L.P.		7,500,000	$30,000,000
ARCH Venture Fund VIII, L.P.	Robert Nelsen	1,250,000	$ 5,000,000
Flagship Ventures Fund V, L.P.	Douglas Cole, M.D.	625,000	$ 2,500,000
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (1)	Stephen Knight, M.D.; Stacie Weninger, Ph.D. (2)	1,250,000	$ 5,000,000
Executive Officers and Directors:			
Ryan J. Watts, Ph.D.		50,000	$ 200,000

(1) Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. holding our securities whose shares are aggregated for purposes of reporting share ownership information are F-Prime

Capital Partners Healthcare Fund IV L.P. (f/k/a Beacon Bioventures Fund IV Limited Partnership), Asia Ventures III L.P., Japan Ventures I L.P., FIL Capital Investments (Mauritius) II Limited and F-Prime Capital (f/k/a Fidelity Biosciences Corp.).

(2) Each of Drs. Knight and Weninger resigned as members of our board of directors on August 11, 2017.

Investors' Rights Agreement

We are party to an investors' rights agreement, as amended, with certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D. Under our investors' rights agreement, certain holders of our capital stock have the right to demand that we file a registration statement or request that their shares of our capital stock be covered by a registration statement that we are otherwise filing. See the section titled "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Right of First Refusal and Co-Sale Agreement

Pursuant to our equity compensation plans and certain agreements with certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Steve E. Krognes, Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D., including a right of first refusal and co-sale agreement, as amended, we or our assignees have a right to purchase shares of our common stock which stockholders propose to sell to other parties. This right will terminate upon the completion of this offering. See the section titled "Principal Stockholders" for additional information regarding beneficial ownership of our capital stock.

Voting Agreement

We are party to a voting agreement, as amended under which certain holders of our capital stock, including Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D., Steve E. Krognes, Marc Tessier-Lavigne, Ph.D., Jay Flatley, Vicki Sato, Ph.D., David Schenkein, M.D., AKDL, L.P., ARCH Venture Fund VIII, L.P., an entity affiliated with Robert Nelsen, entities associated with F-Prime Capital Partners Healthcare Fund IV L.P., and Flagship Ventures Fund V, L.P., an entity affiliated with Douglas Cole, M.D., have agreed as to the manner in which they will vote their shares of our capital stock on certain matters, including with respect to the election of directors. This agreement will terminate upon the completion of this offering, and thereafter none of our stockholders will have any special rights regarding the election or designation of members of our board of directors after the completion of this offering.

Indemnification Agreements

We have entered, and intend to continue to enter, into separate indemnification agreements with each of our directors and executive officers, in addition to the indemnification that will be provided for in our amended and restated certificate of incorporation and amended and restated bylaws. The indemnification agreements and our amended restated certificate of incorporation and amended and restated bylaws that will be in effect upon the completion of this offering require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law. See the section titled "Executive Compensation—Limitation of Liability and Indemnification" for additional information.

Related Party Transaction Policy

Our audit committee will have the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. The written charter of our audit committee will provide that our audit committee shall review and approve in advance any related party transaction.

Prior to the completion of this offering, we intend to adopt a formal written policy providing that we are not permitted to enter into any transaction that exceeds $120,000 and in which any related person has a direct or indirect material interest without the consent of our audit committee. In approving or rejecting any such transaction, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to our audit committee, including whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of August 18, 2017 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of the named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Exchange Act.

We have based our calculation of the percentage of beneficial ownership prior to this offering on 288,733,465 shares of our common stock outstanding as of August 18, 2017, which includes 234,401,367 shares of our common stock resulting from the conversion of all outstanding shares of our convertible preferred stock into our common stock immediately prior to the completion of this offering, as if this conversion had occurred as of August 18, 2017. We have based our calculation of the percentage of beneficial ownership after this offering on shares of our common stock outstanding immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares. We have deemed shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of August 18, 2017, to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Denali Therapeutics Inc., 151 Oyster Point Blvd., 2nd Floor, South San Francisco, CA 94080.

	Shares Beneficially Owned Prior to this Offering		Shares Beneficially Owned After this Offering	
Name of Beneficial Owner	**Shares**	**Percentage**	**Shares**	**Percentage**
5% Stockholders:				
Entities associated with AKDL, L.P. (1)	81,197,200	28.1%		
ARCH Venture Fund VIII, L.P. (2)	44,275,000	15.3%		
Flagship Ventures Fund V, L.P. (3)	35,675,000	12.4%		
Entities associated with F-Prime Capital Partners Healthcare Fund IV L.P. (4)	19,560,016	6.8%		
Entities associated with FIL Limited (5)	16,739,985	5.8%		
Named Executive Officers and Directors:				
Ryan J. Watts, Ph.D. (6)	11,260,555	3.9%		
Alexander O. Schuth, M.D. (7)	3,240,358	1.1%		
Steve E. Krognes (8)	4,000,000	1.4%		
Carole Ho, M.D. (9)	1,906,250	*		
Vicki Sato, Ph.D. (10)	600,000	*		
Douglas Cole, M.D. (11)	—	—		
Jay Flatley (12)	1,300,000	*		
Robert Nelsen (13)	44,275,000	15.3%		
David Schenkein, M.D. (14)	1,300,000	*		
Marc Tessier-Lavigne, Ph.D. (15)	12,556,172	4.3%		
All executive officers and directors as a group (10 persons) (16)	80,438,335	27.7%		

* Represents beneficial ownership of less than one percent (1%) of the outstanding shares of our common stock.

(1) Consists of (a) 76,750,000 shares held of record by AKDL, L.P. and (b) 4,447,200 shares held of record by Neuro Line Partners, L.P. Crestline SI (GP), L.P., or Crestline SI, is the general partner of AKDL, L.P. and Crestline Investors, Inc., or Crestline, is the general partner of Crestline SI. Bratton Capital Management, L.P. is the general partner of Neuro Line Partners, L.P. and Bratton Capital, Inc. is the general partner of Bratton Capital Management, L.P. Douglas K. Bratton, as the sole director of Crestline and Bratton Capital, Inc., has sole voting and investment control with respect to the shares held by AKDL, L.P. and Neuro Line Partners, L.P. The address of these entities is 201 Main Street, Suite 1900, Fort Worth, TX 76102.

(2) Consists of 44,275,000 shares held of record by ARCH Venture Fund VIII, L.P., or ARCH Venture Fund VIII. ARCH Venture Partners VIII, L.P., or AVP VIII LP, as the sole general partner of ARCH Venture Fund VIII, may be deemed to beneficially own certain of the shares held by ARCH Venture Fund VIII. AVP VIII LP disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII in which AVP VIII LP does not have an actual pecuniary interest. ARCH Venture Partners VIII, LLC, or AVP VIII LLC, as the sole general partner of AVP VIII LP, may be deemed to beneficially own certain of the shares held by ARCH Venture Fund VIII. AVP VIII LLC disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII in which AVP VIII LLC does not have an actual pecuniary interest. As the managing directors of AVP VIII LLC, Keith Crandell, Robert Nelsen, one of our directors, and Clinton Bybee (collectively, the Managing Directors), share voting and investment control with respect to the shares held by ARCH Venture Fund VIII. The Managing Directors disclaim beneficial ownership of all shares held by ARCH Venture Fund VIII except to the extent of any pecuniary interest therein. The address of these entities is 8755 West Higgins Road, Suite 1025, Chicago, IL 60631.

(3) Consists of 35,675,000 shares held of record by Flagship Ventures Fund V, L.P., or Flagship V. Flagship Ventures Fund V General Partner LLC, or Flagship V GP, is the general partner of Flagship V. As the manager of Flagship V GP, Noubar B. Afeyan, Ph.D. has sole voting and investment control with respect to the shares held by Flagship V. In addition, Dr. Cole, a member of our board of directors, is a member of Flagship V GP but does not have voting or investment control with respect to the shares held by Flagship V. Dr. Cole disclaims beneficial ownership of all shares held by Flagship V. The address of these entities is 55 Cambridge Parkway, Suite 800E, Cambridge, MA 02142.

(4) Consists of (a) 11,998,104 shares held of record by Impresa Fund III Limited Partnership, (b) 4,429,036 shares held of record by F-Prime Capital Partners Healthcare Fund IV LP (f/k/a Beacon Bioventures Fund IV Limited Partnership), (c) 132,871 shares held of record by F-Prime Capital Partners Healthcare Advisors Fund IV LP, and (d) 3,000,005 shares held of record by F-Prime Inc. (f/k/a Fidelity Biosciences Corp.) (collectively, the Entities associated with F-Prime Capital Partners Healthcare Fund IV LP). The general partner of F-Prime Capital Partners Healthcare Fund IV LP is F-Prime Capital Partners Healthcare Advisors Fund IV LP. F-Prime Capital Partners Healthcare Advisors Fund IV LP is solely managed by Impresa Management LLC, the general partner of its general partner and its investment manager. Impresa Management LLC is owned, directly or indirectly, by various shareholders and employees of FMR LLC. The general partner of Impresa Fund III Limited Partnership is Impresa Management LLC. F-Prime Inc. is a wholly-owned subsidiary of FMR LLC. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of these entities is 245 Summer Street, Boston, MA 02210.

(5) Consists of (a) 7,659,352 shares held of record by FIL Limited, (b) 5,842,285 shares held of record by Asia Ventures III L.P., (c) 1,606,771 shares held of record by Japan Ventures I L.P., (d) 1,601,834 shares held of record by FIL Capital Investments (Mauritius) II Limited, (e) 20,586 shares held of record by Asia Partners III LP, (f) 3,633 shares held of record by Japan Partners I LP and (g) 5,524 shares held of record by India Partners II LP (collectively, the Entities associated with FIL Limited). The general partner of Asia Ventures III L.P. is Asia Partners III LP. The general partner of Japan Ventures I L.P. is Japan Partners I LP. The general partner of Asia Partners III LP is FIL Capital Management Ltd. The general partner of Japan Partners I LP is FIL Capital Management Ltd. The general partner of India Partners II LP is FIL Capital Management Ltd. Each of the entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. The address of each of these entities except for FIL Capital Investments (Mauritius) II Limited is Pembroke Hall, 42 Crow Lange, Pembroke, Bermuda HM 19. The address of FIL Capital Investments (Mauritius) II Limited is c/o Cim Fund Services Ltd, 33 Edith Cavell Street, Port Louis, Mauritius.

(6) Consists of (a) 50,000 shares held of record by Dr. Watts and (b) 11,210,555 shares of restricted stock held of record by the Watts Family 2015 Trust dated July 7, 2015, for which Dr. Watts serves as trustee and which vest on February 23, 2019.

(7) Consists of (a) 2,740,358 shares of restricted stock held of record by Dr. Schuth, which vest on March 17, 2019 and (b) 500,000 shares subject to options exercisable within 60 days of August 15, 2017, of which none are vested as of such date.
(8) Consists of 4,000,000 shares held of record by The Steve Edward Krognes Revocable Trust, for which Mr. Krognes serves as a trustee, of which 1,083,334 shares are subject to repurchase by us at the original purchase price as of August 15, 2017.
(9) Consists of (a) 1,087,500 shares held of record by Dr. Ho, of which 618,750 shares are subject to repurchase by us at the original purchase price as of August 15, 2017, (b) 100,000 shares held of record by The Rohatgi-Ho Irrevocable GST Trust, for which Dr. Ho serves as trustee, of which 47,917 shares are subject to repurchase by us at the original purchase price as of August 15, 2017 and (c) 718,750 shares subject to options exercisable within 60 days of August 15, 2017, of which 156,250 are vested as of such date.
(10) Consists of (a) 250,000 shares held of record by Dr. Sato, (b) 300,000 shares of restricted stock held of record by Dr. Sato, which vest on April 17, 2019 and (c) 50,000 shares subject to options exercisable within 60 days of August 15, 2017, all of which have vested as of such date.
(11) Dr. Cole, a member of our board of directors, is a member of Flagship V GP but does not have voting or investment control with respect to the shares held by Flagship V. Dr. Cole disclaims beneficial ownership of all shares held by Flagship V.
(12) Consists of (a) 300,000 shares of restricted stock held of record by Mr. Flatley, which vest on April 17, 2019 and (b) 1,000,000 shares held of record by The Flatley Family Trust, for which Mr. Flatley serves as a trustee.
(13) Consists of the shares described in footnote (2) above. Mr. Nelsen is a managing director of AVP VIII LLC and shares voting and investment control with respect to these shares. Mr. Nelsen disclaims beneficial ownership of all shares held by ARCH Venture Fund VIII except to the extent of any pecuniary interest therein.
(14) Consists of (a) 300,000 shares of restricted stock held of record by Dr. Schenkein, which vest on April 17, 2019, (b) 464,046 shares held of record by the David P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as a trustee, (c) 35,954 shares held of record by the David P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as a trustee, (d) 464,046 shares held of record by the Amy P. Schenkein 2015 Denali Qualified Annuity Trust, for which Dr. Schenkein serves as a trustee and (e) 35,954 shares held of record by the Amy P. Schenkein 2004 Revocable Trust, for which Dr. Schenkein serves as a trustee.
(15) Consists of (a) 100,000 shares held of record by Dr. Tessier-Lavigne and (b) 12,456,172 shares of restricted stock held of record by Dr. Tessier-Lavigne, which vest on March 24, 2019.
(16) Consists of (a) 80,438,335 shares beneficially owned by our current executive officers and directors, of which 1,750,001 shares may be repurchased by us at the original purchase price as of such date, and (b) 1,268,750 shares subject to options exercisable within 60 days of August 18, 2017, of which 206,250 are vested as of such date.

DESCRIPTION OF CAPITAL STOCK

The following descriptions of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon completion of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the completion of this offering.

Upon the completion of this offering and the filing of our amended and restated certificate of incorporation to be effective upon completion of this offering, our authorized capital stock will consist of shares of capital stock, par value $0.01 per share, of which:

- shares are designated as common stock; and
- shares are designated as preferred stock.

Assuming the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock, which will occur upon the completion of this offering, as of June 30, 2017 there are 288,674,403 shares of our common stock outstanding held by 210 stockholders of record, and no shares of our preferred stock outstanding. Our board of directors is authorized, without stockholder approval except as required by the listing standard of the , to issue additional shares of our capital stock.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our certificate of incorporation and bylaws to be in effect upon the completion of this offering do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred Stock

Upon the closing of this offering, our board of directors will have the authority, without further action by the stockholders, to issue up to shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing change in our control or other corporate action. Upon closing of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of June 30, 2017, we had outstanding options to purchase an aggregate of 23,816,215 shares of our common stock, with a weighted-average exercise price of approximately $0.6533 per share, under our 2015 Plan. After June 30, 2017, we issued options to purchase an aggregate of 1,320,000 shares of our common stock, with a weighted-average exercise price of $2.40 per share, under our 2015 Plan.

Registration Rights

After the completion of this offering, under our investors' rights agreement, as amended, the holders of approximately shares of common stock or their transferees, have the right to require us to register the offer and sale of their shares, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

After the completion of this offering, the holders of up to shares of our common stock will be entitled to certain demand registration rights. At any time beginning 180 days after the effective date of this offering, holders of at least a majority of the shares having registration rights then outstanding can request that we file a registration statement to register the offer and sale of their shares. We are obligated to effect only two such registrations. Each such request for registration must cover securities the anticipated aggregate public offering price of which, before payment of underwriting discounts and commissions, is at least $10 million. These demand registration rights are subject to specified

conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. If we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any 12-month period, for a period of up to 60 days.

Form S-3 Registration Rights

After the completion of this offering, the holders of up to shares of our common stock will be entitled to certain Form S-3 registration rights. At any time we are eligible to file a registration statement on Form S-3, at least twenty percent of the shares having these rights then outstanding can request that we register the offer and sale of their shares of our common stock on a registration statement on Form S-3 so long as the request covers securities the anticipated aggregate public offering price of which, before payment of underwriting discounts and commissions, is at least $5 million. These stockholders may make an unlimited number of requests for registration on a registration statement on Form S-3. However, we will not be required to effect a registration on Form S-3 if we have effected two such registrations within the 12-month period preceding the date of the request. Additionally, if we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any 12-month period, for a period of up to 60 days.

Piggyback Registration Rights

After the completion of this offering, the holders of up to shares of our common stock will be entitled to certain "piggyback" registration rights. If we propose to register the offer and sale of shares of our common stock under the Securities Act, all holders of these shares then outstanding can request that we include their shares in such registration, subject to certain marketing and other limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (1) a registration related to any employee benefit plan or a corporate reorganization or other transaction covered by Rule 145 promulgated under the Securities Act, (2) a registration in which the only stock being registered is common stock issuable upon conversion of debt securities also being registered or (3) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of our common stock, the holders of these shares are entitled to notice of the registration and have the right, subject to certain limitations, to include their shares in the registration.

Expenses of Registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations and piggyback registrations, subject to specified exceptions.

Termination

The registration rights terminate upon the earliest of (1) the date that is five years after the closing of this offering, (2) as to a given holder of registration rights, when such holder of registration rights can sell all of such holder's registrable securities in a three-month period pursuant to Rule 144 promulgated under the Securities Act and (3) the closing of a deemed liquidation event.

Anti-Takeover Effects of Certain Provisions of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated Bylaws

Certain provisions of Delaware law and certain provisions that will be included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be

deemed to have an anti-takeover effect and may delay, deter, or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

Preferred Stock

Our amended and restated certificate of incorporation will contain provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series, and the powers, preferences or relative, participation, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series.

Classified Board of Directors

Our amended and restated certificate of incorporation will provide that our board of directors is divided into three classes, designated Class I, Class II, and Class III. Each class will be an equal number of directors, as nearly as possible, consisting of one-third of the total number of directors constituting our entire board of directors. The term of initial Class I directors shall terminate on the date of the 2018 annual meeting, the term of the initial Class II directors shall terminate on the date of the 2019 annual meeting, and the term of the initial Class III directors shall terminate on the date of the 2020 annual meeting. At each annual meeting of stockholders beginning in 2018, successors to the class of directors whose term expires at that annual meeting will be elected for a three-year term.

Removal of Directors

Our amended and restated certificate of incorporation will provide that stockholders may only remove a director for cause by a vote of no less than a majority of the shares present in person or by proxy at the meeting and entitled to vote.

Director Vacancies

Our amended and restated certificate of incorporation will authorize only our board of directors to fill vacant directorships.

No Cumulative Voting

Our amended and restated certificate of incorporation will provide that stockholders do not have the right to cumulate votes in the election of directors.

Special Meetings of Stockholders

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that, except as otherwise required by law, special meetings of the stockholders may be called only by an officer at the request of a majority of our board of directors, by the chairperson of our board of directors, or by our Chief Executive Officer.

Advance Notice Procedures for Director Nominations

Our bylaws will provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be timely, a stockholder’s notice generally will have to be delivered to and received at our principal

executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although the amended and restated bylaws will not give our board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the DGCL. Our amended and restated bylaws may be adopted, amended, altered, or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of the above provisions, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation will provide that our bylaws may be amended, altered, or repealed by our board of directors.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of the , and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Jurisdiction

Our amended and restated bylaws will provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim arising pursuant to the DGCL, any action regarding our amended and restated certificate of incorporation or our amended and restated bylaws or any action asserting a claim against us that is governed by the internal affairs doctrine. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

Business Combinations with Interested Stockholders

Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an “interested stockholder” (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of

such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (A) by persons who are directors and also officers of such corporation and (B) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Our amended and restated certificate of incorporation and our amended and restated bylaws will provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to carry, and we intend to carry, directors' and officers' insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive directors.

The limitation on liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, your investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Listing

We expect to apply to list our common stock on under the symbol "DNLI."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is .. The transfer agent and registrar's address is .

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and although we expect that our common stock will be approved for listing on , we cannot assure investors that there will be an active public market for our common stock following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of June 30, 2017 and after giving effect to the conversion of all outstanding shares of our convertible preferred stock, shares of our common stock will be outstanding, or shares of common stock if the underwriters exercise their option to purchase additional shares in full. All of the shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining outstanding shares of our common stock will be deemed "restricted securities" as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701 and no exercise of the underwriters' option to purchase additional shares, the shares of our common stock that will be deemed "restricted securities" will be available for sale in the public market following the completion of this offering as follows:

- shares will be eligible for sale on the date of this prospectus; and
- shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, beginning more than 180 days after the date of this prospectus.

Lock-Up Agreements and Market Standoff Agreements

Our officers, directors and the holders of substantially all of our capital stock and options have entered into market standoff agreements with us and have entered into or will enter into lock-up agreements with the underwriters under which they have agreed or will agree, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior consent of Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC. See the section titled "Underwriting" for additional information.

Rule 144

Rule 144, as currently in effect, generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who is not deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our capital stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 without complying with

the volume limitation, manner of sale or notice conditions of Rule 144. If such stockholder has beneficially owned the shares of our capital stock proposed to be sold for at least one year, then such person is entitled to sell such shares in reliance upon Rule 144 without complying with any of the conditions of Rule 144.

Rule 144 also provides that a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our common stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 within any three-month period beginning 90 days after the date of this prospectus a number of shares that does not exceed the greater of the following:

- 1% of the number of shares of our capital stock then outstanding, which will equal shares immediately after the completion of this offering; or
- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of our capital stock made in reliance upon Rule 144 by a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days are also subject to the current public information, manner of sale, and notice conditions of Rule 144.

Rule 701

Rule 701 generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is not deemed to have been one of our affiliates at any time during the preceding 90 days may sell such shares in reliance upon Rule 144 without complying with the current public information or holding period conditions of Rule 144. Rule 701 also provides that a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is deemed to have been one of our affiliates during the preceding 90 days may sell such shares under Rule 144 without complying with the holding period condition of Rule 144. However, all stockholders who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701.

Registration Rights

After the completion of this offering, the holders of up to shares of our common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. The registration of these shares of our common stock under the Securities Act would result in these shares becoming eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration, subject to the Rule 144 limitations applicable to affiliates. See the section titled “Description of Capital Stock—Registration Rights” for a description of these registration rights.

Registration Statement

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to equity awards outstanding or reserved for issuance under our equity compensation plans. The shares of our common stock covered by such registration statement will be eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration statement, subject to vesting restrictions, the conditions of Rule 144 applicable to affiliates and any applicable market standoff agreements and lock-up agreements. See the section titled “Executive Compensation—Employee Benefit and Stock Plans” for a description of our equity compensation plans.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock acquired in this offering by a "non-U.S. holder" (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the United States Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax rules, except to the limited extent set forth below. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- persons subject to the alternative minimum tax or the tax on net investment income;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership, entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership or other entity. A partner in a partnership or other such entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. Holder Defined

For purposes of this discussion, you are a "non-U.S. holder" if you are a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership or:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (x) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (y) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid cash dividends on our common stock, and we do not anticipate paying any dividends on our common stock following the completion of this offering. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussions below on effectively connected income and Foreign Account Tax Compliance Act, or FATCA, withholding, any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide the applicable withholding agent with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. A non-U.S. holder of shares of our common stock eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to the applicable withholding agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, such dividends are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below on backup withholding and FATCA withholding. In order to obtain this exemption, you must provide the applicable withholding

agent with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock, including any applicable tax treaties that may provide for different rules.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA withholding, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a United States real property interest by reason of our status as a “United States real property holding corporation,” or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as U.S. real property interests only if you actually (directly or indirectly) or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular graduated U.S. federal income tax rates, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax or other treaties that may provide for different rules.

Federal Estate Tax

Our common stock beneficially owned by an individual who is not a citizen or resident of the United States (as defined for U.S. federal estate tax purposes) at the time of his or her death will generally be includable in the decedent's gross estate for U.S. federal estate tax purposes. Such stock, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to you may be subject to information reporting and backup withholding at a current rate of 28% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding and information reporting may apply if the applicable withholding agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

Provisions of the Code commonly referred to as FATCA, Treasury Regulations issued thereunder and official IRS guidance generally impose a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from a sale or other disposition of our common stock, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on, and the gross proceeds from, a sale or other disposition of our common stock paid to a "non-financial foreign entity" (as specially defined under these rules), unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption.

The withholding obligations under FATCA generally apply to dividends on our common stock and under current transition rules are expected to apply to the payment of gross proceeds of a sale or other disposition of our common stock made on or after January 1, 2019. The withholding tax will apply regardless of whether the payment otherwise would be exempt from U.S. nonresident and backup withholding tax, including under the other exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Prospective investors are encouraged to consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman Sachs & Co. LLC	
Morgan Stanley & Co. LLC	
J.P. Morgan Securities LLC	
Total	

The underwriters will be committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters will have an option to buy up to an additional shares from us to cover sales by the underwriters of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

Paid by the Company	No Exercise	Full Exercise
Per Share	$	$
Total	$	$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

We, our officers, directors, and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock have agreed or will agree with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior written consent of the representatives. This agreement does not apply to any existing employee benefit plans. See the section titled "Shares Eligible for Future Sale" for a discussion of certain transfer restrictions.

Prior to the offering, there has been no public market for the shares. The initial public offering price will be negotiated among the representatives and us. Among the factors to be considered in determining the initial public offering price of the shares, in addition to prevailing market conditions, will

be our historical performance, estimates of our business potential and earnings prospects, an assessment of our management and the consideration of the above factors in relation to market valuation of companies in related businesses.

We intend to apply to list our common stock on under the symbol “DNLI.”

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A “covered short position” is a short position that is not greater than the amount of additional shares for which the underwriters’ option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. “Naked” short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it, because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on , in the over-the-counter market or otherwise.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common stock may be made at any time under the following exemptions under the Prospectus Directive:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common stock to be offered so as to enable an investor to decide to purchase our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus or any of its contents.

Canada

The common stock may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the common stock must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The common stock may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of

Hong Kong), or Companies (Winding Up and Miscellaneous Provisions) Ordinance, or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong), or Securities and Futures Ordinance, or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the common stock may not be circulated or distributed, nor may the common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore, or Regulation 32.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the common stock under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The common stock has not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The common stock may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $. We will agree to reimburse the underwriters for expenses related to any applicable state securities filings and to the Financial Industry Regulatory Authority incurred by them in connection with this offering in an amount up to $.

We will agree to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Menlo Park, California, is acting as counsel for the underwriters.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2016 and 2015, and for each of the two years in the period ended December 31, 2016, as set forth in their report. We have included our consolidated financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. You may obtain copies of this information by mail from the Public Reference Section of the SEC, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates or view them online. You may obtain information on the operation of the public reference rooms by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains the registration statement of which this prospectus forms a part, as well as the exhibits thereto. These documents, along with future reports, proxy statements and other information about us, are available at the SEC's website, www.sec.gov.

As a result of this offering, we will become subject to the information and reporting requirements of the Exchange Act, as amended, and, in accordance with this law, will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference facilities and the website of the SEC referred to above. We also maintain a website at www.denalitherapeutics.com. Upon the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

DENALI THERAPEUTICS INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Denali Therapeutics Inc.

We have audited the accompanying consolidated balance sheets of Denali Therapeutics Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' (deficit) and cash flows for each of the two years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States) and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Denali Therapeutics Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California
September 8, 2017

Denali Therapeutics Inc.

Consolidated Balance Sheets
(In thousands, except share amounts)

	December 31,		Pro Forma Stockholders' Equity as of December 31,
	2015	2016	2016
			(Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 30,740	$ 39,853	
Short-term marketable securities	—	138,478	
Prepaid expenses and other current assets	2,691	3,624	
Total current assets	33,431	181,955	
Long-term marketable securities	—	72,580	
Property and equipment, net	3,168	15,262	
Other non-current assets	84	1,270	
Total assets	$ 36,683	$ 271,067	
Liabilities, convertible preferred stock and stockholders' equity (deficit)			
Current liabilities:			
Accounts payable	$ 1,713	$ 1,963	
Accrued liabilities	603	3,850	
Accrued compensation	1,017	2,592	
Deferred rent and other current liabilities	148	701	
Total current liabilities	3,481	9,106	
Deferred rent	18	7,045	
Other non-current liabilities	510	397	
Total liabilities	4,009	16,548	
Commitments and contingencies (Note 7)			
Convertible preferred stock, $0.01 par value; 244,113,867 and 253,153,867 shares authorized as of December 31, 2015 and 2016, respectively; 48,791,557 and 234,401,367 shares issued and outstanding as of December 31, 2015 and 2016, respectively; aggregate liquidation preference of $51,131 and $370,071 as of December 31, 2015 and 2016, respectively; no shares issued and outstanding, pro forma (unaudited)	48,308	348,673	$ —
Stockholders' equity (deficit):			
Common stock, $0.01 par value; 318,109,451 and 334,349,451 shares authorized as of December 31, 2015 and 2016, respectively; 17,042,259 and 34,389,501 shares issued and outstanding, as of December 31, 2015 and 2016, respectively; 268,790,868 shares issued and outstanding, pro forma (unaudited)	170	344	2,688
Additional paid-in capital	1,056	9,387	355,716
Accumulated other comprehensive loss	—	(373)	(373)
Accumulated deficit	(16,860)	(103,512)	(103,512)
Total stockholders' equity (deficit)	(15,634)	(94,154)	254,519
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 36,683	$ 271,067	$ 271,067

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year ended December 31,	
	2015	2016
Operating expenses:		
Research and development	$ 11,571	$ 75,702
General and administrative	5,108	11,731
Total operating expenses	16,679	87,433
Loss from operations	(16,679)	(87,433)
Interest income (expense), net	(109)	781
Net loss	(16,788)	(86,652)
Other comprehensive loss:		
Net unrealized loss on marketable securities, net of tax	—	(373)
Comprehensive loss	$ (16,788)	$ (87,025)
Net loss per share, basic and diluted	$ (1.40)	$ (3.37)
Weighted average number of shares outstanding, basic and diluted	12,025,514	25,698,880
Pro forma net loss per share, basic and diluted (unaudited)		$ (0.44)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted (unaudited)		195,696,975

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2014	—	$ —	3,549,302	$ 35	$ —	$ —	$ (70)	$ (35)
Issuance of common stock	—	—	11,263,154	113	(1)	—	(2)	110
Issuance of common stock as consideration in asset acquisition	—	—	1,891,775	19	581	—	—	600
Issuance of series A-1 convertible preferred stock, net of issuance costs of $484	48,791,557	48,308	—	—	—	—	—	—
Vesting of restricted stock awards	—	—	338,028	3	(3)	—	—	—
Stock-based compensation	—	—	—	—	479	—	—	479
Net loss	—	—	—	—	—	—	(16,788)	(16,788)
Balance at December 31, 2015	**48,791,557**	**48,308**	**17,042,259**	**170**	**1,056**	**—**	**(16,860)**	**(15,634)**
Issuance of series A-1 convertible preferred stock, net of issuance costs of $23	135,666,177	135,643	—	—	—	—	—	—
Issuance of series A-2 convertible preferred stock, net of issuance costs of $7	17,446,133	34,885	—	—	—	—	—	—
Issuance of series B-1 convertible preferred stock, net of issuance costs of $153	32,497,500	129,837	—	—	—	—	—	—
Issuance of common stock as contingent consideration in asset acquisition	—	—	3,783,555	38	5,242	—	—	5,280
Issuance of common stock upon exercise of stock options	—	—	650,679	6	105	—	—	111
Vesting of early exercised common stock	—	—	958,330	10	153	—	—	163
Vesting of restricted stock awards	—	—	11,954,678	120	(120)	—	—	—
Stock-based compensation	—	—	—	—	2,951	—	—	2,951
Net loss	—	—	—	—	—	—	(86,652)	(86,652)
Other comprehensive loss	—	—	—	—	—	(373)	—	(373)
Balance at December 31, 2016	**234,401,367**	**$348,673**	**34,389,501**	**$ 344**	**$ 9,387**	**$ (373)**	**$ (103,512)**	**$ (94,154)**

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year ended December 31,	
	2015	2016
Operating activities		
Net loss	$ (16,788)	$ (86,652)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	121	1,469
Stock-based compensation expense	479	2,951
Non-cash interest expense	110	—
Net amortization of premiums and discounts on marketable securities	—	304
Loss on disposal of fixed asset	—	3
Fair value of common stock issued in connection with asset acquisition	600	5,280
Changes in operating assets and liabilities:		
Restricted cash	(84)	(451)
Prepaid expenses and other assets	(2,691)	(533)
Accounts payable	1,678	161
Accrued and other current liabilities	1,607	5,357
Other non-current liabilities	(84)	(248)
Net cash used in operating activities	(15,052)	(72,359)
Investing activities		
Purchase of marketable securities	—	(226,370)
Purchase of property and equipment	(3,062)	(6,134)
Purchase of other investments	—	(500)
Maturities and sales of marketable securities	—	14,000
Net cash used in investing activities	(3,062)	(219,004)
Financing activities		
Proceeds from convertible promissory note received from a related party	5,000	—
Proceeds from exercise of common stock options	510	111
Proceeds from issuance of common stock	110	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	43,234	300,365
Net cash provided by financing activities	48,854	300,476
Net increase in cash and cash equivalents	30,740	9,113
Cash and cash equivalents at beginning of year	—	30,740
Cash and cash equivalents at end of year	$ 30,740	$ 39,853
Supplemental disclosures of cash flow information		
Convertible preferred stock issuance costs incurred but not yet paid	$ 36	$ —
Property and equipment purchases accrued but not yet paid	$ 126	$ 233
Conversion of convertible promissory note and interest into convertible preferred stock	$ 5,110	$ —

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

1. Significant Accounting Policies

Organization and Description of Business

Denali Therapeutics Inc. ("Denali" or the "Company") is a biopharmaceutical company, incorporated in Delaware, that discovers and develops therapeutics to defeat degeneration. The Company was incorporated in October 2013 as SPR Pharma Inc. The Company's name was changed to Denali Therapeutics Inc. in March 2015. The Company is headquartered in South San Francisco, California.

Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Principles of Consolidation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. This subsidiary was dissolved in September 2016. All intercompany balances and transactions have been eliminated on consolidation.

The Company assesses whether it is the primary beneficiary of a variable interest entity ("VIE") at the inception of the arrangement and at each reporting date. This assessment is based on the Company's power to direct the activities of the VIE that most significantly impact the VIE's economic performance and the Company's obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Unaudited Pro Forma Information

Immediately prior to the completion of this offering, all outstanding shares of convertible preferred stock will automatically convert into common stock. Unaudited pro forma balance sheet information as of December 31, 2016 assumes the conversion of all outstanding convertible preferred stock into shares of common stock. The shares of common stock issuable and the proceeds expected to be received in the initial public offering are excluded from such pro forma financial information. Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The unaudited pro forma net loss per share for the year ended December 31, 2016 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates, judgments, and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported amounts of expenses during the reporting period. Actual results could differ from those estimates, and such differences could be material to the consolidated financial position and results of operations.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. Substantially all of the Company's cash and cash equivalents are deposited in accounts with three financial institutions that management believes are of high credit quality. Such deposits have and will continue to exceed federally insured limits. The Company maintains its cash with accredited financial institutions and accordingly, such funds are subject to minimal credit risk. The Company has not experienced any losses on its cash deposits.

The Company's investment policy limits investments to certain types of securities issued by the U.S. government, its agencies and institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. The Company is exposed to credit risk in the event of a default by the financial institutions holding its cash, cash equivalents and marketable securities and issuers of marketable securities to the extent recorded on the consolidated balance sheets. As of December 31, 2016, the Company has no off-balance sheet concentrations of credit risk.

The Company is subject to a number of risks similar to other early-stage biopharmaceutical companies, including, but not limited to, the need to obtain adequate additional funding, possible failure of current or future preclinical testing or clinical trials, its reliance on third parties to conduct its clinical trials, the need to obtain regulatory and marketing approvals for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of the Company's product candidates, its right to develop and commercialize its product candidates pursuant to the terms and conditions of the licenses granted to the Company, protection of proprietary technology, the ability to make milestone, royalty or other payments due under any license or collaboration agreements, and the need to secure and maintain adequate manufacturing arrangements with third parties. If the Company does not successfully commercialize or partner any of its product candidates, it will be unable to generate product revenue or achieve profitability.

Need for Additional Capital

Since inception, the Company has incurred net losses and negative cash flows from operations. During the year ended December 31, 2016, the Company incurred a net loss of $86.7 million and used $72.4 million of cash in operations. At December 31, 2016, the Company had an accumulated deficit of $103.5 million and does not expect to experience positive cash flows in the foreseeable future. The Company has financed its operations to date primarily through the sale and issuance of convertible preferred stock. Management expects to incur additional operating losses in the future as the Company continues the development of, and seeks regulatory approvals for, its product candidates, and begins to commercialize any approved products, and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through public or private equity financings, strategic alliances with third parties and potentially through debt financings. The Company had $250.9 million of cash, cash equivalents and marketable securities at December 31, 2016. Based on the Company's business plans, management believes that this is sufficient to meet its obligations for at least the next twelve months from the issuance date of these consolidated financial statements.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Fair Value of Financial Instruments

ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

Level 1 – inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 – inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 – inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities approximate their fair values, due to their short-term nature.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash and cash equivalents. Cash equivalents, which consist primarily of highly liquid investments with maturities of three months or less when purchased, are stated at fair value.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents, short-term marketable securities, or long-term marketable securities on the balance sheets, are considered available-for-sale, and reported at fair value with unrealized gains and losses included as a component of stockholders' deficit. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income

(expense), net on the consolidated statements of operations. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on marketable securities are included in interest income (expense), net. The cost of securities sold is determined using specific identification.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and management's strategy and intentions for holding the marketable security.

Restricted Cash

The Company's restricted cash consists of restricted cash in connection with the building leases for the Company's former and current headquarters. The current portion of $0.1 million is classified within prepaid expenses and other current assets and the non-current portion of $0.5 million is classified within other non-current assets on the accompanying consolidated balance sheets.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the related estimated useful lives as presented in the table below. Significant additions and improvements are capitalized, while repairs and maintenance are charged to expense as incurred.

Leasehold improvements	Shorter of life of asset or lease term
Manufacturing and laboratory equipment	5 years
Computer hardware and software	3 years
Office furniture and equipment	5 years

Impairment of Long-Lived Assets

The Company periodically evaluates property and equipment for impairment whenever events or changes in circumstances indicate that a potential impairment may have occurred. If such events or changes in circumstances arise, the Company compares the carrying amount of the long-lived assets to the estimated future undiscounted cash flows expected to be generated by the long-lived assets. If the estimated aggregate undiscounted cash flows are less than the carrying amount of the long-lived assets, an impairment charge, calculated as the amount by which the carrying amount of the assets exceeds the fair value of the assets, is recorded. The fair value of the long-lived assets is determined based on the estimated discounted cash flows expected to be generated from the long-lived assets. The Company has not recorded any such impairment charges during the years presented.

Deferred Rent

Certain of the Company's operating lease agreements include scheduled rent escalations over the lease term, as well as tenant improvement allowances. Rent expense is charged ratably over the life of

the lease. Deferred rent consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the buildings the Company occupies. Tenant improvement allowances are recorded as a deferred rent liability and are amortized on a straight-line basis over the term of the lease as a reduction to rent expense.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of salaries and other personnel related expenses, including associated stock-based compensation, consulting fees, lab supplies, and facility costs, as well as fees paid to other entities that conduct certain research, development and manufacturing activities on behalf of the Company.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects.

Stock-Based Compensation

The Company measures employee and director stock-based compensation expense for all stock-based awards at the grant date based on the fair value measurement of the award. The expense is recorded on a straight-line basis over the requisite service period, which is generally the vesting period, for the entire award. Expense is adjusted for actual forfeitures of unvested awards as they occur. The Company calculates the fair value measurement of stock options using the Black-Scholes valuation model.

The Company granted restricted stock awards that vest in conjunction with certain performance and market conditions to certain key employees and directors. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

The Company accounts for stock options issued to non-employees in accordance with the provisions of ASC 505-50, Equity-Based Payments to Non-employees, which requires valuing the stock options on their grant date and remeasuring such stock options at the current fair value at the end of each reporting period until they vest.

Income Taxes

Income taxes are accounted for using the liability method, under which deferred tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities and consideration is given to net operating losses and tax credit carryforwards. Deferred tax assets and liabilities are measured using the enacted tax rates that are expected to be in effect when the differences are expected to reverse.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

The Company assesses the likelihood that deferred tax assets will be recovered from future taxable income, and a valuation allowance is established when necessary to reduce deferred tax assets to the amounts more likely than not expected to be realized.

The Company recognizes and measures uncertain tax positions using a two–step approach. The first step is to evaluate the tax position taken or expected to be taken by determining whether the weight of available evidence indicates that it is more likely than not that the tax position will be sustained in an audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. Significant judgment is required to evaluate uncertain tax positions. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss, primarily unrealized losses on the Company's marketable securities.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-09 ("ASU 2014-09"), Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12 ("ASU 2016-12"), which amends the existing accounting standards for revenue recognition. ASU 2014-09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non-public entities. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While the Company continues to assess all potential impacts under ASU 2014-09, it does not believe adopting the new revenue standard will have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB issued ASU No. 2016-02 ("ASU 2016-02"), Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance

for operating leases today. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. The ASU is expected to impact the Company's consolidated financial statements as the Company has certain operating lease arrangements for which the Company is the lessee. Management is currently evaluating the impact the adoption of ASU 2016-02 will have on the Company's financial position and results of operations. Management expects that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on the Company's balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the balance sheet presentation is expected to change, management does not expect a material change to the consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to have a significant impact.

2. Fair Value Measurements

Assets measured at fair value as of December 31, 2016 are as follows (in thousands):

	Fair Value Measurements			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$28,705	$ —	$ —	$ 28,705
Short-term:				
U.S. government treasuries	22,268	—	—	22,268
U.S. government agency securities	—	70,787	—	70,787
Corporate debt securities	—	38,941	—	38,941
Commercial paper	—	6,482	—	6,482
Long-term:				
U.S. government treasuries	4,989	—	—	4,989
U.S. government agency securities	—	52,868	—	52,868
Corporate debt securities	—	14,723	—	14,723
Total marketable securities	27,257	183,801	—	211,058
Total fair value measurements	**$55,962**	**$183,801**	**$ —**	**$239,763**

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

The carrying amounts of accounts payable and accrued liabilities approximate their fair values due to their short-term maturities.

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly.

There were no transfers of assets or liabilities between the fair value measurement levels during the year ended December 31, 2016.

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2016. The amortized cost, unrealized holding gains or losses, and fair value of the Company's marketable securities by major security type at December 31, 2016 are summarized in the table below (in thousands):

	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value at December 31, 2016
Short-term marketable securities:				
U.S. government treasuries	$ 22,277	$ —	$ (9)	$ 22,268
U.S. government agency securities	70,835	—	(48)	70,787
Corporate debt securities	39,037	—	(96)	38,941
Commercial paper	6,482	—	—	6,482
Total short-term marketable securities	138,631	—	(153)	138,478
Long-term marketable securities:				
U.S. government treasuries	4,996	1	(8)	4,989
U.S. government agency securities	53,005	—	(137)	52,868
Corporate debt securities	14,799	—	(76)	14,723
Total long-term marketable securities	72,800	1	(221)	72,580
Total	**$ 211,431**	**$ 1**	**$ (374)**	**$ 211,058**

As of December 31, 2016, some of the Company's marketable securities were in an unrealized loss position. The Company determined that it did have the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2016. All marketable securities with unrealized losses as of December 31, 2016 have been in a loss position for less than twelve months or the loss is not material.

All of the Company's short-term marketable securities have an effective maturity date of less than one year, and all of the Company's long-term marketable securities have an effective maturity of less than two years.

4. Acquisition

In June 2015, the Company acquired Incro Pharmaceuticals Corporation ("Incro"), a preclinical private biotechnology company incorporated in Delaware. The primary asset purchased in the

acquisition was an in-process research and development license agreement which would allow the Company to further its RIPK1 program. The Company concluded that the assets acquired and liabilities assumed did not meet the accounting definition of a business as a limited number of inputs were acquired but no processes were acquired, and the licensed technology had not achieved technological feasibility. As such, the acquisition was accounted for as an asset purchase and the Company recorded the purchase price as $1.5 million in research and development expense in the accompanying statement of operations and comprehensive loss in the year ended December 31, 2015.

As purchase consideration the Company issued an aggregate of 1,891,775 shares of common stock, valued at $0.6 million on the transaction date, to the former Incro stockholders, and recognized within additional paid-in capital an obligation to issue an additional 108,219 shares of common stock, valued at $32,466, to one former Incro stockholder. The deemed fair value (see Note 10) of the Company's common stock was $0.30 per common share as of the date of the transaction. In addition to the issuance of this equity, the Company assumed liabilities of $0.9 million.

The Company also agreed to issue an additional 3,783,555 shares of common stock to the former Incro stockholders, and to recognize an obligation to issue 216,439 shares of common stock to one former Incro shareholder ("Milestone Shares"), upon acceptance of an investigational new drug ("IND") application by the U.S. Food and Drug Administration or an equivalent in the EU, Canada, Australia, or New Zealand within six years of the date of the acquisition. Of these shares, 1,400,000 shares of common stock ("Indemnification Shares") were to be held in escrow by Denali, and would be released to former stockholders of Incro within 30 days of the later of (i) expiration of 18 months after the closing; and (ii) the date the Milestone Shares vest as noted above. The number of Indemnification Shares to be released to Incro's stockholders were to be reduced to the extent of breaches of standard representations by Incro's stockholders. As this transaction was accounted for as an asset purchase rather than a business combination, no amounts were recognized relating to the contingent consideration.

In August 2016, the Company filed a Clinical Trial Application ("CTA") in Europe to initiate a Phase 1 clinical trial. Upon acceptance of the CTA in September 2016, the issuance of the Milestone Shares was triggered. The Company issued a total of 2,383,555 shares of common stock, recognized an obligation to issue 216,439 shares of common stock, and recorded a liability for the 1,400,000 Indemnification Shares held in escrow. The Company recognized $5.3 million of research and development expense related to the estimated fair value of these shares of $1.32 per share during the year ended December 31, 2016. In December 2016, the 1,400,000 Indemnification Shares were released and issued and the related liability was extinguished upon the expiration of the 18-month period after the closing of the acquisition.

5. License and Collaboration Agreements

F-star

On August 24, 2016, the Company entered into a License and Collaboration Agreement ("Collaboration Agreement") with F-star Gamma Limited ("F-star Gamma"), F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology Limited (collectively, "F-star"). The goal of the collaboration is the development of certain constant Fc-domains of an antibody with non-native antigen binding activity ("Fcabs"), to enhance delivery of therapeutics across the blood-brain barrier ("BBB") into the brain. The collaboration leverages F-star's modular antibody technology and the Company's expertise in the development of therapies for neurodegenerative diseases.

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Under the terms of the Collaboration Agreement, the Company can nominate up to three Fcab targets ("Accepted Fcab Targets"), within the first three years of the date of the Collaboration Agreement; and the Company has selected transferrin receptor ("TfR") as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, the Company can nominate up to eight Fab targets ("Accepted Fab Targets"), which are targets bound by the variable domains of an antibody or other therapeutic modalities ("Fabs"). For each accepted Fcab target, the Company is obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans. Under the terms of the Collaboration Agreement, the Company received non-exclusive licenses under certain intellectual property to conduct technology development to discover and develop Fcabs. The Company is obligated to assign to F-star certain patents and know-how that the Company generates under the Collaboration Agreement related to F-star's platform technology or certain Fcabs identified solely by F-star and the Company received a non-exclusive license under certain of F-star Biotechnology's platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the BBB, subject to certain specified restrictions. F-star retains the right to use its intellectual property, including any intellectual property that the Company and F-star jointly own pursuant to the terms of the Collaboration Agreement, outside the scope of the licenses granted to the Company.

Under the terms of the Collaboration Agreement, the Company paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target. The Company is obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target the Company selects, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. The Company is also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Either party may terminate the agreement if the other party materially breaches the agreement, subject to specified notice and cure provisions, or for the other party's bankruptcy or insolvency. In addition, F-star Gamma may terminate the agreement if the Company challenges any of the patent rights licensed to it by F-star. The Company is able to terminate the agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days' prior written notice to F-star. Unless earlier terminated, the agreement with F-star will remain in effect until all royalty and milestone payment obligations to F-star Gamma expire.

In connection with the entry into the Collaboration Agreement, the Company also purchased an option for an upfront option fee of $0.5 million (the "buy-out-option"), to acquire all of the outstanding shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement (the "Option Agreement"). The Company must elect whether to exercise its buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by the Company of a notice that it is progressing an Fcab identified from the Company's library that binds to an Accepted Fcab Target. If the Company exercises this buy-out option, it will be obligated to make inital exercise payments ranging from $18.0 million to $50.0 million plus the estimated net cash held by F-star Gamma at the time of such exercise. In addition, it will be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones,

up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by the Company or solely by F-star or jointly by the Company and F-star and the timing of the Company's exercise of the buy-out option. Following exercise of the buy-out option, the Company will not be required to make any further milestone or royalty payments under the Collaboration Agreement. If the Company exercises the buy-out option, then F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology will continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action. If the Company does not exercise its option to acquire F-star Gamma prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until the Company's rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target.

If the Company does not exercise the buy-out option, then with respect to each Accepted Fab Target, the Company has the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that the Company or F-star identifies, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target. Each time the Company exercises such license option, it will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to the Company an Fcab that meets pre-defined criteria. The Company has the right to credit a certain amount of royalty payments that it pays to third parties with respect to certain licensed products against the Company's royalty obligation to F-star Gamma, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country.

The Company recognized the upfront option fee of $0.5 million within other non-current assets recorded at cost. This asset will be assessed for potential impairment on an ongoing basis. No impairment charge was recognized during the year ended December 31, 2016.

The Company determined that F-star Gamma is and continues to be a variable interest entity and that the Company holds a variable interest in F-star Gamma's intellectual property assets and the related potential future product candidates these assets may produce through the Collaboration Agreement and the Option Agreement. However, the Company concluded that its governance role in the collaboration, which is specified by the terms of a joint steering committee, does not provide the Company the power to direct the activities of F-star Gamma that most significantly impact F-star Gamma's economic performance. Based on this conclusion, the Company is not considered to be the

primary beneficiary of F-star Gamma; and therefore F-star Gamma is not subject to consolidation by the Company.

The Company recognized the entirety of the $5.5 million upfront license fee in research and development expense for the year ended December 31, 2016. The Company recognized an additional $0.3 million of research and development expense related to the funding of F-star Gamma research costs during the year ended December 31, 2016.

The $0.5 million other non-current asset is the only asset or liability recorded in the Company's consolidated balance sheet that relates to the Company's variable interest in F-star Gamma at December 31, 2016. The upfront payments of $0.5 million and $5.5 million and the obligation to fund certain future research costs, represent the Company's maximum exposure to loss under the arrangements with F-star.

Genentech

On June 17, 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. ("Genentech"). The agreement gives the Company access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress the Company's in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted the Company (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. The Company is obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

As consideration, the Company paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million, both of which are included in research and development expense for the year ended December 31, 2016 as there is no alternative future use of the rights acquired in other research and development projects.

The Company may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by the Company, (ii) the date a compound was first discovered, derived or optimized by the Company, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. The Company also has the right to credit a certain amount of third-party royalty and milestone payments against royalty and milestone payments owed to Genentech, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country and (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country.

Genentech may terminate the agreement if the Company challenges any of the patent rights licensed to the Company by Genentech, or if the Company materially breaches the agreement, subject

to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for the Company's material breach, bankruptcy or insolvency after the Company has made a milestone payment to Genentech, then the Company is obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of the Company's patents, know-how and regulatory filings directed to Genentech-provided compounds. The Company does not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

Unless earlier terminated, the agreement with Genentech will continue in effect until all of the Company's royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, the Company will retain the licenses under the intellectual property Genentech licensed to the Company on a non-exclusive, royalty-free basis.

6. Balance Sheet Components:

Property and Equipment, Net

	December 31,	
	2015	2016
	(in thousands)	
Lab equipment	$3,034	$ 8,868
Leasehold improvements	101	7,543
Computers equipment and purchased software	146	373
Furniture and fixtures	8	66
	3,289	16,850
Less: accumulated depreciation	(121)	(1,588)
Total property and equipment, net	$3,168	$15,262

Depreciation expense was $0.1 million and $1.5 million for the years ended December 31, 2015 and 2016, respectively.

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Prepaid Expenses and Other Current Assets

	December 31,	
	2015	2016
	(in thousands)	
Prepaid research and development expenses	$1,652	$2,396
Accrued interest on short-term marketable securities	—	438
Prepaid employee bonuses	973	234
Other prepaid and current assets	66	556
Total prepaid expenses and other current assets	$2,691	$3,624

Other Non-Current Assets

	December 31,	
	2015	2016
	(in thousands)	
Other investments	$—	$ 500
Restricted cash	84	451
Other prepaid and non-current assets	—	319
Total other non-current assets	$ 84	$1,270

Deferred Rent and Other Current Liabilities

	December 31,	
	2015	2016
	(in thousands)	
Current portion of deferred rent liability	$ —	$538
Other current liabilities	148	163
Total deferred rent and other current liabilities	$148	$701

7. Commitments and Contingencies

Lease Obligations

In September 2015, the Company entered into a non-cancelable operating lease for its corporate headquarters comprising 38,109 of rentable square feet in a building in South San Francisco (“Headquarters Lease”). The Headquarters Lease commenced on August 1, 2016 with a lease term of eight years. The Company has an option to extend the lease term for a period of five years by giving the landlord written notice of the election to exercise the option at least nine months, but not more than twelve months, prior to the original expiration of the lease term. The Headquarters Lease provides for monthly base rent amounts escalating over the term of the lease. In addition, the Headquarters Lease provides both a tenant improvement allowance (“TIA”) of up to $7.4 million, of which $1.9 million will be repaid to the landlord in the form of additional monthly rent with interest applied. This additional monthly rent commenced in November 2016 when the entire TIA was utilized, and results in an increase of base rent of $0.4 million per year.

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The Company utilized $0.1 million and $7.3 million of the TIA in the years ended December 31, 2015 and 2016, respectively. The total $7.4 million TIA has been recorded as leasehold improvements and deferred rent liability on the consolidated balance sheet. The Company is amortizing the deferred rent liability as a reduction of rent expense and the leasehold improvement through an increase of depreciation expense of leasehold improvements ratably over the lease term. Under the terms of the Headquarters Lease, the Company was required to pay a security deposit of $0.5 million, which is recorded as other non-current assets in the accompanying consolidated balance sheets.

In May 2015, the Company entered into a non-cancelable operating lease for office and research and development space in South San Francisco that expires in December 2017 (the “First Lease”). The First Lease provides for 9,855 of rentable square feet at a base rent that increases annually. Under the terms of the First Lease, the Company was required to pay a security deposit of $0.1 million, which is recorded as prepaid expenses other current assets in the accompanying consolidated balance sheets.

On July 22, 2016, the Company entered into a sublease agreement with a third party for the entirety of the remaining term of the First Lease. The sublease commenced on August 22, 2016. The Company received sublease payments totaling $0.1 million through the year ended December 31, 2016 and expects to receive future minimum payments from this sublease of $0.4 million in 2017, which is recognized as an offset to rent expense.

The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records tenant improvement allowances as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably assured at lease inception.

Rent expense for the years ended December 31, 2015 and 2016 was $0.2 million and $1.0 million, respectively.

As of December 31, 2016, the future minimum lease payments under non–cancelable operating leases are as follows (in thousands):

Year Ended December 31:	
2017	$ 2,510
2018	2,586
2019	2,664
2020	2,745
2021 and later	10,534
	$21,039

Indemnification

In the ordinary course of business, the Company may provide indemnifications of varying scope and terms to vendors, lessors, business partners, board members, officers, and other parties with

respect to certain matters, including, but not limited to, losses arising out of breach of such agreements, services to be provided by the Company, negligence or willful misconduct of the Company, violations of law by the Company, or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with directors and certain officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. No demands have been made upon the Company to provide indemnification under such agreements, and thus, there are no claims that the Company is aware of that could have a material effect on the Company's balance sheet, statements of comprehensive loss, or statements of cash flows.

Commitments

In the normal course of business, the Company enters into various firm purchase commitments primarily related to research and development activities. As of December 31, 2016, the Company has non-cancelable purchase commitments of $1.0 million and contractual obligations under license agreements of $0.2 million. Pursuant to certain license and collaboration agreements, the Company has obligations to make future milestone and royalty payments to other third parties. However, because these amounts are contingent and not fixed or determinable, they have not been included on the Company's consolidated balance sheet.

8. Convertible Promissory Note

In January 2015, the Company entered into a convertible promissory note with a related party, a stockholder of the Company. The principal amount of the promissory note was $5.0 million at a fixed interest rate of 8.0%, which was repayable in January 2016. Interest of $0.1 million accrued on the note and was recognized within interest income (expense), net in the consolidated statement of operations and comprehensive loss in the year ended December 31, 2015.

The entire amount due, including interest, was converted into 5,109,589 shares of Series A-1 convertible preferred stock in May 2015 (see Note 9).

9. Convertible Preferred Stock and Stockholders' Deficit

Convertible Preferred Stock

The Company is authorized to and has issued two classes of stock: convertible preferred stock and common stock. Convertible preferred stock is carried at the issuance price, net of issuance costs. The carrying value of the convertible preferred stock has not been accreted up to its redemption value as no redemption events are considered probable by management.

The Company entered into a preferred stock purchase agreement ("Preferred Stock Purchase Agreement"), with certain investors on May 8, 2015 (the "Initial Closing"), under which the Company agreed to sell up to 180,895,892 shares of Series A-1 convertible preferred stock and 17,446,133 shares of Series A-2 convertible preferred stock. Additionally, at the Initial Closing, the Company concurrently issued 25,183,223 shares of Series A-1 convertible preferred stock for net proceeds of $24.8 million.

The Preferred Stock Purchase Agreement provided that, upon Board of Directors approval, each investor would purchase its pro-rata portion of the shares to be issued in one or more additional series

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A-1 closings, and in any Series A-2 closings. Further, the Company agreed to sell and issue said shares of Series A-1 convertible preferred stock on the same terms as the first tranche, and to issue said shares of Series A-2 convertible preferred stock on the terms included in the Preferred Stock Purchase Agreement. The second and third Series A-1 closings added further obligations for new investors to participate in the Series A-2 tranches. The Company did not separately account for tranche purchase rights described above as they were not freestanding from the associated shares of convertible preferred stock.

On May 20, 2015 (the "First Additional Closing") the Company and the Series A convertible preferred stock shareholders amended the Preferred Stock Purchase Agreement pursuant to which the Company agreed to sell up to an additional 1,825,000 shares of Series A-1 convertible preferred stock. Additionally, at the First Additional Closing, the Company issued 13,925,000 shares of Series A-1 convertible preferred stock for net proceeds of $13.9 million and on July 22, 2015 ("Second Additional Closing"), the Company issued an additional 9,683,334 shares of Series A-1 convertible preferred stock for net proceeds of $9.6 million.

On January 6, 2016 (the "Third Additional Closing"), the Company issued 2,000,000 shares of Series A-1 convertible preferred stock, for net proceeds of $2.0 million. On January 26, 2016 (the "first Tranche Closing"), the Company issued 45,000,000 shares of Series A-1 convertible preferred stock, for net proceeds of $45.0 million. On June 6, 2016 (the "Second Tranche Closing and Series A-2 Closing"), the Company issued 88,666,177 shares of Series A-1 convertible preferred stock and 17,446,133 shares of Series A-2 convertible preferred stock, for net proceeds of $88.7 million and $34.9 million, respectively. All of these shares were sold under the Preferred Stock Purchase Agreement.

On June 23, 2016 (the "First Series B-1 Closing"), the Company entered into a preferred stock purchase agreement ("Series B Preferred Stock Purchase Agreement") with certain investors, under which the Company sold 30,585,000 shares of Series B-1 convertible preferred stock at a price of $4.00 per share for net proceeds of $122.2 million. In connection with this financing, the Company amended and restated its certificate of incorporation to increase the authorized shares of its common stock to 327,149,451 shares and the authorized shares of its preferred stock to 253,153,867 shares, each with a par value of $0.01 per share. The authorized preferred shares consisted of 184,457,734 designated as Series A-1 convertible preferred stock, 17,446,133 designated as Series A-2 convertible preferred stock, 32,500,000 designated Series B-1 convertible preferred stock and 18,750,000 designated Series B-2 convertible preferred stock.

On August 26, 2016, (the "Second Series B-1 Closing"), the Company sold 1,912,500 shares of Series B-1 convertible preferred stock at a price of $4.00 per share for net proceeds of $7.6 million.

On December 23, 2016, upon the passing of six months from the First Series B-1 Closing, the shares authorized for Series B-2 were no longer available for issuance under the Series B Preferred Stock Purchase Agreement.

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At December 31, 2015, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	184,457,734	48,791,557	$ 1.00	$48,308	$ 51,131
Series A-2	17,446,133	—	2.00	—	—
Series B	42,210,000	—	4.00	—	—
	244,113,867	48,791,557		$48,308	$ 51,131

At December 31, 2016, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	184,457,734	184,457,734	$ 1.00	$ 183,951	$ 198,264
Series A-2	17,446,133	17,446,133	2.00	34,885	36,483
Series B-1	32,500,000	32,497,500	4.00	129,837	135,324
Series B-2	18,750,000	—	—	—	—
	253,153,867	234,401,367		$ 348,673	$ 370,071

The rights, preferences and privileges of the convertible preferred stock are as follows:

Dividend Rights

The holders of preferred stock are entitled to receive dividends, if and when declared by the Board of Directors, at the rate of $0.08 per share per annum for Series A-1, $0.16 per share per annum for Series A-2, and $0.32 per share per annum for Series B-1 from and after the date of issuance of such shares. As of December 31, 2015 and 2016, no such dividends had been declared or accrued.

Dividends on any other class of capital stock cannot be paid unless the holders of the preferred stock first receive, or simultaneously receive, the preferred stock dividend. The holders of preferred stock also participate in dividends paid on common stock as if the shares of preferred stock had been converted into shares of common stock and are considered participating securities.

Conversion Rights

The holders of preferred stock have the right to convert at any time into shares of common stock initially at a one-for-one ratio. All shares of the preferred stock shall be automatically converted into shares common stock (i) upon the consent of the holders of at least a majority of the outstanding preferred stock, or (ii) upon the closing of a firmly underwritten initial public offering of common stock at a price of at least $5.00 per share resulting in at least $50.0 million of gross proceeds. The conversion price for each series of preferred stock is subject to an adjustment in the event of stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, or reorganization.

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Liquidation Rights

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a deemed liquidation event, the holders of shares of preferred stock then outstanding are entitled to be paid out of the assets of the Company available for distribution to its stockholders, before any payment can be made to the holders of common stock, an amount per share equal to the greater of (i) the original issue price for the Series of preferred stock held plus any dividends accrued but unpaid, whether or not declared; or (ii) such amount per share as would have been paid if all shares of preferred stock had been converted to common stock immediately prior to such liquidation, dissolution, winding up or deemed liquidation event. If assets of the Company available are insufficient to pay holders of Preferred Stock the full amount they are entitled to, the holders of preferred stock will share ratably in any distribution of the assets available for distribution in proportion to the amounts due such holders. After the payment of all preferential amounts required to be paid to the holders of shares of preferred stock, the remaining assets of the Company will be distributed among the holders of the shares of common stock, pro rata based on the number of shares held by each such holder.

The Company classifies its convertible preferred stock outside of stockholders' deficit as certain change in control events are outside the Company's control.

Voting Rights

Each share of preferred stock has voting rights equal to the number of shares of common stock into which the preferred stock could be converted immediately after the close of business on the record date.

As long as certain investors in Series A convertible preferred stock hold 100,000 or more shares of convertible preferred stock purchased pursuant to the Preferred Stock Purchase Agreement, they are entitled to elect individually one member of the Board totaling five Series A Directors. Series B convertible preferred stockholders are entitled to elect one member of the Board by majority vote of the Series B convertible preferred stockholders. Together, Series A and Series B convertible preferred stock investors shall be entitled to elect two additional members of the Board that are not otherwise an affiliate of the Company or of any investor.

Redemption

Upon certain change in control events that are outside of the Company's control, including liquidation, sale or transfer of control of the Company, holders of the convertible preferred stock can cause its redemption. Shares of preferred stock must be redeemed by the Company at the original issue price for each series of preferred stock plus any dividends accrued but unpaid, whether or not declared, in three annual installments, upon a written request from the holders of a majority of the then outstanding shares of preferred stock, which request can be made at any time after the fifth anniversary of the Series B-1 original issue date (on or after June 22, 2021). On each of the three annual redemption dates the Company must redeem the number of outstanding shares of preferred stock determined by dividing the total number of outstanding shares of preferred stock by the number of remaining redemption dates.

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Common Stock

As of December 31, 2016, the Company had reserved shares of common stock for issuance as follows:

Series A-1 convertible preferred stock outstanding	184,457,734
Series A-2 convertible preferred stock outstanding	17,446,133
Series B-1 convertible preferred stock outstanding	32,500,000
Series B-2 convertible preferred stock outstanding	18,750,000
Options issued and outstanding	21,496,084
Restricted shares subject to future vesting	15,690,435
Early exercised common stock subject to future vesting	2,041,669
Options available for future grants	7,253,237
Shares to be issued under Incro acquisition agreement	324,658
Total	299,959,950

10. Stock Incentive Plan

2015 Stock Incentive Plan

In May 2015, the Company adopted the 2015 Stock Incentive Plan (the "2015 Plan"), which as amended, reserved 33,300,000 shares for the issuance of stock options, non-qualified stock options, restricted stock and other stock awards, to employees, non-employee directors, and consultants under terms and provisions established by the Board of Directors and approved by the stockholders. Awards granted under the 2015 Plan expire no later than ten years from the date of grant. For incentive stock options and non-statutory stock options, the option price shall not be less than 100% of the estimated fair value on the day of grant. For all stock options granted between August 2015 and February 2016 with an exercise price of $0.17, a deemed fair value of $0.30 per share was used in calculating stock-based compensation expense, which was determined using management hindsight. Options granted typically vest over a four-year period but may be granted with different vesting terms

The Company permits early exercise of certain stock options prior to vesting by certain directors and officers. Any shares issued pursuant to unvested options are restricted and subject to repurchase by the Company until the conditions for vesting are met. The amounts paid for shares purchased under an early exercise of stock options and subject to repurchase by the Company are reported in stockholders' deficit once those shares vest. Upon termination of employment of an option holder, the Company has the right to repurchase, at the original purchase price, any unvested restricted shares.

In 2015, there were 3,000,000 options exercised prior to vesting for total proceeds of $0.5 million to the Company which was recognized as a long-term liability as of December 31, 2015. No shares vested relating to these exercises in the year ended December 31, 2015. The Company reclassified $0.2 million to stockholders' deficit upon vesting during the year ended December 31, 2016 and the remaining proceeds related to the unvested options of $0.3 million as of December 31, 2016 will be reclassified to stockholders' deficit as the options vest.

As of December 31, 2015 and 2016, there were 8,099,487 shares and 7,253,237 shares, respectively, available for the Company to grant under the 2015 Plan.

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Notes to Consolidated Financial Statements

Stock Option Activity

The following table summarizes option activity under the 2015 plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2014	—	$ —	—	
Options granted	17,100,513	0.17		
Options exercised	(3,000,000)	0.17		
Balance at December 31, 2015	14,100,513	0.17	9.73	
Options granted	8,451,250	0.86		
Options exercised	(650,679)	0.17		
Options forfeited	(405,000)	0.21		
Balance at December 31, 2016	21,496,084	$ 0.44	9.03	$ 18,873
Options vested and expected to vest at December 31, 2016	14,517,121	$ 0.57	9.21	$ 10,847
Options exercisable at December 31, 2016	1,676,413	$ 0.17	8.83	$ 1,926

Aggregate intrinsic value represents the difference between the Company's estimated fair value of its common stock and the exercise price of outstanding options. The total intrinsic value of options exercised was $0.4 million and $0.7 million for the years ended December 31, 2015 and 2016, respectively. The total intrinsic value of options exercisable was $1.9 million as of December 31, 2016. During the year ended December 31, 2016, the weighted-average grant-date fair value of the options vested was $0.34 per share. No options vested during the year ended December 31, 2015. The weighted-average grant date fair value of options granted during the years ended December 31, 2015 and 2016 was $0.51 and $0.71 per share, respectively.

Stock Options Granted to Employees with Service-Based Vesting

The estimated fair value of stock options granted to employees were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Year Ended December 31,	
	2015	2016
Expected term (in years)	6.08	6.00-6.08
Volatility	85.7%-90.2%	91.2%-92.2%
Risk-free interest rate	1.7%-1.9%	1.2%-2.1%
Dividend yield	—	—

Expected Term: The expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term).

Expected Volatility: The Company used an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that were deemed to be

representative of future stock price trends as the Company does not have any trading history for its common stock.

Risk-Free Interest Rate: The Company based the risk-free interest rate over the expected term of the options based on the constant maturity rate of U.S. Treasury securities with similar maturities as of the date of the grant.

Expected Dividend: The Company has not paid and does not anticipate paying any dividends in the near future. Therefore, the expected dividend yield was zero.

Performance Contingent Stock Options Granted to Employees

In August and November 2015, the Board of Directors granted 1,000,000 and 2,000,000 of stock option awards to certain executive officers, respectively. These awards have an exercise price of $0.17 per share. These awards vest over time and include a performance provision which states that upon the occurrence of a change in control event, the vesting term would accelerate. As of December 31, 2016, the Company determined that the achievement of the requisite performance condition was not probable and, as a result, the expense relating to these grants is being recognized over the initial time-based vesting period. If the performance goal is ever deemed to be probable of achievement, the recognition of compensation expense will be accelerated in accordance with the accelerated vesting schedule.

The estimated fair value of employee performance-contingent options was estimated at the date of grant using a Black-Scholes option-pricing model using the same assumptions as the Stock Options Granted to Employees with Service-based Vesting Valuation Assumptions.

Performance and Market Contingent Stock Options Granted to Employees

In August and November 2015, the Board of Directors granted 6,478,963 and 500,000 of performance- and market- contingent awards to members of the senior management team, respectively. These awards have an exercise price of $0.17 per share.

These awards have two separate market triggers for vesting based upon either (i) the successful achievement of stepped target closing prices on a national securities exchange for 90 consecutive trading days later than 180 days after the Company's initial public offering for its common stock, or (ii) stepped target prices for a change in control transaction. By definition, the market condition in these awards can only be achieved after the performance condition of a liquidity event has been achieved. As such, the requisite service period is based on the estimated period over which the market condition can be achieved. When a performance goal is deemed to be probable of achievement, time-based vesting and recognition of stock-based compensation expense commences. In the event any the milestones are not achieved by the specified timelines, such vesting award will terminate and no longer be exercisable with respect to that portion of the shares. The maximum potential expense associated with the performance- and market- contingent awards is $6.2 million ($5.8 million and $0.4 million of general and administrative and research and development expense, respectively) if all of the performance and market conditions are achieved as stated in the option agreement. As of December 31, 2016, the Company determined that the achievement of the requisite performance conditions was not probable and, as a result, no compensation cost was recognized for these awards.

The Company uses a lattice model with a Monte Carlo simulation to value stock options with performance and market conditions. This valuation methodology utilizes the estimated fair value of the

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Company's common stock on grant date and several key assumptions, including expected volatility of the Company's stock price based on comparable public companies, risk-free rates of return and expected dividend yield.

Stock Options Granted to Non-Employees with Service-Based Vesting

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The estimated fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2015	2016
Expected term (in years)	9.50-9.84	8.50-9.70
Volatility	88.6%-89.3%	95.3%-98.2%
Risk-free interest rate	2.0%-2.3%	2.4%
Dividend yield	—	—

The expected term for stock options granted to non-employees is equivalent to the remaining contractual term of the award.

Restricted Stock Activity

The following table summarizes restricted stock activity:

	Shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2015	27,645,114	$ 0.04
Granted	—	—
Vested	(11,954,679)	0.04
Forfeited	—	—
Unvested at December 31, 2016	15,690,435	$ 0.04

At December 31, 2016, there was $0.7 million of total unrecognized compensation cost related to non-vested restricted stock, all which is expected to be recognized over a remaining weighted-average period of 2.5 years.

Stock-Based Compensation Expense

The Company's results of operations include expenses relating to employee and non-employee stock-based awards and restricted stock awards as follows (in thousands):

	Year Ended December 31,	
	2015	2016
Research and development	$ 94	$ 2,078
General and administrative	385	873
Total	$ 479	$ 2,951

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As of December 31, 2016, total unamortized stock-based compensation expense related to unvested employee and non-employee awards that are expected to vest was $7.2 million and $0.4 million, respectively. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 3.1 years and 3.2 years as of December 31, 2015 and 2016, respectively.

The Company recorded stock-based compensation expense for options issued to non-employees under the 2015 Plan of $0.1 million and $1.0 million for the years ended December 31, 2015 and 2016, respectively.

11. Income Taxes

The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the accompanying financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

The effective tax rate for the years ended December 31, 2015 and 2016 is different from the federal statutory tax rate primarily due to the valuation allowance against deferred tax assets as a result of insufficient sources of income. The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,	
	2015	2016
Taxes at the U.S. statutory tax rate	34.0%	34.0%
Change in valuation allowance	(34.1)	(32.0)
Contingent consideration issued in tax-free reorganization	—	(2.1)
Research tax credits	1.5	0.6
Stock-based compensation	(0.2)	(0.5)
Other	(1.2)	—
Total provision for income taxes	0.0%	0.0%

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

The components of the Company's net deferred tax assets are as follows (in thousands):

	December 31,	
	2015	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 4,452	$ 26,044
Tax credit carryforwards	410	1,486
Reserves and accruals	370	4,038
Capitalized start-up costs	1,987	5,128
Intangibles	—	6,565
Share based compensation	67	390
Gross deferred tax assets	7,286	43,651
Valuation allowance	(6,823)	(40,113)
Net deferred tax assets	463	3,538
Deferred tax liabilities:		
Property and equipment	(65)	(3,379)
Stock-based compensation	(398)	(159)
Net deferred tax assets	$ —	$ —

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, especially the uncertainties surrounding the realization of deferred tax assets through future taxable income, the Company believes it is not more likely than not that the deferred tax assets will be fully realizable. Accordingly, the Company has provided a 100% valuation allowance against its net deferred tax assets as of December 31, 2015 and 2016.

As of December 31, 2016, the Company has federal net operating loss ("NOL") carryforwards of approximately $65.4 million, which are available to reduce future taxable income, and has federal tax credits of approximately $1.2 million which may be used to offset future tax liabilities. The federal NOL and federal tax credit carryforwards will begin to expire in 2035. The Company also has state NOL carryforwards of approximately $65.4 million, which are available to reduce future taxable income, and has state tax credits of approximately $1.4 million which may be used to offset future tax liabilities. The state NOL will begin to expire in 2035 and the state tax credit carryforwards will be carried forward indefinitely. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service ("IRS") and state tax authorities and may become subject to an annual limitation in the event of certain future cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code of 1986. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities.

The Company follows the provisions of ASC 740, Accounting for Income Taxes, and the accounting guidance related to accounting for uncertainty in income taxes. The Company determines its uncertain tax positions based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings is more likely than not to be sustained upon examination by the relevant income tax authorities.

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2015	2016
Gross unrecognized tax benefits at January 1	$ —	$ 122
Additions for tax positions taken in a prior year	—	7
Additions for tax positions taken in the current year	122	411
Reductions for tax positions taken in the prior year	—	(9)
Gross unrecognized tax benefits at December 31	$ 122	$ 531

If recognized, none of the unrecognized tax benefits as of December 31, 2015 and 2016 would reduce the annual effective tax rate, primarily due to corresponding adjustments to the valuation allowance. The Company will recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. As of December 31, 2016, no liability has been recorded for potential interest or penalties. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months.

Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

12. Net Loss and Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share data):

	Year Ended December 31,	
	2015	2016
Numerator:		
Net loss	$ (16,788)	$ (86,652)
Denominator:		
Weighted average common shares outstanding	12,025,514	25,698,880
Net loss per share, basic and diluted	$ (1.40)	$ (3.37)

Denali Therapeutics Inc.
Notes to Consolidated Financial Statements

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential common shares outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,	
	2015	2016
Series A-1 convertible preferred stock	48,791,557	184,457,734
Series A-2 convertible preferred stock	—	17,446,133
Series B-1 convertible preferred stock	—	32,497,500
Options issued and outstanding	14,100,513	21,496,084
Restricted shares subject to future vesting	27,645,114	15,690,435
Early exercised common stock subject to future vesting	3,000,000	2,041,669
Shares to be issued under Incro acquisition agreement	108,219	324,658
Total	93,645,403	273,954,213

Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share (in thousands, except for share and per share amounts):

	Year ended December 31, 2016 (Unaudited)
Net loss	$ (86,652)
Shares used in computing net loss per share, basic and diluted	25,698,880
Pro forma adjustment to reflect assumed conversion of preferred stock	169,998,095
Shares used to compute pro forma net loss per share, basic and diluted	195,696,975
Pro forma net loss per share, basic and diluted	$ (0.44)

Denali Therapeutics Inc.

Condensed Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2016	June 30, 2017 (Unaudited)	Pro Forma Stockholders' Equity as of June 30, 2017 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 39,853	$ 41,307	
Short-term marketable securities	138,478	145,657	
Prepaid expenses and other current assets	3,624	2,353	
Total current assets	181,955	189,317	
Long-term marketable securities	72,580	25,875	
Property and equipment, net	15,262	14,969	
Other non-current assets	1,270	1,218	
Total assets	$ 271,067	$ 231,379	
Liabilities, convertible preferred stock and stockholders' equity (deficit)			
Current liabilities:			
Accounts payable	$ 1,963	$ 1,428	
Accrued liabilities	3,850	6,652	
Accrued compensation	2,592	1,820	
Deferred rent and other current liabilities	701	886	
Total current liabilities	9,106	10,786	
Deferred rent	7,045	6,738	
Other non-current liabilities	397	531	
Total liabilities	16,548	18,055	
Commitments and contingencies (Note 5)			
Convertible preferred stock, $0.01 par value; 253,153,867 shares authorized as of December 31, 2016 and June 30, 2017 (unaudited); 234,401,367 shares issued and outstanding as of December 31, 2016 and June 30, 2017 (unaudited); aggregate liquidation preference of $383,930 as of June 30, 2017 (unaudited)	348,673	348,673	$ —
Stockholders' equity (deficit):			
Common stock, $0.01 par value; 334,349,451 shares authorized as of December 31, 2016 and June 30, 2017 (unaudited); 34,389,501 and 39,986,068 shares issued and outstanding as of December 31, 2016 and June 30, 2017, respectively (unaudited); 274,387,435 shares issued and outstanding, pro forma (unaudited)	344	400	2,744
Additional paid-in capital	9,387	11,594	357,923
Accumulated other comprehensive loss	(373)	(377)	(377)
Accumulated deficit	(103,512)	(146,966)	(146,966)
Total stockholders' equity (deficit)	(94,154)	(135,349)	213,324
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 271,067	$ 231,379	$ 231,379

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(In thousands, except share and per share amounts)

	Six Months Ended June 30,	
	2016	2017
Operating expenses:		
Research and development	$ 31,153	$ 37,474
General and administrative	5,572	6,838
Total operating expenses	36,725	44,312
Loss from operations	(36,725)	(44,312)
Interest income, net	38	858
Net loss	(36,687)	(43,454)
Other comprehensive income (loss):		
Net unrealized gain (loss) on marketable securities, net of tax	16	(4)
Comprehensive loss	$ (36,671)	$ (43,458)
Net loss per share, basic and diluted	$ (1.69)	$ (1.16)
Weighted average number of shares outstanding, basic and diluted	21,742,166	37,380,492
Pro forma net loss per share, basic and diluted		$ (0.16)
Weighted-average number of shares used in computing pro forma net loss per share, basic and diluted		271,781,859

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Six Months Ended June 30,	
	2016	2017
Operating activities		
Net loss	$ (36,687)	$ (43,454)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	382	1,497
Stock-based compensation expense	1,100	1,824
Net amortization of premiums and discounts on marketable securities	—	685
Changes in operating assets and liabilities:		
Restricted cash	(451)	—
Prepaid expenses and other assets	247	1,266
Accounts payable	845	(446)
Accrued and other current liabilities	1,894	2,423
Other non-current liabilities	(36)	(173)
Net cash used in operating activities	(32,706)	(36,378)
Investing activities		
Purchase of marketable securities	(49,267)	(28,156)
Purchase of property and equipment	(1,482)	(1,437)
Maturities and sales of marketable securities	—	67,050
Net cash provided by (used in) investing activities	(50,749)	37,457
Financing activities		
Proceeds from exercise of common stock options	43	375
Proceeds from issuance of convertible preferred stock, net of issuance costs	292,743	—
Net cash provided by financing activities	292,786	375
Net increase in cash and cash equivalents	209,331	1,454
Cash and cash equivalents at beginning of period	30,740	39,853
Cash and cash equivalents at end of period	$ 240,071	$ 41,307
Supplemental disclosures of cash flow information		
Property and equipment purchases accrued but not yet paid	$ 272	$ —

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

1. Significant Accounting Policies

Organization and Description of Business

Denali Therapeutics Inc. (the "Company") is a biopharmaceutical company, incorporated in Delaware, that discovers and develops therapeutics to defeat neurodegenerative diseases. The Company was incorporated in October 2013 as SPR Pharma Inc. The Company's name was changed to Denali Therapeutics Inc. in March 2015. The Company is headquartered in South San Francisco, California.

Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Principles of Consolidation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. This subsidiary was dissolved in September 2016. All intercompany balances and transactions have been eliminated on consolidation.

The Company assesses whether it is the primary beneficiary of any variable interest entity ("VIE") in which it has a variable interest at the inception of the arrangement and at each reporting date. This assessment is based on the Company's power to direct the activities of the VIE that most significantly impact the VIE's economic performance and the Company's obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

Unaudited Interim Consolidated Financial Statements

The interim condensed consolidated balance sheet as of June 30, 2017, and the statements of operations and comprehensive loss, and cash flows for the six months ended June 30, 2016 and 2017 are unaudited. The unaudited interim consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair presentation of the Company's financial position as of June 30, 2017 and its results of operations and cash flows for the six months ended June 30, 2016 and 2017. The financial data and the other financial information disclosed in these notes to the consolidated financial statements related to the six-month periods are also unaudited. The consolidated results of operations for the six months ended June 30, 2017 are not necessarily indicative of the results to be expected for the year ended December 31, 2017 or for any other future annual or interim period. The consolidated balance sheet as of December 31, 2016 included herein was derived from the audited consolidated financial statements as of that date. These interim condensed consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Information

Immediately prior to the completion of this offering, all outstanding shares of convertible preferred stock will convert into common stock. Unaudited pro forma balance sheet information as of June 30, 2017 assumes the conversion of all outstanding convertible preferred stock into shares of common stock. The shares of common stock issuable and the proceeds expected to be received in the initial public offering are excluded from such pro forma financial information.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the Company to make certain estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported amounts of expenses during the reporting period. Actual results could differ from those estimates, and such differences could be material to the consolidated financial position and results of operations.

Need for Additional Capital

Since inception, the Company has incurred net losses and negative cash flows from operations. During the six months ended June 30, 2017, the Company incurred a net loss of $43.5 million and used $36.4 million of cash in operations. At June 30, 2017, the Company had an accumulated deficit of $147.0 million and does not expect to experience positive cash flows in the near future. The Company has financed operations to date primarily through the sale and issuance of convertible preferred stock. Management expects to incur additional operating losses in the future as the Company continues the development of, and seeks regulatory approvals for, its product candidates, and begins to commercialize any approved products and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. The Company had $212.8 million of cash, cash equivalents and marketable securities at June 30, 2017. Based on the Company's business plans, management believes that this is sufficient to meet its obligations for at least the next twelve months from the issuance date of these condensed consolidated financial statements.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources.

Fair Value of Financial Instruments

ASC Topic 820, Fair Value Measurement ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

Level 1 – inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 – inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

Level 3 – inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities approximate their fair values, due to their short-term nature.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of 90 days or less at the date of purchase to be cash and cash equivalents. Cash equivalents, which consist primarily of highly liquid investments with maturities of three months or less when purchased, are stated at fair value.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents, short-term marketable securities, or long-term marketable securities on the balance sheets, are considered available-for-sale, and reported at fair value with unrealized gains and losses included as a component of stockholders' deficit. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income, net on the consolidated statements of operations. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on marketable securities are included in interest income, net. The cost of securities sold is determined using specific identification.

The Company periodically evaluates whether declines in fair values of its marketable securities below their book value are other-than-temporary. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the security or it is more likely than not it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and our strategy and intentions for holding the marketable security.

Restricted Cash

The Company's restricted cash consists of restricted cash in connection with the building leases for the Company's former and current headquarters. The current portion is classified within prepaid expenses and other current assets and the non-current portion within other non-current assets on the accompanying consolidated balance sheets.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of salaries and other personnel related expenses, including associated stock–based compensation, consulting fees, lab supplies, and facility costs, as well as fees paid to other entities that conduct certain research, development and manufacturing activities on behalf of the Company.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities are deferred and recognized as expense in the period in which the related goods are delivered or services are performed.

The Company has acquired and may continue to acquire the rights to develop and commercialize new product candidates from third parties. The upfront payments to acquire license, product or rights, as well as any future milestone payments, are immediately recognized as research and development expense provided that there is no alternative future use of the rights in other research and development projects.

Stock-Based Compensation

The Company measures employee and director stock-based compensation expense for all stock-based awards at the grant date based on the fair value measurement of the award. The expense is recorded on a straight-line basis over the requisite service period, which is generally the vesting period, for the entire award. Expense is adjusted for actual forfeitures of unvested awards as they occur. The Company calculates the fair value measurement of stock options using the Black-Scholes valuation model.

The Company granted restricted stock awards that vest in conjunction with certain performance conditions to certain key employees and directors. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

The Company accounts for stock options issued to non-employees in accordance with the provisions of ASC 505-50, Equity-Based Payments to Non-employees, which requires valuing the stock options on their grant date and remeasuring such stock options at the current fair value at the end of each reporting period until they vest.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss, primarily unrealized losses on the Company's marketable securities.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

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Unaudited Pro Forma Net Loss per Share

Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. Pro forma basic and diluted net loss per share has been computed to give effect to the conversion of all outstanding convertible preferred stock into shares of common stock. The unaudited pro forma net loss per share does not include the shares expected to be sold and related proceeds to be received from the initial public offering. The unaudited pro forma net loss per share for the six months ended June 30, 2017 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the period, or their issuance dates if later.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014–09 ("ASU 2014-09"), Revenue from Contracts with Customers (Topic 606), and further updated through ASU 2016-12 ("ASU 2016-12"), which amends the existing accounting standards for revenue recognition. ASU 2014–09 is based on principles that govern the recognition of revenue at an amount to which an entity expects to be entitled when products are transferred to customers. This guidance is effective for annual reporting periods, and interim periods within those years, beginning after December 15, 2017, for public entities and no later than for annual reporting periods beginning after December 15, 2018, for non–public entities. Early adoption is not permitted. The new revenue standard may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of adoption. While the Company continues to assess all potential impacts under ASU 2014-09, it does not believe adopting the new revenue standard will have a material impact on its consolidated financial statements as the Company is not yet generating revenues.

In February 2016, the FASB issued ASU No. 2016-02 ("ASU 2016-02"), Leases (Topic 842), which supersedes the guidance in former ASC 840, Leases. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. The ASU is expected to impact the Company's consolidated financial statements as the Company has certain operating lease arrangements for which the Company is the lessee. Management is currently evaluating the impact the adoption of ASU 2016-02 will have on the Company's financial position and results of operations. Management expects that the adoption of this standard will result in the recognition of an asset for the right to use the leased facility on the Company's balance sheet, as well as the recognition of a liability for the lease payments remaining on the lease. While the balance sheet presentation is expected to change, management does not expect a material change to the consolidated statement of operations.

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. The purpose of Update No. 2016-18 is to clarify guidance and presentation related to

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restricted cash in the statement of cash flows. The amendment requires beginning-of-period and end-of-period total amounts shown on the statement of cash flows to include cash and cash equivalents as well as restricted cash and restricted cash equivalents. The update is effective for fiscal years beginning after December 15, 2017, including interim reporting periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to be material.

In May 2017, the FASB issued ASU 2017-09, Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. It is effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the impact of adopting this standard on the consolidated financial statements and disclosures, but does not expect it to have a significant impact.

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2. Fair Value Measurements

Assets measured at fair value at each balance sheet date are as follows (in thousands):

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$28,705	$ —	$ —	$ 28,705
Short-term:				
U.S. government treasuries	22,268	—	—	22,268
U.S. government agency securities	—	70,787	—	70,787
Corporate debt securities	—	38,941	—	38,941
Commercial paper	—	6,482	—	6,482
Long-term:				
U.S. government treasuries	4,989	—	—	4,989
U.S. government agency securities	—	52,868	—	52,868
Corporate debt securities	—	14,723	—	14,723
Total marketable securities	27,257	183,801	—	211,058
Total fair value measurements	**$55,962**	**$183,801**	**$ —**	**$239,763**

	June 30, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$29,135	$ —	$ —	$ 29,135
Short-term:				
U.S. government treasuries	18,444	—	—	18,444
U.S. government agency securities	—	76,376	—	76,376
Corporate debt securities	—	50,837	—	50,837
Long-term:				
U.S. government agency securities	—	25,875	—	25,875
Total marketable securities	18,444	153,088	—	171,532
Total fair value measurements	**$47,579**	**$153,088**	**$ —**	**$200,667**

The carrying amounts of accounts payable and accrued liabilities approximate their fair values due to their short-term maturities.

The Company's Level 2 securities are valued using third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly. There were no transfers of assets or liabilities between the fair value measurement levels during the six months ended June 30, 2017.

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2016 and June 30, 2017. The amortized cost, gross unrealized holding gains or losses, and fair value of the Company's

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marketable securities by major security type at each balance sheet date are summarized in the tables below (in thousands):

	December 31, 2016			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 22,277	$ —	$ (9)	$ 22,268
U.S. government agency securities	70,835	—	(48)	70,787
Corporate debt securities	39,037	—	(96)	38,941
Commercial paper	6,482	—	—	6,482
Total short-term marketable securities	138,631	—	(153)	138,478
Long-term marketable securities:				
U.S. government treasuries	4,996	1	(8)	4,989
U.S. government agency securities	53,005	—	(137)	52,868
Corporate debt securities	14,799	—	(76)	14,723
Total long-term marketable securities	72,800	1	(221)	72,580
Total	**$ 211,431**	**$ 1**	**$ (374)**	**$ 211,058**

	June 30, 2017			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 18,472	$ —	$ (28)	$ 18,444
U.S. government agency securities	76,526	—	(150)	76,376
Corporate debt securities	50,923	—	(86)	50,837
Total short-term marketable securities	145,921	—	(264)	145,657
Long-term marketable securities:				
U.S. government agency securities	25,988	—	(113)	25,875
Total long-term marketable securities	25,988	—	(113)	25,875
Total	**$ 171,909**	**$ —**	**$ (377)**	**$ 171,532**

As of December 31, 2016 and June 30, 2017, some of the Company's marketable securities were in an unrealized loss position. At each date, the Company determined that it did have the ability and intent to hold all marketable securities that have been in a continuous loss position until maturity or recovery, thus there has been no recognition of any other-than-temporary impairment in the year ended December 31, 2016 or the six months ended June 30, 2017. All marketable securities with unrealized losses as of as of each balance sheet date have been in a loss position for less than twelve months or the loss is not material.

All of the Company's short-term marketable securities have an effective maturity date of less than one year, and all of the Company's long-term marketable securities have an effective maturity of less than two years.

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4. License and Collaboration Agreements

F-star

On August 24, 2016, the Company entered into a License and Collaboration Agreement ("Collaboration Agreement") with F-star Gamma Limited ("F-star Gamma"), F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology Limited (collectively, "F-star"). The goal of the collaboration is the development of certain constant Fc-domains of an antibody with non-native antigen binding activity ("Fcabs"), to enhance delivery of therapeutics across the blood-brain barrier ("BBB") into the brain. The collaboration leverages F-star's modular antibody technology and the Company's expertise in the development of therapies for neurodegenerative diseases.

Under the terms of the Collaboration Agreement, the Company can nominate up to three Fcab targets ("Accepted Fcab Targets"), within the first three years of the date of the Collaboration Agreement; and the Company has selected transferrin receptor ("TfR") as the first Accepted Fcab Target. With respect to each Accepted Fcab Target, the Company can nominate up to eight Fab targets ("Accepted Fab Targets"), which are targets bound by the variable domains of an antibody or other therapeutic modalities ("Fabs"). For each accepted Fcab target, the Company is obligated to use commercially reasonable efforts during the research term to perform development activities in accordance with certain specified development plans. Under the terms of the Collaboration Agreement, the Company received non-exclusive licenses under certain intellectual property to conduct technology development to discover and develop Fcabs. The Company is obligated to assign to F-star certain patents and know-how that the Company generates under the Collaboration Agreement related to F-star's platform technology or certain Fcabs identified solely by F-star and the Company received a non-exclusive license under certain of F-star Biotechnology's platform patents and know-how to develop and commercialize products in connection with the delivery of therapeutics across the BBB, subject to certain specified restrictions. F-star retains the right to use its intellectual property, including any intellectual property that the Company and F-star jointly own pursuant to the terms of the Collaboration Agreement, outside the scope of the licenses granted to the Company.

Under the terms of the Collaboration Agreement, the Company paid F-star Gamma an upfront fee of $5.5 million, which includes selection of the first Accepted Fcab Target. The Company is obligated to pay a one-time fixed fee in the low single-digit millions for each additional Accepted Fcab Target the Company selects, technical milestone payments for each Accepted Fcab Target, up to a maximum of $15.0 million in the aggregate for all Accepted Fcab Targets, and, at specified times, monthly exclusivity fees for Accepted Fcab Targets and Accepted Fab Targets, which may be eliminated in certain circumstances. The Company is also responsible for certain research costs incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research costs for the agreed TfR development plan will be up to $2.1 million.

Either party may terminate the agreement if the other party materially breaches the agreement, subject to specified notice and cure provisions, or for the other party's bankruptcy or insolvency. In addition, F-star Gamma may terminate the agreement if the Company challenges any of the patent rights licensed to it by F-star. The Company is able to terminate the agreement for convenience, either in its entirety or on an Accepted Fcab Target-by-Accepted Fcab Target basis or an Accepted Fab Target-by-Accepted Fab Target basis, on 90 days' prior written notice to F-star. Unless earlier terminated, the agreement with F-star will remain in effect until all royalty and milestone payment obligations to F-star Gamma expire.

In connection with the entry into the Collaboration Agreement, the Company also purchased an option for an upfront option fee of $0.5 million (the "buy-out-option"), to acquire all of the outstanding

shares of F-star Gamma pursuant to a pre-negotiated buy-out option agreement (the "Option Agreement"). The Company must elect whether to exercise its buy-out option before the earlier of (i) dosing of the fifth patient dosed in the first Phase 1 trial of an antibody that binds to an Accepted Fab Target and an Accepted Fcab Target, (ii) the fourth anniversary of the first delivery by F-star of an Fcab meeting certain delivery criteria, and (iii) five and one half years after the delivery by the Company of a notice that it is progressing an Fcab identified from the Company's library that binds to an Accepted Fcab Target. If the Company exercises this buy-out option, it will be obligated to make initial exercise payments ranging from $18.0 million to $50.0 million in the aggregate, plus the estimated net cash held by F-star Gamma at the time of such exercise. In addition, it will be required to make certain contingent payments upon the achievement of certain preclinical, clinical, regulatory and commercial milestones, up to a maximum amount of $447.0 million in the aggregate. The amount of the initial exercise and contingent payments varies based on whether F-star delivers an Fcab that meets pre-defined criteria, whether the Fcab has been identified solely by the Company or solely by F-star or jointly by the Company and F-star and the timing of the Company's exercise of the buy-out option. Following exercise of the buy-out option, the Company will not be required to make any further milestone or royalty payments under the Collaboration Agreement. If the Company exercises the buy-out option, then F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H and F-star Biotechnology continue to be prohibited from developing, commercializing and manufacturing any antibody or other molecule that incorporates any Selected Fcab, or any Selected Fcab as a standalone product, and from authorizing any third party to take any such action. If the Company does not exercise its option to acquire F-star Gamma prior to the expiration of the buy-out option period, then, from the lapse of the buy-out option period until the Company's rights with respect to an Accepted Fab Target expire or terminate, F-star is prohibited from developing, commercializing and manufacturing any antibody or other molecule that contains both a Selected Fcab and a Fab that specifically binds to the relevant Accepted Fab Target.

If the Company does not exercise the buy-out option, then with respect to each Accepted Fab Target, the Company has the right to obtain from F-star an exclusive, worldwide license to certain intellectual property to develop and commercialize licensed products that contain (i) a Fab that specifically binds to such Accepted Fab Target and (ii) an Fcab that the Company or F-star identifies, either solely or jointly, and that specifically binds to an Accepted Fcab Target, for up to eight Accepted Fab Targets per each Accepted Fcab Target. Each time the Company exercises such license option, it will be obligated to pay F-star Gamma (i) a one-time fixed fee in the low single-digit millions, (ii) milestone payments upon the achievement of certain clinical development and commercial milestones, up to a maximum of $362.5 million in the aggregate; (iii) additional sales-based milestones if net sales of licensed products achieve certain specified levels, up to a maximum amount payable to F-star of $650.0 million in the aggregate and (iv) low-to-mid single-digit percentage royalties on net sales of licensed products. Such amounts may be reduced by a specified percentage depending on the origin of the Fcab incorporated in the applicable licensed product and whether F-star delivers to the Company an Fcab that meets pre-defined criteria. The Company has the right to credit a certain amount of royalty payments that it pays to third parties with respect to certain licensed products against the Company's royalty obligation to F-star Gamma, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country, (b) the expiration of regulatory exclusivity for such licensed product in such country and (c) the twelfth anniversary of the first commercial sale of such licensed product in such country.

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The Company recognized the upfront option fee of $0.5 million within other non-current assets recorded at cost. This asset will be assessed for potential impairment on an ongoing basis. No impairment charge was recognized during the six months ended June 30, 2017.

The Company determined that F-star Gamma is and continues to be a variable interest entity and that the Company holds a variable interest in F-star Gamma's intellectual property assets and the related potential future product candidates these assets may produce through the Collaboration Agreement and the Option Agreement. However, the Company concluded that its governance role in the collaboration, which is specified by the terms of a joint steering committee, does not provide the Company the power to direct the activities of F-star Gamma that most significantly impact F-star Gamma's economic performance. Based on this conclusion, the Company is not considered to be the primary beneficiary of F-star Gamma; and therefore F-star Gamma is not subject to consolidation by the Company.

The Company recognized $0.5 million of research and development expense related to the funding of F-star Gamma research costs during the six months ended June 30, 2017.

The $0.5 million other non-current asset is the only asset or liability recorded in the Company's interim condensed consolidated balance sheet that relates to the Company's variable interest in F-star Gamma at June 30, 2017. The upfront payments of $0.5 and $5.5 million and the obligation to fund certain future research costs, represent the Company's maximum exposure to loss under the arrangements with F-star.

Genentech

On June 17, 2016, the Company entered into an Exclusive License Agreement with Genentech, Inc. ("Genentech"). The agreement gives the Company access to Genentech's preclinical stage LRRK2 small molecule program, which can be used to enhance and further progress the Company's in-house LRRK2 program for Parkinson's disease. Under the agreement, Genentech granted the Company (i) an exclusive, worldwide, sublicenseable license under Genentech's rights to certain patents and patent applications directed to small molecule compounds which bind to and inhibit LRRK2 and (ii) a non-exclusive, worldwide, sublicenseable license to certain related know-how, in each case, to develop and commercialize certain compounds and licensed products incorporating any such compound. The Company is obligated to use commercially reasonable efforts during the first three years of the agreement to research, develop and commercialize at least one licensed product.

As consideration, the Company paid an upfront fee of $8.5 million and a technology transfer fee of $1.5 million.

The Company may owe Genentech milestone payments upon the achievement of certain development, regulatory, and commercial milestones, up to a maximum of $315.0 million in the aggregate, as well as royalties on net sales of licensed products ranging from low to high single-digit percentages, with the exact royalty rate dependent on various factors, including (i) whether the compound incorporated in the relevant licensed product is a Genentech-provided compound or a compound acquired or developed by the Company, (ii) the date a compound was first discovered, derived or optimized by the Company, (iii) the existence of patent rights covering the relevant licensed product in the relevant country, (iv) the existence of orphan drug exclusivity covering a licensed product that is a Genentech-provided compound and (v) the level of annual net sales of the relevant licensed product. The Company also has the right to credit a certain amount of third-party royalty and

milestone payments against royalty and milestone payments owed to Genentech, up to a maximum reduction of fifty percent. The Company's royalty payment obligations will expire on a country-by-country and licensed product-by-licensed product basis upon the later of (a) ten years after the first commercial sale of such licensed product in such country and (b) the expiration of the last valid claim of a licensed patent covering such licensed product in such country.

Genentech may terminate the agreement if the Company challenges any of the patent rights licensed to the Company by Genentech, or if the Company materially breaches the agreement, subject to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. If Genentech terminates the agreement for the Company's material breach, bankruptcy or insolvency after the Company has made a milestone payment to Genentech, then the Company is obligated to grant to Genentech an exclusive right of first negotiation with respect to certain of the Company's patents, know-how and regulatory filings directed to Genentech-provided compounds. The Company does not have the right to terminate the agreement without cause, but may terminate the agreement for Genentech's material breach, subject to specified notice and cure provisions.

Unless earlier terminated, the agreement with Genentech will continue in effect until all of the Company's royalty and milestone payment obligations to Genentech expire. Following expiration of the agreement, the Company will retain the licenses under the intellectual property Genentech licensed to the Company on a non-exclusive, royalty-free basis.

The entire upfront fee, and $0.3 million relating to the technology transfer fee are included in research and development expense for the six months ended June 30, 2016. The first clinical milestone of $2.5 million became due in June 2017 upon first patient dosing in the Phase 1 clinical trial for DNL201. The full amount was included in research and development expenses in the six months ended June 30, 2017.

5. Commitments and Contingencies

Lease Obligations

In September 2015, the Company entered into a non-cancelable operating lease for its corporate headquarters comprising 38,109 of rentable square feet in a building in South San Francisco ("Headquarters Lease"). The Headquarters Lease commenced on August 1, 2016 with a lease term of eight years. The Company has an option to extend the lease term for a period of five years by giving the landlord written notice of the election to exercise the option at least nine months, but not more than twelve months, prior to the original expiration of the lease term. The Headquarters Lease provides for monthly base rent amounts escalating over the term of the lease. In addition, the Headquarters Lease provides both a tenant improvement allowance ("TIA") of up to $7.4 million, of which $1.9 million will be repaid to the landlord in the form of additional monthly rent with interest applied. This additional monthly rent commenced in November 2016 when the entire TIA was utilized, and results in an increase of base rent of $0.4 million per year.

The total $7.4 million TIA has been recorded as leasehold improvements and deferred rent liability on the consolidated balance sheet. The Company is amortizing the deferred rent liability as a reduction of rent expense and the leasehold improvement through an increase of depreciation expense of leasehold improvements ratably over the lease term. Under the terms of the Headquarters Lease, the Company was required to pay a security deposit of $0.5 million, which is recorded as other non-current assets in the accompanying consolidated balance sheets.

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In May 2015, the Company entered into a non-cancelable operating lease for office and research and development space in South San Francisco that expires in December 2017 (the “First Lease”). The First Lease provides for 9,855 of rentable square feet at a base rent that increases annually. Under the terms of the First Lease, the Company was required to pay a security deposit of $0.1 million, which is recorded as prepaid expenses other current assets in the accompanying consolidated balance sheets.

On July 22, 2016, the Company entered into a sublease agreement with a third party for the entirety of the remaining term of the First Lease. The sublease commenced on August 22, 2016. The Company received sublease payments totaling $0.2 million through the six months ended June 30, 2017 and expects to receive future minimum payments from this sublease of $0.2 million in the remainder of 2017, which is recognized as an offset to rent expense.

The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Where leases contain escalation clauses, rent abatements, and/or concessions such as rent holidays and landlord or tenant incentives or allowances, the Company applies them in the determination of straight-line rent expense over the lease term. The Company records tenant improvement allowances as deferred rent and associated expenditures as leasehold improvements that are being amortized over the shorter of their estimated useful life or the term of the lease. The Company does not assume renewals in its determination of the lease term unless the renewals are deemed by management to be reasonably assured at lease inception.

As of June 30, 2017, the future minimum lease payments under non-cancelable operating leases are as follows (in thousands):

Year Ended December 31:	
2017 (six months)	$ 1,450
2018	2,586
2019	2,664
2020	2,745
2021	2,829
2022 and later	7,704
	$19,978

Rent expense for the six months ended June 30, 2016 and 2017 was $0.2 million and $1.1 million, respectively.

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6. Convertible Preferred Stock and Stockholders' Deficit

Convertible Preferred Stock

At December 31, 2016, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	184,457,734	184,457,734	$ 1.00	$ 183,951	$ 198,264
Series A-2	17,446,133	17,446,133	2.00	34,885	36,483
Series B-1	32,500,000	32,497,500	4.00	129,837	135,324
Series B-2	18,750,000	—	—	—	—
	253,153,867	**234,401,367**		**$ 348,673**	**$ 370,071**

At June 30, 2017, convertible preferred stock consisted of the following (in thousands, except share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per Share	Carrying Value	Liquidation Preference
Series A-1	184,457,734	184,457,734	$ 1.00	$ 183,951	$ 205,582
Series A-2	17,446,133	17,446,133	2.00	34,885	37,867
Series B-1	32,500,000	32,497,500	4.00	129,837	140,481
Series B-2	18,750,000	—	—	—	—
	253,153,867	**234,401,367**		**$ 348,673**	**$ 383,930**

Common Stock

As of June 30, 2017, the Company had reserved shares of common stock for issuance as follows:

Series A-1 convertible preferred stock outstanding	184,457,734
Series A-2 convertible preferred stock outstanding	17,446,133
Series B-1 convertible preferred stock outstanding	32,500,000
Series B-2 convertible preferred stock outstanding	18,750,000
Options issued and outstanding	23,816,215
Restricted shares subject to future vesting	12,432,793
Early exercised common stock subject to future vesting	1,854,176
Options available for future grant	2,781,675
Shares to be issued under Incro acquisition agreement	324,658
Total	294,363,384

7. Stock Incentive Plan

2015 Stock Incentive Plan

As of June 30, 2017, there were 2,781,675 shares available for the Company to grant under the 2015 Stock Incentive Plan (the "2015 Plan").

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Stock Option Activity

The following table summarizes option award activity under the 2015 plan:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average remaining contractual life (years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2016	21,496,084	$ 0.44	9.03	$ 18,873
Options granted	4,922,500	1.37		
Options exercised	(2,151,431)	0.29		
Options forfeited	(450,938)	0.17		
Balance at June 30, 2017	23,816,215	$ 0.65	8.78	$ 41,600
Options vested and expected to vest at June 30, 2017	16,837,252	$ 0.85	9.03	$ 26,037
Options exercisable at June 30, 2017	2,443,604	$ 0.73	8.98	$ 4,070

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock, as determined by the Board of Directors, as of June 30, 2017.

During the six months ended June 30, 2016 and 2017, the estimated weighted-average grant-date fair value of the options vested was $0.24 and $0.29 per share, respectively, and the estimated weighted-average grant-date fair value of common stock underlying options granted was $0.35 and $1.03 per share, respectively.

Stock Options Granted to Employees with Service-Based Vesting Valuation Assumptions

The estimated fair value of stock options granted to employees were calculated using the Black-Scholes option-pricing model using the following assumptions:

	Six Months Ended June 30,	
	2016	2017
Expected term (in years)	6.08	6.08
Volatility	91.2%-92.2%	89.8%-91.3%
Risk-free interest rate	1.4%-1.5%	1.9%-2.3%
Dividend yield	—	—

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Stock Options Granted to Non-Employees with Service-Based Vesting Valuation Assumptions

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The estimated fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Six Months Ended June 30,	
	2016	2017
Expected term (in years)	9.01-9.60	8.01-9.45
Volatility	94.5%-96.9%	91.4%-98.0%
Risk-free interest rate	1.4%-1.7%	2.3%-2.4%
Dividend yield	—	—

Restricted Stock Activity

The following table summarizes restricted stock activity:

	Shares	Weighted-Average Fair Value at Date of Grant per Share
Unvested at December 31, 2016	15,690,435	$ 0.04
Granted	—	—
Vested	(3,257,642)	0.04
Forfeited	—	—
Unvested at June 30, 2017	12,432,793	$ 0.04
Vested and expected to vest – June 30, 2017	12,432,793	$ 0.04

At June 30, 2017, there was $0.5 million of total unrecognized compensation cost related to non-vested restricted stock, all which is expected to be recognized over a remaining weighted-average period of 1.59 years.

Stock-Based Compensation Expense

The Company's results of operations include expenses relating to employee and non-employee stock-based awards and restricted stock awards, as follows (in thousands):

	Six Months Ended June 30,	
	2016	2017
Research and development	$ 629	$1,222
General and administrative	471	602
Total	$1,100	$1,824

As of June 30, 2017, total unamortized stock-based compensation expense related to unvested employee and non-employee awards that are expected to vest was $10.7 million and $0.5 million respectively. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 3.11 years.

Denali Therapeutics Inc.
Notes to Unaudited Interim Condensed Consolidated Financial Statements

The Company recorded stock-based compensation expense for options issued to non-employees under the 2015 Plan of $0.3 million for each of the six months ended June 30, 2016 and 2017.

8. Net Loss and Unaudited Pro Forma Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share (in thousands, except share and per share data):

	Six Months Ended June 30,	
	2016	2017
Numerator:		
Net loss	$ (36,687)	$ (43,454)
Denominator:		
Weighted average common shares outstanding	21,742,166	37,380,492
Net loss per share, basic and diluted	$ (1.69)	$ (1.16)

Since the Company was in a loss position for all periods presented, basic net loss per share is the same as diluted net loss per share for all periods as the inclusion of all potential shares of common stock outstanding would have been anti-dilutive. Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	June 30,	
	2016	2017
Series A-1 convertible preferred stock	184,457,734	184,457,734
Series A-2 convertible preferred stock	17,446,133	17,446,133
Series B-1 convertible preferred stock	30,585,000	32,497,500
Options issued and outstanding	17,684,763	23,816,215
Restricted shares subject to future vesting	19,286,109	12,432,793
Early exercised common stock subject to future vesting	2,750,000	1,854,176
Shares to be issued under Incro acquisition agreement	108,219	324,658
Total	272,317,958	272,829,209

Pro Forma Net Loss Per Share

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per share (in thousands, except for share and per share amounts):

	Six Months Ended June 30, 2017
Net loss	$ (43,454)
Shares used in computing net loss per share, basic and diluted	37,380,492
Pro forma adjustment to reflect assumed conversion of preferred stock	234,401,367
Shares used to compute pro forma net loss per share, basic and diluted	271,781,859
Pro forma net loss per share, basic and diluted	$ (0.16)

Shares

Denali Therapeutics Inc.

Common Stock

Goldman Sachs & Co. LLC **Morgan Stanley** **J.P. Morgan**

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 13. *Other Expenses of Issuance and Distribution*

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the SEC's registration fee, the Financial Industry Regulatory Authority, Inc.'s filing fee and the exchange listing fee.

	Amount to be Paid
SEC Registration Fee	$ *
FINRA filing fee	*
Exchange listing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees	*
Miscellaneous expenses	*
Total	$ *

* To be provided by amendment.

Item 14. *Indemnification of Directors and Officers*

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify its directors and officers and to purchase insurance with respect to liability arising out of their capacity or status as directors and officers, provided that the person acted in good faith and in a manner the person reasonably believed to be in our best interests, and, with respect to any criminal action, had no reasonable cause to believe the person's actions were unlawful. The Delaware General Corporation Law further provides that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The certificate of incorporation of the registrant to be in effect upon the completion of this offering provides for the indemnification of the registrant's directors and officers to the fullest extent permitted under the Delaware General Corporation Law. In addition, the bylaws of the registrant to be in effect upon the completion of this offering require the registrant to fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of the registrant, or is or was a director or officer of the registrant serving at the registrant's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, to the fullest extent permitted by applicable law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for

payments of unlawful dividends or unlawful stock repurchases or redemptions or (4) for any transaction from which the director derived an improper personal benefit. The registrant's certificate of incorporation to be in effect upon the completion of this offering provides that the registrant's directors shall not be personally liable to it or its stockholders for monetary damages for breach of fiduciary duty as a director and that if the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of the registrant's directors shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, the registrant has entered into separate indemnification agreements with each of the registrant's directors and certain of the registrant's officers which require the registrant, among other things, to indemnify them against certain liabilities which may arise by reason of their status as directors, officers or certain other employees.

The registrant expects to obtain and maintain insurance policies under which its directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities which might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not the registrant would have the power to indemnify such person against such liability under the provisions of the Delaware General Corporation Law.

These indemnification provisions and the indemnification agreements entered into between the registrant and the registrant's officers and directors may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act of 1933, as amended.

The underwriting agreement between the registrant and the underwriters to be filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant's directors and officers and certain controlling persons against specified liabilities, including liabilities under the Securities Act with respect to information provided by the underwriters specifically for inclusion in the registration statement.

Item 15. ***Recent Sales of Unregistered Securities***

The following list sets forth information regarding all unregistered securities sold by us in the past three years. No underwriters were involved in the sales and the certificates representing the securities sold and issued contain legends restricting transfer of the securities without registration under the Securities Act or an applicable exemption from registration.

(a) In March 2015, we issued 23,187,500 restricted shares of our common stock outside of the 2015 Stock Incentive Plan, or 2015 Plan, to Drs. Watts, Schuth and Tessier-Lavigne.

(b) In April 2015, we issued 900,000 restricted shares of our common stock under the 2015 Plan to Drs. Sato and Schenkein and Mr. Flatley.

(c) In May 2015, we issued 39,108,223 shares of our Series A-1 convertible preferred stock at $1.00 per share, for aggregate proceeds of $39,108,223, to a total of 30 accredited investors.

(d) In May 2015, we issued and sold 11,263,154 shares of our common stock to six accredited investors at $0.01 per share.

(e) In June 2015, we issued an aggregate of 5,675,330 shares of our common stock in connection with the closing of the acquisition of Incro Pharmaceuticals Corporation, or Incro, of which 3,783,555 shares were held in escrow by us until such shares vested and were released in September 2016.

(f) In July 2015, we issued 9,683,334 shares of our Series A-1 convertible preferred stock at $1.00 per share, for aggregate proceeds of $9,683,334, to a total of 11 accredited investors.

(g) In August 2015, we issued 3,219,585 restricted shares of our common stock outside of the 2015 Stock Incentive Plan, as amended, or 2015 Plan, to Ryan J. Watts, Ph.D., Alexander O. Schuth, M.D. and Marc Tessier-Lavigne, Ph.D.

(h) In January 2016, we issued 47,000,000 shares of our Series A-1 convertible preferred stock at $1.00 per share, for aggregate proceeds of $47,000,000, to a total of nine accredited investors.

(i) In June 2016, we issued 88,666,177 shares of our Series A-1 convertible preferred stock at $1.00 per share, for aggregate proceeds of $88,666,177, to a total of eight accredited investors.

(j) In June 2016, we issued 17,446,133 shares of our Series A-2 convertible preferred stock at $2.00 per share, for aggregate proceeds of $34,892,266, to a total of 15 accredited investors.

(k) In June 2016, we issued 30,585,000 shares of our Series B-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $122,340,000, to a total of 17 accredited investors.

(l) In August 2016, we issued 1,912,500 shares of our Series B-1 convertible preferred stock at $4.00 per share, for aggregate proceeds of $7,650,000, to a total of 10 accredited investors.

(m) From August 2015 through August 2017, we granted stock options to purchase an aggregate of 31,419,263 shares of common stock to certain employees, directors, and consultants under our 2015 Plan at exercise prices per share ranging from $0.17 to $2.40, for an aggregate exercise price of approximately $20.066 million.

(n) From October 2015 through August 2017, we issued and sold an aggregate of 5,861,172 shares of common stock upon the exercise of options under our 2015 Plan to our directors, employees, consultants and other service providers at exercise prices per share ranging from $0.17 to $1.32, for an aggregate exercise price of approximately $1.253 million.

The offers, sales and issuances of the securities described in Items 15(a) through 15(l) were exempt from registration under the Securities Act under Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited person and had adequate access, through employment, business or other relationships, to information about the registrant.

The offers, sales and issuances of the securities described in Items 15(m) and 15(n) were exempt from registration under the Securities Act under either (1) Rule 701 in that the transactions were under

compensatory benefit plans and contracts relating to compensation as provided under Rule 701 or (2) Section 4(a)(2) of the Securities Act as transactions by an issuer not involving any public offering. The recipients of such securities were the registrant's employees, consultants or directors and received the securities under the registrant's 2015 Plan. The recipients of securities in each of these transactions represented their intention to acquire the securities for investment only and not with view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions.

Item 16. *Exhibit and Financial Statement Schedules*

(a) Exhibits.

We have filed the exhibits listed on the accompanying Exhibit Index of this Registration Statement.

(b) Financial Statement Schedules.

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. *Undertakings*

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreements, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on , 2017.

DENALI THERAPEUTICS INC.

By: _____
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Ryan J. Watts, Ph.D. and Steve E. Krognes as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and substitution, for him or her and in his or her name, place and stead, in any and all capacities (including his capacity as a director and/or officer of Denali Therapeutics Inc.) to sign any or all amendments (including post-effective amendments) to this registration statement and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agents or any of them, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
Ryan J. Watts, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	, 2017
Steve E. Krognes	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	, 2017
Vicki Sato, Ph.D.	Chairperson of our Board of Directors	, 2017
Marc Tessier-Lavigne, Ph.D.	Director	, 2017
Douglas Cole, M.D.	Director	, 2017
Jay Flatley	Director	, 2017

Signature	Title	Date
Robert Nelsen	Director	, 2017
David Schenkein, M.D.	Director	, 2017

EXHIBIT INDEX

Exhibit Number	Description
1.1*	Form of Underwriting Agreement, including Form of Lock-up Agreement.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Registrant, to be in effect upon the completion of this offering.
3.3	Amended and Restated Bylaws of the Registrant, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Registrant, to be in effect upon the completion of this offering.
4.1	Investors' Rights Agreement among the Registrant and certain of its stockholders, dated May 8, 2015, as amended on June 4, 2015, July 22, 2015 and June 22, 2016.
4.2*	Specimen common stock certificate of the Registrant.
5.1*	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.
10.1+*	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.
10.2+	2015 Stock Incentive Plan, as amended, and forms of agreement thereunder.
10.3+*	2017 Equity Incentive Plan and forms of agreements thereunder, to be in effect upon the completion of this offering.
10.4+*	2017 Employee Stock Purchase Plan and form of agreement thereunder, to be in effect upon the completion of this offering.
10.5+*	Offer Letter between the Registrant and Ryan J. Watts, Ph.D.
10.6+*	Offer Letter between the Registrant and Alexander O. Schuth, M.D.
10.7+*	Offer Letter between the Registrant and Steve E. Krognes.
10.8+*	Offer Letter between the Registrant and Carole Ho, M.D.
10.9	Lease Agreement between the Registrant and HCP Oyster Point III LLC, dated September 24, 2015.
10.10*#	Exclusive License Agreement between the Registrant and Genentech, Inc., dated June 17, 2016.
10.11*#	License and Collaboration Agreement between the Registrant, F-star Gamma Limited, F-star Biotechnologische Forschungs-Und Entwicklungsges M.B.H. and F-star Biotechnology Limited, dated August 24, 2016.
23.1*	Consent of Independent Registered Public Accounting Firm.
23.2*	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
24.1	Power of Attorney (see page II-5 to this Form S-1).

* To be filed by amendment.
\+ Indicated management contract or compensatory plan.
\# Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF DENALI THERAPEUTICS INC.

(Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware)

Denali Therapeutics Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "**General Corporation Law**"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Denali Therapeutics Inc., and that this corporation was originally incorporated pursuant to the General Corporation Law on October 14, 2013 under the name SPR Pharma, Inc. and changed its name to Denali Therapeutics Inc. pursuant to a Certificate of Amendment filed on March 6, 2015.

2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Certificate of Incorporation of this corporation, declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

RESOLVED, that the Certificate of Incorporation of this corporation be amended and restated in its entirety to read as follows:

FIRST: The name of this corporation is Denali Therapeutics Inc. (the "**Corporation**").

SECOND: The address of the registered office of the Corporation in the State of Delaware is 1209 Orange Street, Wilmington, Delaware 19801, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 327,149,451 shares of Common Stock, $0.01 par value per share ("**Common Stock**") and (ii) 253,153,867 shares of Preferred Stock, $0.01 par value per share ("**Preferred Stock**").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth herein.

2. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the General Corporation Law. There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

B. PREFERRED STOCK

184,457,734 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-1 Preferred Stock**," 17,446,133 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series A-2 Preferred Stock**" (together with the Series A-1 Preferred Stock, the "**Series A Preferred Stock**"), 32,500,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-1 Preferred Stock**," and 18,750,000 shares of the authorized Preferred Stock of the Corporation are hereby designated "**Series B-2 Preferred Stock**" (together with the Series B-1 Preferred Stock, the "**Series B Preferred Stock**"), each with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. Unless otherwise indicated, references to "sections" or "subsections" in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth.

1. Dividends. From and after the date of the issuance of any shares of Series A-1 Preferred Stock, dividends at the rate per annum of $0.08 per share shall accrue on such shares of Series A-1 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-1 Preferred Stock), from and after the date of issuance of any shares of Series A-2 Preferred Stock, dividends at the rate per annum of $0.16 per share shall accrue on such shares of Series A-2 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-2 Preferred Stock), from and after the date of issuance of any shares of Series B-1 Preferred Stock, dividends at the rate per annum of $0.32 per share shall accrue on such shares of Series B-1 Preferred Stock

(subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B-1 Preferred Stock) and from and after the date of issuance of any shares of Series B-2 Preferred Stock, dividends at a rate per annum equal to 8% of the Series B-2 Original Issue Price shall accrue on such shares of Series B-2 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B-2 Preferred Stock) (together, the "**Accruing Dividends**"). Accruing Dividends shall accrue from day to day, whether or not declared, and shall be cumulative; provided, however, that except as set forth in the following sentence of this Section 1 or in Subsection 2.1 and Section 6, such Accruing Dividends shall be payable only when, as, and if declared by the Board of Directors and the Corporation shall be under no obligation to pay such Accruing Dividends. The Corporation shall not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Corporation (other than dividends on shares of Common Stock payable in shares of Common Stock) unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount at least equal to the sum of (i) the amount of the aggregate Accruing Dividends then accrued on such share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, and not previously paid and (ii) (A) in the case of a dividend on Common Stock or any class or series that is convertible into Common Stock, that dividend per share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into Common Stock and (2) the number of shares of Common Stock issuable upon conversion of a share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, in each case calculated on the record date for determination of holders entitled to receive such dividend or (B) in the case of a dividend on any class or series that is not convertible into Common Stock, at a rate per share of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively, determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to such class or series) and (2) multiplying such fraction by an amount equal to the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable (each as defined below); provided that if the Corporation declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Corporation, the dividend payable to the holders of Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock pursuant to this Section 1 shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest dividend to the Series A-1, Series A-2, Series B-1 or Series B-2 Preferred Stock, respectively. The "**Series A-1 Original Issue Price**" shall mean $1.00 per share, the "**Series A-2 Original Issue Price**" shall mean $2.00 per share, the "**Series B-1 Original Issue Price**" shall mean $4.00 per share and the "**Series B-2 Original Issue Price**" shall mean the price per share (which price shall be not less than $4.00 per share) approved by the Board as such in a resolution adopted by the Board in connection with the initial issuance of shares of Series B-2 Preferred Stock (which resolution will be maintained on file at the Corporation's principal offices and will be available to any stockholder upon request), in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the applicable series of Preferred Stock.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

2.1 Preferential Payments to Holders of Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event (as defined below), the holders of shares of Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to the greater of (i) the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon, or (ii) such amount per share as would have been payable had all shares of Preferred Stock been converted into Common Stock pursuant to Section 4 immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event (the amount payable pursuant to this sentence is hereinafter referred to as the "**Series A-1 Liquidation Amount**," "**Series A-2 Liquidation Amount**," "**Series B-1 Liquidation Amount**" and "**Series B-2 Liquidation Amount**," respectively). If upon any such liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1, the holders of shares of Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

2.2 Payments to Holders of Common Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock, the remaining assets of the Corporation available for distribution to its stockholders shall be distributed among the holders of the shares of Common Stock, pro rata based on the number of shares held by each such holder.

2.3 Deemed Liquidation Events.

2.3.1 Definition. Each of the following events shall be considered a "**Deemed Liquidation Event**" unless the holders of a majority of the outstanding shares of Preferred Stock elect otherwise by written notice sent to the Corporation at least twenty (20) days prior to the effective date of any such event:

(a) a merger or consolidation in which

(i) the Corporation is a constituent party or

(ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation,

except any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, at least a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation; or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation; or

(b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole or the sale or disposition (whether by merger, consolidation or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation.

2.3.2 Effecting a Deemed Liquidation Event.

(a) The Corporation shall not have the power to effect a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(i) unless the agreement or plan of merger or consolidation for such transaction (the "**Merger Agreement**") provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2.

(b) In the event of a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(ii) or 2.3.1(b), if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within ninety (90) days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Preferred Stock no later than the ninetieth (90th) day after the Deemed Liquidation Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause; (ii) to require the redemption of such shares of Preferred Stock, and (iii) if the holders of a majority of the then outstanding shares of Preferred Stock so request in a written instrument delivered to the Corporation not later than one hundred twenty (120) days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors of the Corporation), together with any other assets of the Corporation available for distribution to its stockholders, all to the extent permitted by Delaware law governing distributions to

stockholders (the "**Available Proceeds**"), on the one hundred fiftieth (150th) day after such Deemed Liquidation Event, to redeem all outstanding shares of Preferred Stock at a price per share equal to the Series A-1 Liquidation Amount, Series A-2 Liquidation Amount, Series B-1 Liquidation Amount or Series B-2 Liquidation Amount, as applicable. Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence, if the Available Proceeds are not sufficient to redeem all outstanding shares of Preferred Stock, the Corporation shall ratably redeem each holder's shares of Preferred Stock to the fullest extent of such Available Proceeds, and shall redeem the remaining shares as soon as it may lawfully do so under Delaware law governing distributions to stockholders. The provisions of Section 6 shall apply, with such necessary changes in the details thereof as are necessitated by the context, to the redemption of the Preferred Stock pursuant to this Subsection 2.3.2(b). Prior to the distribution or redemption provided for in this Subsection 2.3.2(b), the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event or in the ordinary course of business.

2.3.3 Amount Deemed Paid or Distributed. The amount deemed paid or distributed to the holders of capital stock of the Corporation upon any such merger, consolidation, sale, transfer, exclusive license, other disposition or redemption shall be the cash or the value of the property, rights or securities paid or distributed to such holders by the Corporation or the acquiring person, firm or other entity. The value of such property, rights or securities shall be determined in good faith by the Board of Directors of the Corporation.

2.3.4 Allocation of Escrow and Contingent Consideration. In the event of a Deemed Liquidation Event pursuant to Subsection 2.3.1(a)(i), if any portion of the consideration payable to the stockholders of the Corporation is payable only upon satisfaction of contingencies (the "**Additional Consideration**"), the Merger Agreement shall provide that (a) the portion of such consideration that is not Additional Consideration (such portion, the "**Initial Consideration**") shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event; and (b) any Additional Consideration which becomes payable to the stockholders of the Corporation upon satisfaction of such contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 after taking into account the previous payment of the Initial Consideration as part of the same transaction. For the purposes of this Subsection 2.3.4, consideration placed into escrow or retained as holdback to be available for satisfaction of indemnification or similar obligations in connection with such Deemed Liquidation Event shall be deemed to be Additional Consideration.

3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class.

3.2 Election of Directors. The holders of record of the shares of Series A Preferred Stock, exclusively and as a separate class, shall be entitled to elect four (4) Series A Directors (as such term is defined in that certain Amended and Restated Voting Agreement dated on or about June 22, 2016 by and between the Corporation and the other parties named therein (as it may be amended from time to time, the "**Voting Agreement**")). Any Series A Director may be removed without cause by, and only by, the affirmative vote of the holders of a majority of the shares of Series A Preferred Stock, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders. If the holders of shares of Series A Preferred Stock fail to elect a sufficient number of directors to fill all directorships for which they are entitled to elect directors, voting exclusively and as a separate class, then any directorship not so filled shall remain vacant until such time as the holders of the Series A Preferred Stock elect a person to fill such directorship by vote or written consent in lieu of a meeting; and no such directorship may be filled by stockholders of the Corporation other than by the holders of Series A Preferred Stock, voting exclusively and as a separate class. The holders of record of the shares of Series B Preferred Stock exclusively and as a separate class, shall be entitled to elect one Series B Director (as such term is defined in the Voting Agreement). The Series A Directors and the Series B Director are collectively referred to as the "**Preferred Directors**." The Series B Director may be removed without cause by, and only by, the affirmative vote of the holders of a majority of the shares of Series B Preferred Stock, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders. If the holders of shares of Series B Preferred Stock fail to elect a sufficient number of directors to fill all directorships for which they are entitled to elect directors, voting exclusively and as a separate class, then any directorship not so filled shall remain vacant until such time as the holders of the Series B Preferred Stock elect a person to fill such directorship by vote or written consent in lieu of a meeting; and no such directorship may be filled by stockholders of the Corporation other than by the holders of Series B Preferred Stock, voting exclusively and as a separate class. The holders of record of the shares of Common Stock and of any other class or series of voting stock (including the Preferred Stock), exclusively and voting together as a single class, shall be entitled to elect the balance of the total number of directors of the Corporation. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. Except as otherwise provided in this Subsection 3.2, a vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series or by any remaining director or directors elected by the holders of such class or series pursuant to this Subsection 3.2. The rights of the holders of the Series A Preferred Stock under this Subsection 3.2 shall terminate on the first date on which there are issued and outstanding less than 100,000 shares of Series A Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Series A Preferred Stock or any series thereof). The rights of the holders of the Series B Preferred Stock under this Subsection 3.2 shall terminate on

the first date following the Series B-1 Original Issue Date (as defined below) on which there are issued and outstanding less than 100,000 shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Series B Preferred Stock or any series thereof).

3.3 Preferred Stock Protective Provisions. At any time when at least 100,000 shares of Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination, or other similar recapitalization with respect to the Preferred Stock) are outstanding, the Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of a majority of the then outstanding shares of Preferred Stock, given in writing or by vote at a meeting, consenting or voting (as the case may be) separately as a class, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio,* and of no force or effect.

3.3.1 liquidate, dissolve or wind-up the business and affairs of the Corporation, effect any merger or consolidation or any other Deemed Liquidation Event, or consent to any of the foregoing;

3.3.2 amend, alter or repeal any provision of the Certificate of Incorporation or By-laws of the Corporation;

3.3.3 create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless the same ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and rights of redemption, or increase the authorized number of shares of Preferred Stock;

3.3.4 create, or authorize the creation of, or issue or obligate itself to issue shares of Common Stock representing more than an aggregate of four percent (4%) of the outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities) in any single calendar year (the "**4% Annual Cap**") as compensation to officers, directors, employees, consultants and other advisors to the Corporation;

3.3.5 increase or decrease (other than for decreases resulting from conversion of the Preferred Stock) the authorized number of shares of Preferred Stock or any series thereof;

3.3.6 (a) reclassify, alter or amend any existing security of the Corporation that is pari passu with the Preferred Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends or rights of redemption, if such reclassification, alteration or amendment would render such other security senior to the Preferred Stock in respect of any such right, preference, or privilege or (b) reclassify, alter or amend any existing security of the Corporation that is junior to the Preferred

Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends or rights of redemption, if such reclassification, alteration or amendment would render such other security senior to or pari passu with the Preferred Stock in respect of any such right, preference or privilege;

3.3.7 purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Corporation other than (a) redemptions of or dividends or distributions on the Preferred Stock as expressly authorized herein, (b) dividends or other distributions payable on the Common Stock solely in the form of additional shares of Common Stock and (c) repurchases of stock from former employees, officers, directors, consultants or other persons who performed services for the Corporation or any subsidiary in connection with the cessation of such employment or service at the lower of the original purchase price or the then-current fair market value thereof;

3.3.8 create, or authorize the creation of, or issue, or authorize the issuance of any debt security, or permit any subsidiary to take any such action with respect to any debt security, unless such debt security has received the prior approval of the Board of Directors, including the approval of a majority of the Preferred Directors;

3.3.9 create, or hold capital stock in, any subsidiary that is not wholly owned (either directly or through one or more other subsidiaries) by the Corporation, or sell, transfer or otherwise dispose of any capital stock of any direct or indirect subsidiary of the Corporation, or permit any direct or indirect subsidiary to sell, lease, transfer, exclusively license or otherwise dispose (in a single transaction or series of related transactions) of all or substantially all of the assets of such subsidiary;

3.3.10 increase or decrease the authorized number of directors constituting the Board of Directors;

3.3.11 issue shares of capital stock of the Company or any rights, options or warrants to acquire shares of capital stock of the Company representing more than five percent (5%) of the then outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities) to a third party in connection with any singular sponsored research, collaboration, technology license, development, OEM, manufacturing, marketing, or other similar agreement or strategic partnership in which the Company enters into a simultaneous business relationship with the acquiror of such securities;

3.3.12 change the principal line of business of the Company from the basic discovery, research and commercialization of drugs to treat human disease, with an emphasis on human neurologic diseases;

3.3.13 enter into any transaction or series of related transactions having an aggregate value of $150,000.00 or more with any director or executive officer of the Corporation (other than in connection with their services as a director or employee of the Corporation) or any stockholder owning more than five percent (5%) of the outstanding shares of capital stock of the Corporation; or

3.3.14 amend this Section 3.3.

4. Optional Conversion.

The holders of the Preferred Stock shall have conversion rights as follows (the "**Conversion Rights**"):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and non-assessable shares of Common Stock as is determined (w) by dividing the Series A-1 Original Issue Price by the Series A-1 Conversion Price (as defined below) in the case of the Series A-1 Preferred Stock, (x) by dividing the Series A-2 Original Issue Price by the Series A-2 Conversion Price (as defined below), in the case of the Series A-2 Preferred Stock, (y) by dividing the Series B-1 Original Issue Price by the Series B-1 Conversion Price (as defined below), in the case of the Series B-1 Preferred Stock, or (z) by dividing the Series B-2 Original Issue Price by the Series B-2 Conversion Price (as defined below), in the case of the Series B-2 Preferred Stock, in each case in effect at the time of conversion. The "**Series A-1 Conversion Price**" shall initially be equal to $1.00. The "**Series A-2 Conversion Price**" shall initially be equal to $2.00. The "**Series B-1 Conversion Price**" shall initially be equal to $4.00. The "**Series B-2 Conversion Price**" shall initially be equal to the Series B-2 Original Issue Price. The Series A-1 Conversion Price, the Series A-2 Conversion Price, the Series B-1 Conversion Price and the Series B-2 Conversion Price shall be known individually or collectively, as applicable, as the "Conversion Price". Such initial Conversion Price, and the rate at which shares of Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Termination of Conversion Rights. In the event of a notice of redemption of any shares of Preferred Stock pursuant to Section 6, the Conversion Rights of the shares designated for redemption shall terminate at the close of business on the last full day preceding the date fixed for redemption, unless the redemption price is not fully paid on such redemption date, in which case the Conversion Rights for such shares shall continue until such price is paid in full. In the event of liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Preferred Stock.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by

the Board of Directors of the Corporation. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Preferred Stock to voluntarily convert shares of Preferred Stock into shares of Common Stock, such holder shall (a) provide written notice to the Corporation's transfer agent at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent) that such holder elects to convert all or any number of such holder's shares of Preferred Stock and, if applicable, any event on which such conversion is contingent and (b), if such holder's shares are certificated, surrender the certificate or certificates for such shares of Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent). Such notice shall state such holder's name or the names of the nominees in which such holder wishes the shares of Common Stock to be issued. If required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such notice and, if applicable, certificates (or lost certificate affidavit and agreement) shall be the time of conversion (the "**Conversion Time**"), and the shares of Common Stock issuable upon conversion of the specified shares shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time (i) issue and deliver to such holder of Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Preferred Stock represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when the Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation shall take such

corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action which would cause an adjustment reducing the applicable Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and non-assessable shares of Common Stock at such adjusted applicable Conversion Price.

4.3.3 Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any dividends declared but unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to the applicable Conversion Price shall be made for any declared but unpaid dividends on the Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

4.4 Adjustments to Applicable Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(a) "**Option**" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "**Series B-1 Original Issue Date**" shall mean the date on which the first share of Series B-1 Preferred Stock was issued.

(c) "**Convertible Securities**" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) "**Additional Shares of Common Stock**" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series B-1 Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively, "**Exempted Securities**"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on Preferred Stock;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors of the Corporation, including the approval of a majority of the Preferred Directors; provided that such issuance does not exceed the 4% Annual Cap;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security.

(v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors of the Corporation, including the approval of a majority of the Preferred Directors;

(vi) shares of Common Stock, Options or Convertible Securities issued to suppliers or third party service providers in connection with the provision of goods or services pursuant to transactions approved by the Board of Directors of the Corporation, including the approval of a majority of the Preferred Directors;

(vii) shares of Common Stock, Options or Convertible Securities issued to a third party in connection with any singular sponsored research, collaboration, technology license, development, OEM, manufacturing, marketing or other similar agreement or strategic partnership in which the Company enters into a simultaneous business relationship with the acquirer of such securities approved by the Board of Directors of the Corporation, including the approval of a majority of the Preferred Directors; provided that such

issuance to such third party does not exceed five percent (5%) of the then-outstanding shares of Common Stock on a fully diluted basis (assuming the conversion of all outstanding shares of Preferred Stock and the exercise and conversion of all outstanding Convertible Securities);

(viii) shares of Common Stock Options or Convertible Securities issued pursuant to the acquisition of another corporation by the Corporation by merger, purchase of substantially all of the assets or other reorganization or to a joint venture agreement, provided, that such issuances are approved by the Board of Directors of the Corporation, including the approval of a majority of the Preferred Directors; and

(ix) shares of Preferred Stock issued pursuant to that certain Preferred Stock Purchase Agreement, dated as of May 8, 2015, among the Corporation and the Investors named therein, as amended and as in effect on or about June 22, 2016 (the "**Purchase Agreement**").

4.4.2 No Adjustment of Conversion Price. No adjustment in the Series A-1 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of majority of the then outstanding shares of Series A-1 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series A-2 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series A-2 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B-1 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series B-1 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B-2 Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series B-2 Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the applicable Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such applicable Conversion Price as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the applicable Conversion Price to an amount which exceeds the lower of (i) the applicable Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the applicable Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4 (either because the consideration per share (determined pursuant to Subsection 4.4.5) of the Additional Shares of Common Stock subject thereto was equal to or greater than the applicable Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series B-1 Original Issue Date), are revised after the Series B-1 Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Conversion Price pursuant to the terms of Subsection 4.4.4, the applicable Conversion Price shall be readjusted to such applicable Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the applicable Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the applicable Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the applicable Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Conversion Price Upon Issuance of Additional Shares of Common Stock.

(a) In the event the Corporation shall at any time after the Series B-1 Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Conversion Price for a series of Preferred Stock in effect immediately prior to such issue, then such Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(i) "CP_2" shall mean the applicable Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(ii) "CP_1:" shall mean the applicable Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(iii) “A” shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(iv) “B” shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP_1); and

(v) “C” shall mean the number of such Additional Shares of Common Stock issued in such transaction.

Notwithstanding the foregoing, no adjustment shall be made to the Series B-2 Conversion Price with respect to any issuance of Additional Shares of Common Stock issued prior to the first issuance of shares of Series B-2 Preferred Stock.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors of the Corporation; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors of the Corporation.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing:

(i) The total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the applicable Conversion Price pursuant to the terms of Subsection 4.4.4, and such issuance dates occur within a period of no more than ninety (90) days from the first such issuance to the final such issuance, then, upon the final such issuance, the applicable Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series B-1 Original Issue Date effect a subdivision of the outstanding Common Stock, the applicable Conversion Price in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series B-1 Original Issue Date combine the outstanding shares of Common Stock, the applicable Conversion Price in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the applicable Conversion Price in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the applicable Conversion Price then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the applicable Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the applicable Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the holders of Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series B-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization. etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not the Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Preferred Stock shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board of Directors of the Corporation) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in

and other adjustments of the applicable Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the Preferred Stock. For the avoidance of doubt, nothing in this Subsection 4.8 shall be construed as preventing the holders of Preferred Stock from seeking any appraisal rights to which they are otherwise entitled under the DGCL in connection with a merger triggering an adjustment hereunder, nor shall this Subsection 4.8 be deemed conclusive evidence of the fair value of the shares of Preferred Stock in any such appraisal proceeding.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the applicable Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than ten (10) days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Preferred Stock (but in any event not later than ten (10) days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the applicable Conversion Price then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of the Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Preferred Stock and the Common Stock. Such notice shall be sent at least ten (10) days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events. Upon either (a) the closing of the sale of shares of Common Stock to the public at a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock), in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $50,000,000 of gross proceeds to the Corporation or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the then outstanding shares of Preferred Stock (the time of such closing or the date and time specified or the time of the event specified in such vote or written consent is referred to herein as the "**Mandatory Conversion Time**"), then (i) all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate as calculated pursuant to Subsection 4.1.1 and (ii) such shares may not be reissued by the Corporation.

5.2 Procedural Requirements. All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock in certificated form shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Subsection 5.1, including the rights, if any, **to** receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender any certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of any certificate or certificates of such holders (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and, if applicable, the surrender of any certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock, the Corporation shall (a) issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof and (b) pay cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable

upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

5A. Special Mandatory Conversion and Special Mandatory Redemption.

5A.1. Trigger Event. In the event that any Investor (as defined in the Purchase Agreement) does not purchase the shares of Preferred Stock that such Investor has agreed to purchase in any Tranche Closing (as defined in and contemplated by the Purchase Agreement), other than as a result of the nonfulfillment of such Investor's conditions to purchase such shares (as set forth in Section 5 of the Purchase Agreement), then (i) each share of Preferred Stock originally purchased by such Investor under the Purchase Agreement shall automatically, and without any further action on the part of the holder thereof, be converted into one percent (1%) of the number of shares of Common Stock that would otherwise be issuable upon conversion of such share pursuant to Section 4.1, effective upon, subject to, and concurrently with, the consummation of such Tranche Closing and (ii) with respect to any shares of Common Stock outstanding at the time of such Tranche Closing that were issued to such Investor upon conversion of any shares of Preferred Stock originally purchased by such Investor under the Purchase Agreement pursuant to Section 4.1 prior to such Tranche Closing, ninety nine percent (99%) of the shares of Common Stock issued upon such conversion (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock occurring after the conversion and before such Tranche Closing) shall be redeemed by the Corporation at a price per share equal to $0.01. For purposes of determining the number of shares of Preferred Stock an Investor has purchased in a Tranche Closing, all Shares purchased by Affiliates of such Investor shall be aggregated with the Shares purchased by such Investor (provided that no Shares shall be attributed to more than one entity or person within any such group of affiliated entities or persons). "**Affiliate**" shall mean, with respect to any specified individual, corporation, partnership, trust, limited liability company, association or other entity (collectively, a "**Person**"), any other Person who, directly or indirectly, controls, is controlled by or is under common control with such Person, including without limitation any general partner, managing member, limited partner, member, manager, employee, officer or director of such Person or any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person. For purposes of this definition, (i) the term "control" when used with respect to any Person means the power to direct the management or policies of such Person, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" shall have meanings correlative to the foregoing, and (ii) Asia Ventures III L.P., Japan Ventures I L.P. and FIL Capital Investments (Mauritius) II Limited and their Affiliates are deemed to be Affiliates of F-Prime Capital Partners Healthcare Fund IV LP. Such conversion is referred to as a "**Special Mandatory Conversion**." Such redemption is referred to as the "**Special Mandatory Redemption**."

5A.2. Procedural Requirements for Special Mandatory Conversion. Upon a Special Mandatory Conversion, each holder of shares of Preferred Stock converted pursuant to Subsection 5A.1 shall be sent written notice of such Special Mandatory Conversion and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5A. Upon receipt of such notice, each holder of such shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Subsection 5A.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the time of the Special Mandatory Conversion (notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates therefor (or lost certificate affidavit and agreement), to receive the items provided for in the next sentence of this Subsection 5A.1. As soon as practicable after the Special Mandatory Conversion and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Preferred Stock so converted, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Preferred Stock accordingly.

5A.3. Procedural Requirements for Special Mandatory Redemption. Upon a Special Mandatory Redemption, each holder of shares of Common Stock redeemed pursuant to Subsection 5A.1 (a "**Redeemed Holder**") shall be sent written notice of such Special Mandatory Redemption and the place designated for mandatory redemption of all such shares of Common Stock pursuant to this Section 5A. Upon receipt of such notice, each Redeemed Holder shall surrender his, her or its certificate or certificates for all such shares (or, if such Redeemed Holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for redemption shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered Redeemed Holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Common Stock redeemed pursuant to

Subsection 5A.1, including the rights, if any, to receive notices and vote, will terminate at the time of the Special Mandatory Redemption (notwithstanding the failure of the Redeemed Holder to surrender the certificates for such shares at or prior to such time). Such redeemed Common Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Common Stock accordingly.

6. Redemption.

6.1 General. Unless prohibited by Delaware law governing distributions to stockholders, shares of Preferred Stock shall be redeemed by the Corporation at a price equal to the Series A-1 Original Issue Price, Series A-2 Original Issue Price, Series B-1 Original Issue Price or Series B-2 Original Issue Price, as applicable, per share, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the "**Redemption Price**"), in three (3) annual installments commencing not more than sixty (60) days after receipt by the Corporation at any time on or after the fifth anniversary of the Series B-1 Original Issue Date, from the holders of a majority of the then outstanding shares of Preferred Stock, of written notice requesting redemption of all shares of Preferred Stock (the "**Redemption Request**"). Upon receipt of a Redemption Request, the Corporation shall apply all of its assets to any such redemption, and to no other corporate purpose, except to the extent prohibited by Delaware law governing distributions to stockholders. The date of each such installment shall be referred to as a "**Redemption Date**." On each Redemption Date, the Corporation shall redeem, on a pro rata basis in accordance with the number of shares of Preferred Stock owned by each holder, that number of outstanding shares of Preferred Stock determined by dividing (i) the total number of shares of Preferred Stock outstanding immediately prior to such Redemption Date by (ii) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies); provided, however, that Excluded Shares (as such term is defined in Subsection 6.2) shall not be redeemed and shall be excluded from the calculations set forth in this sentence. If on any Redemption Date Delaware law governing distributions to stockholders prevents the Corporation from redeeming all shares of Preferred Stock to be redeemed, the Corporation shall ratably redeem the maximum number of shares that it may redeem consistent with such law, and shall redeem the remaining shares as soon as it may lawfully do so under such law.

6.2 Redemption Notice. The Corporation shall send written notice of the mandatory redemption (the "**Redemption Notice**") to each holder of record of Preferred Stock not less than forty (40) days prior to each Redemption Date. Each Redemption Notice shall state:

(a) the number of shares of Preferred Stock held by the holder that the Corporation shall redeem on the Redemption Date specified in the Redemption Notice;

(b) the Redemption Date and the Redemption Price;

(c) the date upon which the holder's right to convert such shares terminates (as determined in accordance with Subsection 4.1); and

(d) for holders of shares in certificated form, that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Preferred Stock to be redeemed.

If the Corporation receives, on or prior to the twentieth (20th) day after the date of delivery of the Redemption Notice to a holder of Preferred Stock, written notice from such holder that such holder elects to be excluded from the redemption provided in this Section 6, then the shares of Preferred Stock registered on the books of the Corporation in the name of such holder at the time of the Corporation's receipt of such notice shall thereafter be "**Excluded Shares**." Excluded Shares shall not be redeemed or redeemable pursuant to this Section 6, whether on such Redemption Date or thereafter.

6.3 Surrender of Certificates; Payment. On or before the applicable Redemption Date, each holder of shares of Preferred Stock to be redeemed on such Redemption Date, unless such holder has exercised his, her or its right to convert such shares as provided in Section 4, shall, if a holder of shares in certificated form, surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. In the event less than all of the shares of Preferred Stock represented by a certificate are redeemed, a new certificate, instrument, or book entry representing the unredeemed shares of Preferred Stock shall promptly be issued to such holder.

6.4 Rights Subsequent to Redemption. If the Redemption Notice shall have been duly given, and if on the applicable Redemption Date the Redemption Price payable upon redemption of the shares of Preferred Stock to be redeemed on such Redemption Date is paid or tendered for payment or deposited with an independent payment agent so as to be available therefor in a timely manner, then notwithstanding that any certificates evidencing any of the shares of Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Preferred Stock shall cease to accrue after such Redemption Date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Redemption Price without interest upon surrender of any such certificate or certificates therefor.

7. Redeemed or Otherwise Acquired Shares. Any shares of Preferred Stock that are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Preferred Stock following redemption.

8. Waiver. Any of the rights, powers, preferences and other terms of the Preferred Stock set forth herein may be waived on behalf of all holders of Preferred Stock by the affirmative written consent or vote of the holders of a majority of the shares of Preferred Stock then outstanding, consenting or voting as a single class.

9. Notices. Any notice required or permitted by the provisions of this Article Fourth to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

FIFTH: Subject to any additional vote required by the Certificate of Incorporation or By-laws, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the By-laws of the Corporation.

SIXTH: Subject to any additional vote required by the Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the By-laws of the Corporation.

SEVENTH: Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

EIGHTH: Meetings of stockholders may be held within or without the State of Delaware, as the By-laws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the By-laws of the Corporation.

NINTH: To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Ninth to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Ninth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

TENTH: To the fullest extent permitted by applicable law, the Corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the Corporation (and any other persons to which General Corporation Law permits the Corporation to provide indemnification) through By-law provisions, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise, in excess of the indemnification and advancement otherwise permitted by Section 145 of the General Corporation Law.

Any amendment, repeal or modification of the foregoing provisions of this Article Tenth shall not adversely affect any right or protection of any director, officer or other agent of the Corporation existing at the time of such amendment, repeal or modification.

ELEVENTH: The Corporation renounces, to the fullest extent permitted by law, any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An "**Excluded Opportunity**" is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, "**Covered Persons**"), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person's capacity as a director of the Corporation.

TWELFTH: Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery in the State of Delaware shall be the sole and exclusive forum for any stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation, its directors, officers or employees arising pursuant to any provision of the Delaware General Corporation Law or the Corporation's certificate of incorporation or by-laws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by the internal affairs doctrine, except for, as to each of (i) through (iv) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. If any provision or provisions of this Article Twelfth shall be held to be invalid, illegal or unenforceable as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Article Twelfth (including, without limitation, each portion of any sentence of this Article Twelfth containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

* * *

3. That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

4. That this Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this Corporation's Certificate of Incorporation, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

IN WITNESS WHEREOF, this Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 21st day of June, 2016.

By: /s/ Ryan Watts

Name: Ryan Watts
Title: President and CEO

CERTIFICATE OF AMENDMENT
TO
AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
DENALI THERAPEUTICS INC.

Denali Therapeutics Inc. (the "**Corporation**"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "**DGCL**"), does hereby certify:

FIRST The original Certificate of Incorporation of the Corporation was filed with the Secretary of State of the State of Delaware on October 14, 2013 under the name SPR Pharma, Inc.

SECOND: The first paragraph of Article FOURTH of the Amended and Restated Certificate of Incorporation is hereby amended in its entirety to read as follows:

"The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 334,349,451 shares of Common Stock, $0.01 par value per share ("**Common Stock**") and (ii) 253,153,867 shares of Preferred Stock, $0.01 par value per share ("**Preferred Stock**")."

THIRD: This Certificate of Amendment of Amended and Restated Certificate of Incorporation has been duly adopted in accordance with Sections 228 and 242 of the DGCL, with the approval of the Corporation's stockholders having been given by written consent without a meeting in accordance with Section 228 of the DGCL. The undersigned affirms, under penalties of perjury, that this Certificate of Amendment of Amended and Restated Certificate of Incorporation is the act and deed of the Corporation and that the facts stated herein are true.

IN WITNESS WHEREOF, the Corporation has caused this Certificate of Amendment of Amended and Restated Certificate of Incorporation be signed by an authorized officer of the Corporation on December 13, 2016.

/s/ Ryan Watts
Ryan Watts, Ph.D.
President and Chief Executive Officer

Exhibit 3.3

AMENDED AND RESTATED

BY-LAWS

OF

DENALI THERAPEUTICS INC.

(a Delaware corporation)

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ARTICLE I

STOCKHOLDERS

1.1 Place of Meetings. All meetings of stockholders shall be held at such place as may be designated from time to time by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President or, if not so designated, at the principal office of the corporation. The Board of Directors may, in its sole discretion, determine that a meeting shall not be held at any place, but may instead be held solely by means of remote communication in a manner consistent with the General Corporation Law of the State of Delaware.

1.2 Annual Meeting. The annual meeting of stockholders for the election of directors and for the transaction of such other business as may properly be brought before the meeting shall be held on a date and at a time designated by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President (which date shall not be a legal holiday in the place where the meeting is to be held).

1.3 Special Meetings. Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President, and may not be called by any other person or persons. The Board of Directors may postpone or reschedule any previously scheduled special meeting of stockholders. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting.

1.4 Notice of Meetings. Except as otherwise provided by law, notice of each meeting of stockholders; whether annual or special, shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting. Without limiting the manner by which notice otherwise may be given to stockholders, any notice shall be effective if given by a form of electronic transmission consented to (in a manner consistent with the General Corporation Law of the State of Delaware) by the stockholder to whom the notice is given. The notices of all meetings shall state the place, .if any, date and time of the meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting. The notice of a special meeting shall state, in addition, the purpose or purposes for which the meeting is called. If notice is given by mail, such notice shall be deemed given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. If notice is given by electronic transmission, such notice shall be deemed given at the time specified in Section 232 of the General Corporation Law of the State of Delaware.

1.5 Voting List. The Secretary shall prepare, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, for a period of at least 10 days prior to the meeting: (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the corporation. If the meeting is to

be held at a physical location (and not solely by means of remote communication), then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. The list shall presumptively determine the identity of the stockholders entitled to vote at the meeting and the number of shares held by each of them.

1.6 Quorum. Except as otherwise provided by law, the Certificate of Incorporation or these Amended and Restated By-laws (these "**By-laws**"), the holders of a majority in voting power of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at the meeting, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum for the transaction of business; provided, however, that where a separate vote by a class or classes or series of capital stock is required by law or the Certificate of Incorporation, the holders of a majority in voting power of the shares of such class or classes or series of the capital stock of the corporation issued and outstanding and entitled to vote on such matter, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum entitled to take action with respect to the vote on such matter. A quorum, once established at a meeting, shall not be broken by the withdrawal of enough votes to leave less than a quorum.

1.7 Adjournments. Any meeting of stockholders may be adjourned from time to time to any other time and to any other place at which a meeting of stockholders may be held under these By-laws by the chairman of the meeting or by the stockholders present or represented at the meeting and entitled to vote, although less than a quorum. It shall not be necessary to notify any stockholder of any adjournment of less than 30 days if the time and place, if any, of the adjourned meeting, and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting, are announced at the meeting at which adjournment is taken, unless after the adjournment a new record date is fixed for the adjourned meeting. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting.

1.8 Voting and Proxies. Each stockholder shall have one vote for each share of stock entitled to vote held of record by such stockholder and a proportionate vote for each fractional share so held, unless otherwise provided by law or the Certificate of Incorporation. Each stockholder of record entitled to vote at a meeting of stockholders, or to express consent or dissent to corporate action without a meeting, may vote or express such consent or dissent in person (including by means of remote communications, if any, by which stockholders may be deemed to be present in person and vote at such meeting) or may authorize another person or persons to vote or act for such stockholder by a proxy executed or transmitted in a manner permitted by the General Corporation Law of the State of Delaware by the stockholder or such stockholder's authorized agent and delivered (including by electronic transmission) to the Secretary of the corporation. No such proxy shall be voted or acted upon after three years from the date of its execution, unless the proxy expressly provides for a longer period.

1.9 Action at Meeting. When a quorum is present at any meeting, any matter other than the election of directors to be voted upon by the stockholders at such meeting shall be decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter (or if there are two or more classes or series of stock entitled to vote as separate classes, then in the case of each such class or series, the holders of a majority in voting power of the shares of stock of that class or series present or represented at the meeting and voting affirmatively or negatively on such matter), except when a different vote is required by law, the Certificate of Incorporation or these By-laws. When a quorum is present at any meeting, any election by stockholders of directors shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

1.10 Conduct of Meetings.

(a) Chairman of Meeting. Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in the Chairman's absence by the Vice Chairman of the Board, if any, or in the Vice Chairman's absence by the Chief Executive Officer, or in the Chief Executive Officer's absence, by the President, or in the President's absence by a Vice President, or in the absence of all of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen by vote of the stockholders at the meeting. The Secretary shall act as secretary of the meeting, but in the Secretary's absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) Rules, Regulations and Procedures. The Board of Directors may adopt by resolution such rules, regulations and procedures for the conduct of any meeting of stockholders of the corporation as it shall deem appropriate including, without limitation, such guidelines and procedures as it may deem appropriate regarding the participation by means of remote communication of stockholders and proxyholders not physically present at a meeting. Except to the extent inconsistent with such rules, regulations and procedures as adopted by the Board of Directors, the chairman of any meeting of stockholders shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, the following; (i) the establishment of an agenda or order of business for the meeting; (ii) rules and procedures for maintaining order at the meeting and the safety of those present; (iii) limitations on attendance at or participation in the meeting to stockholders of record of the corporation, their duly authorized and constituted proxies or such other persons as shall be determined; (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof; and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

1.11 Action without Meeting.

(a) Taking of Action by Consent. Any action required or permitted to be taken at any annual or special meeting of stockholders of the corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Except as otherwise provided by the Certificate of Incorporation, stockholders may act by written consent to elect directors; provided, however, that, if such consent is less than unanimous, such action by written consent may be in lieu of holding an annual meeting only if all of the directorships to which directors could be elected at an annual meeting held at the effective time of such action are vacant and are filled by such action.

(b) Electronic Transmission of Consents. A telegram, cablegram or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, or by a person or persons authorized to act for a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this section, provided that any such telegram, cablegram or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the telegram, cablegram or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder or proxyholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such telegram, cablegram or electronic transmission. The date on which such telegram, cablegram or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by telegram, cablegram or other electronic transmission shall be deemed to have been delivered until such consent is ‘reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation’s registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by telegram, cablegram or other electronic transmission may be otherwise delivered to the principal place of business Of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the Board of Directors. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

(c) Notice of Taking of Corporate Action. Prompt notice of the taking of corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of holders to take the action were delivered to the corporation.

ARTICLE II

DIRECTORS

2.1 General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation except as otherwise provided by law or the Certificate of Incorporation.

2.2 Number, Election and Qualification. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the corporation shall be established from time to time by the stockholders or the Board of Directors. The directors shall be elected at the annual meeting of stockholders by such stockholders as have the right to vote on such election. Election of directors need not be by written ballot. Directors need not be stockholders of the corporation.

2.3 Chairman of the Board: Vice Chairman of the Board. The Board of Directors may appoint from its members a Chairman of the Board and a Vice Chairman of the Board, neither of whom need be an employee or officer of the corporation. If the Board of Directors appoints a Chairman of the Board, such Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors and, if the Chairman of the Board is also designated as the corporation's Chief Executive Officer, shall have the powers and duties of the Chief Executive Officer prescribed in Section 3.7 of these By-laws. If the Board of Directors appoints a Vice Chairman of the Board, such Vice Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors. Unless otherwise provided by the Board of Directors, the Chairman of the Board or, in the Chairman's absence, the Vice Chairman of the Board, if any, shall preside at all meetings of the Board of Directors.

2.4 Tenure. Each director shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.5 Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2.2 of these By-laws shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

2.6 Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting of the Board of Directors duly held at which a quorum is present shall be regarded as the act of the Board of Directors, unless a greater number is required by law or by the Certificate of Incorporation.

2.7 Removal. Except as otherwise provided by the General Corporation Law of the State of Delaware, any one or more or all of the directors of the corporation may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except that the directors elected by the holders of a particular class or series of stock may be removed without cause only by vote of the holders of a majority of the outstanding shares of such class or series.

2.8 Vacancies. Subject to the rights of holders of any series of Preferred Stock to elect directors, unless and until filled by the stockholders, any vacancy or newly-created directorship on the Board of Directors, however occurring, may be filled by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director. A director elected to fill a vacancy shall be elected for the unexpired term of such director's predecessor in office, and a director chosen to fill a position resulting from a newly-created directorship shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.9 Resignation. Any director may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal office or to the Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon delivery unless it is specified to be effective at some later time or upon the happening of some later event.

2.10 Regular Meetings. Regular meetings of the Board of Directors may be held without notice at such time and place as shall be determined from time to time by the Board of Directors; provided that any director who is absent when such a determination is made shall be given notice of the determination. A regular meeting of the Board of Directors may be held without notice immediately after and at the same place as the annual meeting of stockholders.

2.11 Special Meetings. Special meetings of the Board of Directors may be held at any time and place designated in a call by the Chairman of the Board, the Chief Executive Officer, the President, two or more directors, or by one director in the event that there is only a single director in office.

2.12 Notice of Special Meetings. Notice of the date, place, if any, and time of any special meeting of directors shall be given to each director by the Secretary or by the officer or one of the directors calling the meeting. Notice shall be duly given to each director (a) in person or by telephone at least 24 hours in advance of the meeting, (b) by sending written notice by reputable overnight courier, telecopy, facsimile or electronic transmission, or delivering written notice by hand, to such director's last known business, home or electronic transmission address at least 48 hours in advance of the meeting, or (c) by sending written notice by first-class mail to such director's last known business or home address at least 72 hours in advance of the meeting. A notice or waiver of notice of a meeting of the Board of Directors need not specify the purposes of the meeting.

2.13 Meetings by Conference Communications Equipment. Directors may participate in meetings of the Board of Directors or any committee thereof by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

2.14 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent to the action in writing or by electronic transmission, and the written consents or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

2.15 Committees. The Board of Directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation with such lawfully delegable powers and duties as the Board of Directors thereby confers, to serve at the pleasure of the Board of Directors. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members of the committee present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board of Directors and subject to the provisions of law, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation and may authorize the seal of the corporation to be affixed to all papers which may require it. Each such committee shall keep minutes and make such reports as the Board of Directors may from time to time request. Except as the Board of Directors may otherwise determine, any committee may make rules for the conduct of its business, but unless otherwise provided by the directors or in such rules, its business shall be conducted as nearly as possible in the same manner as is provided in these By-laws for the Board of Directors. Except as otherwise provided in the Certificate of Incorporation, these By-laws, or the resolution of the Board of Directors designating the committee, a committee may create one or more subcommittees, each subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

2.16 Compensation of Directors. Directors may be paid such compensation for their services and such reimbursement for expenses of attendance at meetings as the Board of Directors may from time to time determine. No such payment shall preclude any director from serving the corporation or any of its parent or subsidiary entities in any other capacity and receiving compensation for such service.

ARTICLE III

OFFICERS

3.1 Titles. The officers of the corporation shall consist of a Chief Executive Officer, a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, including one or more Vice Presidents, Assistant Treasurers and Assistant Secretaries. The Board of Directors may appoint such other officers as it may deem appropriate.

3.2 Election. The Chief Executive Officer, President, Treasurer and Secretary shall be elected annually by the Board of Directors at its first meeting following the annual meeting of stockholders. Other officers may be appointed by the Board of Directors at such meeting or at any other meeting.

3.3 Qualification. No officer need be a stockholder. Any two or more offices may be held by the same person.

3.4 Tenure. Except as otherwise provided by law, by the Certificate of Incorporation or by these By-laws, each officer shall hold office until such officer's successor is elected and qualified, unless a different term is specified in the resolution electing or appointing such officer, or until such officer's earlier death, resignation or removal.

3.5 Resignation and Removal. Any officer may resign by delivering a written resignation to the corporation at its principal office or to the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event. Any officer may be removed at any time, with or without cause, by vote of a majority of the directors then in office. Except as the Board of Directors may otherwise determine, no officer who resigns or is removed shall have any right to any compensation as an officer for any period following such officer's resignation or removal, or any right to damages on account of such removal, whether such officer's compensation be by the month or by the year or otherwise, unless such compensation is expressly provided for in a duly authorized written agreement with the corporation.

3.6 Vacancies. The Board of Directors may fill any vacancy occurring in any office for any reason and may, in its discretion, leave unfilled for such period as it may determine any offices other than those of Chief Executive Officer, President, Treasurer and Secretary. Each such successor shall hold office for the unexpired term of such officer's predecessor and until a successor is elected and qualified, or until such officer's earlier death, resignation or removal.

3.7 President: Chief Executive Officer. Unless the Board of Directors has designated another person as the corporation's Chief Executive Officer, the President shall be the Chief Executive Officer of the corporation. The Chief Executive Officer shall have general charge and supervision of the business of the corporation subject to the direction of the Board of Directors, and shall perform all duties and have all powers that are commonly incident to the office of chief executive or that are delegated to such officer by the Board of Directors. The President shall perform such other duties and shall have such other powers as the Board of Directors or the Chief Executive Officer (if the President is not the Chief Executive Officer) may from time to time prescribe. In the event of the absence, inability or refusal to act of the Chief Executive Officer or the President (if the President is not the Chief Executive Officer), the Vice President (or if there shall be more than one, the Vice Presidents in the order determined by the Board of Directors) shall perform the duties of the Chief Executive Officer and when so performing such duties shall have all the powers of and be subject to all the restrictions upon the Chief Executive Officer.

3.8 Vice Presidents. Each Vice President shall perform such duties and possess such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. The Board of Directors may assign to any Vice President the title of Executive Vice President, Senior Vice President or any other title selected by the Board of Directors.

3.9 Secretary and Assistant Secretaries. The Secretary shall perform such duties and shall have such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. In addition, the Secretary shall perform such duties and have such powers as are incident to the office of the secretary, including without limitation the duty and power to give notices of all meetings of stockholders and special meetings of the Board of Directors, to attend all meetings of stockholders and the Board of Directors and keep a record of the proceedings, to maintain a stock ledger and prepare lists of stockholders and their addresses as required, to be custodian of corporate records and the corporate seal and to affix and attest to the same on documents.

Any Assistant Secretary shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Secretary may from time to time prescribe. In the event of the absence, inability or refusal to act of the Secretary, the Assistant Secretary (or if there shall be more than one, the Assistant Secretaries in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Secretary.

In the absence of the Secretary or any Assistant Secretary at any meeting of stockholders or directors, the chairman of the meeting shall designate a temporary secretary to keep a record of the meeting.

3.10 Treasurer and Assistant Treasurers. The Treasurer shall perform such duties and shall have such powers as may from time to time be assigned by the Board of Directors or the Chief Executive Officer. In addition, the Treasurer shall perform such duties and have such powers as are incident to the office of treasurer, including without limitation the duty and power to keep and be responsible for all funds and securities of the corporation, to deposit funds of the corporation in depositories selected in accordance with these By-laws, to disburse such funds as ordered by the Board of Directors, to make proper accounts of such funds, and to render as required by the Board of Directors statements of all such transactions and of the financial condition of the corporation.

The Assistant Treasurers shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Treasurer may from time to time prescribe. In the event of the absence, inability or refusal to act of the Treasurer, the Assistant Treasurer (or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Treasurer.

3.11 Salaries. Officers of the corporation shall be entitled to such salaries, compensation or reimbursement as shall be fixed or allowed from time to time by the Board of Directors.

3.12 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

ARTICLE IV

CAPITAL STOCK

4.1 Issuance of Stock. Subject to the provisions of the Certificate of Incorporation, the whole or any part of any unissued balance of the authorized capital stock of the corporation or the whole or any part of any shares of the authorized capital stock of the corporation held in the corporation's treasury may be issued, sold, transferred or otherwise disposed of by vote of the Board of Directors in such manner, for such lawful consideration and on such terms as the Board of Directors may determine.

4.2 Stock Certificates; Uncertificated Shares. The shares of the corporation shall be represented by certificates, provided that the Board of Directors may provide by resolution or resolutions that some or all of any or all classes or series of the corporation's stock shall be uncertificated shares. Every holder of stock of the corporation represented by certificates shall be entitled to have a certificate, in such form as may be prescribed by law and by the Board of Directors, representing the number of shares held by such holder registered in certificate form. Each such certificate shall be signed in a manner that complies with Section 158 of the General Corporation Law of the State of Delaware.

Each certificate for shares of stock which are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these By-laws, applicable securities laws or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction.

If the corporation shall be authorized to issue more than one class of stock or more than one*series of any class, the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of each certificate representing shares of such class or series of stock, provided that in lieu of the foregoing requirements there may be set forth on the face or back of each certificate representing shares of such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests a copy of the full text of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Within a reasonable time after the issuance or transfer of uncertificated shares, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to Sections 151, 202(a) or 218(a) of the General Corporation Law of the State• of Delaware or, with respect to Section 151 of the General Corporation Law of the State of Delaware, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

4.3 Transfers. Shares of stock of the corporation shall be transferable in the manner prescribed by law and in these By-laws. Transfers of shares of stock of the corporation shall be made only on the books of the corporation or by transfer agents designated to transfer shares of stock of the corporation. Subject to applicable law, shares of stock represented by certificates shall be transferred only on the books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Except as may be otherwise required by law, by the Certificate of Incorporation or by these Bylaws, the corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to such stock, regardless of any transfer, pledge or other disposition of such stock until the shares have been transferred on the books of the corporation in accordance with the requirements of these By-laws.

4.4 Restrictions on Transfer. No stockholder shall sell, assign, pledge, or in any manner transfer any of the shares of capital stock of the corporation or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise, except by a transfer which meets the requirements hereinafter set forth in these By-laws:

(a) If the stockholder desires to sell or otherwise transfer any of his shares of capital stock, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer.

(b) In addition shares of capital stock may only be transferred with the prior written consent of the corporation, upon duly authorized action of its Board of Directors, in the event of any transfer (i) to individuals, companies or any other form of entity identified by the corporation as a potential competitor or considered by the corporation to be unfriendly, or (ii) if such transfer increases the risk of the corporation having a class of security held of record by two thousand (2,000) or more persons, or five hundred (500) or more persons who are not accredited investors (as such term is defined by the Securities and Exchange Commission), as described in Section 12(g) of the Securities Exchange Act of 1934 (the "**1934 Act**"), and any related regulations, or otherwise requiring the corporation to register any class of securities under the 1934 Act; or (iii) if such transfer would result in the loss of any federal or state securities law exemption relied upon by the corporation in connection with the initial issuance of such shares or the issuance of any other securities; or (iv) if such transfer is facilitated in any manner by any public posting, message board, trading portal, internet site, or similar method of communication, including without limitation any trading portal or internet site intended to facilitate secondary transfers of securities; or (v) if such transfer is to be effected in a brokered transaction.

(c) For up to forty five (45) days following receipt of the notice referred to in Section 4.4(a) of these By-laws, the corporation and/or its assignee(s) shall have the option to purchase all of the shares specified in the notice at the price and upon the terms set forth in such notice; provided, that, with the consent of the stockholder, the corporation and/or its assignee(s) shall have the option to purchase a lesser portion of the shares specified in said notice

at the price and upon the terms set forth therein. In the event of a gift, property settlement or other transfer in which the proposed transferee is not paying the full price for the shares, and that is not otherwise exempted from the provisions of this section, the price shall be deemed to be the fair market value of the stock at such time as determined in good faith by the Board of Directors. In the event the corporation elects to purchase all of the shares or, with consent of the stockholder, a lesser portion of the shares, it shall give written notice to the transferring stockholder of its election and settlement for said shares shall be made as provided below in paragraph (e).

(d) The corporation may assign its rights under paragraph (c) above.

(e) In the event the corporation and/or its assignee(s) elect to acquire any of the shares of the transferring stockholder as specified in said transferring stockholder's notice, the Secretary of the corporation shall so notify the transferring stockholder and settlement thereof shall be made in cash, property, services, or other non-cash consideration (the fair market value of the non-cash consideration shall be as determined in good faith by the Company's Board of Directors and as set forth in the notice) within thirty (30) days after the Secretary of the corporation receives said transferring stockholder's notice; provided, that if the terms of payment set forth in said transferring stockholder's notice were other than cash against delivery, the corporation and/or its assignee(s) shall pay for said shares on the same terms and conditions set forth in said transferring stockholder's notice.

(f) In the event the corporation and/or its assignees(s) do not elect to acquire all of the shares specified in the transferring stockholder's notice, said transferring stockholder may, within the sixty-day period, following the expiration or waiver of the option rights granted to the corporation and/or its assignees(s) herein, transfer the shares specified in said transferring stockholder's notice which were not acquired by the corporation and/or its assignees(s) as specified in said transferring stockholder's notice. All shares so sold by said transferring stockholder shall continue to be subject to the provisions of these By-laws in the same manner as before said transfer.

(g) Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the provisions of this Section 4.4 (other than clause (b) hereof which shall apply to all transfers):

(1) A stockholder's transfer of any or all shares held either during such stockholder's lifetime or on death by will or intestacy to such stockholder's immediate family or to any custodian or trustee for the account of such stockholder or such stockholder's immediate family or to any limited partnership of which the stockholder, members of such stockholder's immediate family or any trust for the account of such stockholder or such stockholder's immediate family will be the general of limited partner(s) of such partnership. "Immediate family" as used herein shall mean spouse, lineal descendant (natural or adopted), father, mother, brother, or sister of the stockholder making such transfer.

(2) A stockholder's bona fide pledge or mortgage of any shares with a commercial lending institution, provided, that any subsequent transfer of said shares to said institution shall be conducted in the manner set forth in these By-laws.

(3) A stockholder's transfer of any or all of such stockholder's shares to the corporation or to any other stockholder of the corporation.

(4) A corporate stockholder's transfer of all of its shares pursuant to and in accordance with the terms of any merger, consolidation, reclassification of shares or capital reorganization of the corporate stockholder, or pursuant to a sale of all or substantially all of the stock or assets of a corporate stockholder.

(5) A corporate stockholder's transfer of all of its shares to all of its stockholders on a pro rata basis.

(6) A transfer by a stockholder to an Affiliate. "Affiliate" means, with respect to any specified person or entity ("**Person**"), any other Person who, directly or indirectly, controls, is controlled by, or is under common control with such Person, including without limitation any general partner, managing member, limited partner, member, manager, employee, officer or director of such Person or any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person. For purposes of this definition, (i) the term "control" when used with respect to any Person means the power to direct the management or policies of such Person, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" shall have meanings correlative to the foregoing, and (ii) Asia Ventures III L.P., Japan Ventures I L.P. and FIL Capital Investments (Mauritius) II Limited and their Affiliates are deemed to be Affiliates of Beacon Bioventures Fund IV Limited Partnership.

(h) The provisions of this by-law may be waived with respect to any transfer either by the corporation, upon duly authorized action of its Board of Directors, or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the outstanding shares of preferred stock of the corporation (excluding the votes represented by those shares to be transferred by the transferring stockholder, if applicable).

(i) Any sale or transfer, or purported sale or transfer, of capital stock of the corporation shall be null and void unless the terms, conditions, and provisions of this by-law are strictly observed and followed.

(j) In the event of a conflict between this Section 4.4 and any other agreement that may have been entered into by a stockholder with the corporation that contains a right of first refusal, the terms of the agreement between the stockholder and the corporation shall control and prevail over this Section 4.4 and the right of first refusal herein shall be deemed satisfied by compliance with that agreement.

(k) The provisions of this Section 4.4 shall automatically terminate upon the earlier of (a) the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the United States Securities and Exchange Commission under the Securities Act of 1933, as amended and (b) the consummation of a Deemed Liquidation Event (as defined in the Certificate of Incorporation, as amended).

(l) The certificates representing shares of capital stock of the corporation shall bear on their face the following legend so long as the foregoing right of first refusal remains in effect:

"THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A RIGHT OF FIRST REFUSAL IN FAVOR OF THE COMPANY, AS PROVIDED IN THE BY-LAWS OF THE COMPANY."

Notwithstanding the foregoing, no stockholder shall transfer any stock to (a) any entity which, in the determination of the Board of Directors, directly or indirectly competes with the corporation; or (b) any customer, distributor or supplier of the corporation, if the Board of Directors should determine that such transfer would result in such customer, distributor or supplier receiving information that would place the corporation at a competitive disadvantage with respect to such customer, distributor or supplier.

4.5 Lost, Stolen or Destroyed Certificates. The corporation may issue a new certificate of stock in place of any previously issued certificate alleged to have been lost, stolen or destroyed, upon such terms and conditions as the Board of Directors may prescribe, including the presentation of reasonable evidence of such loss, theft or destruction and the giving of such indemnity and posting of such bond as the Board of Directors may require for the protection of the corporation or any transfer agent or registrar.

4.6 Record Date. The Board of Directors may fix in advance a date as a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders or to express consent (or dissent) to corporate action without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not precede the date on which the resolution fixing the record date is adopted, and such record date shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 10 days after the date of adoption of a record date for a consent without a meeting, nor more than 60 days prior to any other action to which such record date relates.

If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held. If no record date is fixed, the record date for determining stockholders entitled to express consent to corporate action without a meeting, when no prior action by the Board of Directors is necessary, shall be the day on which the first consent is properly delivered to the corporation. If no record date is fixed, the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

4.7 Regulations. The issue, transfer, conversion and registration of shares of stock of the corporation shall be governed by such other regulations as the Board of Directors may establish.

ARTICLE V

GENERAL PROVISIONS

5.1 Fiscal Year. Except as from time to time otherwise designated by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January of each year and end on the last day of December in each year.

5.2 Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors.

5.3 Waiver of Notice. Whenever notice is required to be given by law, by the Certificate of Incorporation or by these By-laws, a written waiver, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before, at or after the time of the event for which notice is to be given, shall be deemed equivalent to notice required to be given to such person. Neither the business nor the purpose of any meeting need be specified in any such waiver. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

5.4 Voting of Securities. Except as the Board of Directors may otherwise designate, the Chief Executive Officer, the President or the Treasurer may waive notice of, vote, or appoint any person or persons to vote, on behalf of the corporation at, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this corporation (with or without power of substitution) at, any meeting of stockholders or securityholders of any ..other entity, the securities of which may be held by this corporation.

5.5 Evidence of Authority. A certificate by the Secretary, or an Assistant Secretary, or a temporary Secretary, as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall as to all persons who rely on the certificate in good faith be conclusive evidence of such action.

5.6 Certificate of Incorporation. All references in these By-laws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as amended and in effect from time to time.

5.7 Severability. Any determination that any provision of these By-laws is for any reason inapplicable, illegal or ineffective shall not affect or invalidate any other provision of these By-laws.

5.8 Pronouns. All pronouns used in these By-laws shall be deemed to refer to the masculine, feminine or neuter, singular or plural, as the identity of the person or persons may require.

ARTICLE VI

AMENDMENTS

6.1 By the Board of Directors. These By-laws may be altered, amended or repealed, in whole or in part, or new By-laws may be adopted by the Board of Directors.

6.2 By the Stockholders. These By-laws may be altered, amended or repealed, in whole or in part, or new by-laws may be adopted by the affirmative vote of the holders of a majority of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at any annual meeting of stockholders, or at any special meeting of stockholders, provided notice of such alteration, amendment, repeal or adoption of new by-laws shall have been stated in the notice of such special meeting.

Exhibit 4.1

EXECUTION VERSION

INVESTORS' RIGHTS AGREEMENT

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INVESTORS' RIGHTS AGREEMENT

THIS INVESTORS' RIGHTS AGREEMENT (this "**Agreement**"), is made as of the 8th day of May, 2015, by and among Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and each of the investors listed on Schedule A hereto, each of which is referred to in this Agreement as an "**Investor**."

RECITALS

WHEREAS, the Company and the Investors are parties to the Preferred Stock Purchase Agreement of even date herewith (the "**Purchase Agreement**"); and

WHEREAS, in order to induce the Company to enter into the Purchase Agreement and to induce the Investors to invest funds in the Company pursuant to the Purchase Agreement, the Investors and the Company hereby agree that this Agreement shall govern the rights of the Investors to cause the Company to register shares of Common Stock issuable to the Investors, to receive certain information from the Company, and to participate in future equity offerings by the Company, and shall govern certain other matters as set forth in this Agreement;

NOW, THEREFORE, the parties hereby agree as follows:

1. Definitions. For purposes of this Agreement:

1.1 "**Affiliate**" means, with respect to any specified Person, any other Person who, directly or indirectly, controls, is controlled by, or is under common control with such Person, including without limitation any general partner, managing member, limited partner, member, manager, employee, officer or director of such Person or any venture capital fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company with, such Person. For purposes of this definition, (i) the term "control" when used with respect to any Person means the power to direct the management or policies of such Person, directly or indirectly, whether through ownership of voting securities, by contract or otherwise, and the terms "controlling" and "controlled" shall have meanings correlative to the foregoing, and (ii) Asia Ventures III L.P., Japan Ventures I L.P. and FIL Capital Investments (Mauritius) II Limited and their Affiliates are deemed to be Affiliates of Beacon Bioventures Fund IV Limited Partnership. For the avoidance of doubt, for purposes of this Agreement (and for no other purposes) AKDL, L.P. shall be deemed to be an Affiliate of Crestline Investors, Inc.

1.2 "**Common Stock**" means shares of the Company's common stock, par value $0.01 per share.

1.3 "**Competitor**" means a Person engaged, directly or indirectly (including through any partnership, limited liability company, corporation, joint venture or similar arrangement (whether now existing or formed hereafter)), in the basic discovery, research and commercialization of drugs to treat human neurological diseases, but shall not include any financial investment firm or collective investment vehicle that, together with its Affiliates, holds less than ten percent (10)% of the outstanding equity of any Competitor and does not, nor do any of its Affiliates, have a right to designate any members of the Board of Directors of any Competitor.

1.4 "**Damages**" means any loss, damage, claim or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, damage, claim or liability (or any action in respect thereof) arises out of or is based upon: (i) any untrue statement or alleged untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by the indemnifying party (or any of its agents or Affiliates) of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

1.5 "**Derivative Securities**" means any securities or rights convertible into, or exercisable or exchangeable for (in each case, directly or indirectly), Common Stock, including options and warrants.

1.6 "**Exchange Act**" means the Securities Exchange Act of 1934, as amended and the rules and regulations promulgated thereunder.

1.7 "**Excluded Registration**" means (i) a registration relating to the sale of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; (iii) a registration on any form that does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities; or (iv) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered.

1.8 "**Form S-1**" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

1.9 "**Form S-3**" means such form under the Securities Act as in effect on the date hereof or any registration form under the Securities Act subsequently adopted by the SEC that permits incorporation of substantial information by reference to other documents filed by the Company with the SEC.

1.10 "**GAAP**" means generally accepted accounting principles in the United States.

1.11 "**Holder**" means any holder of Registrable Securities who is a party to this Agreement.

1.12 "**Immediate Family Member**" means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including, adoptive relationships, of a natural person referred to herein.

1.13 "**Initiating Holders**" means, collectively, Holders who properly initiate a registration request under this Agreement.

1.14 "**IPO**" means the Company's first underwritten public offering of its Common Stock under the Securities Act.

1.15 "**Key Employee**" means any executive-level employee (including, division director and vice president-level positions) as well as any employee who, either alone or in concert with others, develops, invents, programs, or designs any Company Intellectual Property (as defined in the Purchase Agreement).

1.16 "**Major Investor**" means any Investor that, individually or together with such Investor's Affiliates, holds at least 10,000,000 shares of Registrable Securities (as adjusted for any stock split, stock dividend, combination, or other recapitalization or reclassification effected after the date hereof).

1.17 "**New Securities**" means, collectively, equity securities of the Company, whether or not currently authorized, as well as rights, options, or warrants to purchase such equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

1.18 "**Person**" means any individual, corporation, partnership, trust, limited liability company, association or other entity.

1.19 "**Preferred Stock**" means, collectively, shares of the Company's Series A Preferred Stock and Series B Preferred Stock.

1.20 "**Registrable Securities**" means (i) the Common Stock issuable or issued upon conversion of the Preferred Stock, excluding any Common Stock issued upon conversion of the Preferred Stock pursuant to Section 5A of Part B of Article FOURTH of the Company's Certificate of Incorporation; (ii) any Common Stock, or any Common Stock issued or issuable (directly or indirectly) upon conversion and/or exercise of any other securities of the Company, acquired by the Investors after the date hereof; and (iii) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares qualified as Registrable Securities pursuant to clause (i) or (ii) above; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which the applicable rights under this Agreement are not assigned pursuant to Subsection 6.1, and excluding for purposes of Section 2 any shares for which registration rights have terminated pursuant to Subsection 2.13 of this Agreement.

1.21 "**Registrable Securities then outstanding**" means the number of shares determined by adding the number of shares of outstanding Common Stock that are Registrable Securities and the number of shares of Common Stock issuable (directly or indirectly) pursuant to then exercisable and/or convertible securities that are Registrable Securities.

1.22 "**Restricted Securities**" means the securities of the Company required to be notated with the legend set forth in Subsection 2.12(b) hereof.

1.23 "**SEC**" means the Securities and Exchange Commission.

1.24 "**SEC Rule 144**" means Rule 144 promulgated by the SEC under the Securities Act.

1.25 "**SEC Rule 145**" means Rule 145 promulgated by the SEC under the Securities Act.

1.26 "**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

1.27 "**Selling Expenses**" means all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of counsel for any Holder, except for the fees and disbursements of the Selling Holder Counsel borne and paid by the Company as provided in Subsection 2.6.

1.28 "**Series A Director**" and "Series A Directors" shall have the meaning set forth in that certain Voting Agreement dated the date hereof between the Company, the Investors and certain other parties named therein, as it shall be amended or restated from time to time.

1.29 "**Series A Preferred Stock**" means, collectively, shares of the Company's Series A-1 Preferred Stock, par value $0.01 per share, and Series A-2 Preferred Stock, par value $0.01 per share.

1.30 "**Series B Preferred Stock**" means shares of the Company's Series B Preferred Stock, par value $0.01 per share.

2. Registration Rights. The Company covenants and agrees as follows:

2.1 Demand Registration.

(a) Form S-1 Demand. If at any time after the earlier of (i) five (5) years after the date of this Agreement or (ii) one hundred eighty (180) days after the effective date of the registration statement for the IPO, the Company receives a request from Holders of at least

fifty percent (50%) of the Registrable Securities then outstanding that the Company file a Form S-1 registration statement with respect to Registrable Securities having an anticipated aggregate offering price of at least $10 million, then the Company shall (x) within ten (10) days after the date such request is given, give notice thereof (the "**Demand Notice**") to all Holders other than the Initiating Holders; and (y) as soon as practicable, and in any event within sixty (60) days after the date such request is given by the Initiating Holders, file a Form S-1 registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders requested to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c) and 2.3.

(b) Form S-3 Demand. If at any time when it is eligible to use a Form S-3 registration statement, the Company receives a request from Holders of at least twenty percent (20%) of the Registrable Securities then outstanding that the Company file a Form S-3 registration statement with respect to outstanding Registrable Securities of such Holders having an anticipated aggregate offering price of at least $5 million, then the Company shall (i) within ten (10) days after the date such request is given, give a Demand Notice to all Holders other than the Initiating Holders; and (ii) as soon as practicable, and in any event within forty-five (45) days after the date such request is given by the Initiating Holders, file a Form S-3 registration statement under the Securities Act covering all Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c) and 2.3.

(c) Notwithstanding the foregoing obligations, if the Company furnishes to Holders requesting a registration pursuant to this Subsection 2.1 a certificate signed by the Company's chief executive officer stating that in the good faith judgment of the Company's Board of Directors it would be materially detrimental to the Company and its stockholders for such registration statement to either become effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period of not more than sixty (60) days after the request of the Initiating Holders is given; provided, however, that the Company may not invoke this right more than twice in any twelve (12) month period; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during such sixty (60) day period other than an Excluded Registration.

(d) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(a), (i) during the period that is sixty (60) days before the Company's good faith estimate of the date of filing of, and ending on a date that is one hundred eighty (180) days after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; (ii) after the Company has effected two registrations pursuant to Subsection 2.1(a); or (iii) if the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Subsection 2.1(b). The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(b) (i) during the period that is thirty (30) days before the Company's good faith estimate of the date of filing of, and ending on a date that is ninety (90) days after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; or (ii) if the Company has effected two registrations pursuant to Subsection 2.1(b) within the twelve (12) month period immediately preceding the date of such request. A registration shall not be counted as "effected" for purposes of this Subsection 2.1(d) until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration, elect not to pay the registration expenses therefor, and forfeit their right to one demand registration statement pursuant to Subsection 2.6, in which case such withdrawn registration statement shall be counted as "effected" for purposes of this Subsection 2.1(d).

2.2 Company Registration. If the Company proposes to register (including for this purpose, a registration effected by the Company for stockholders other than the Holders) any of its securities under the Securities Act in connection with the public offering of such securities solely for cash (other than in an Excluded Registration), the Company shall, at such time, promptly give each Holder notice of such registration. Upon the request of each Holder given within twenty (20) days after such notice is given by the Company, the Company shall, subject to the provisions of Subsection 2.3, cause to be registered all of the Registrable Securities that each such Holder has requested to be included in such registration. The Company shall have the right to terminate or withdraw any registration initiated by it under this Subsection 2.2 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses (other than Selling Expenses) of such withdrawn registration shall be borne by the Company in accordance with Subsection 2.6.

2.3 Underwriting Requirements. If, pursuant to Subsection 2.1, the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Subsection 2.1, and the Company shall include such information in the Demand Notice. The underwriter(s) will be selected by the Company and shall be reasonably acceptable to a majority in interest of the Initiating Holders. In such event, the right of any Holder to include such Holder's Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities

through such underwriting shall (together with the Company as provided in Subsection 2.4(e)) enter into an underwriting agreement in customary form with the underwriter(s) selected for such underwriting. Notwithstanding any other provision of this Subsection 2.3, if the managing underwriter(s) advise(s) the Initiating Holders in writing that marketing factors require a limitation on the number of shares to be underwritten, then the Initiating Holders shall so advise all Holders of Registrable Securities that otherwise would be underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be allocated among such Holders of Registrable Securities, including the Initiating Holders, in proportion (as nearly as practicable) to the number of Registrable Securities owned by each Holder or in such other proportion as shall mutually be agreed to by all such selling Holders; provided, however, that the number of Registrable Securities held by the Holders to be included in such underwriting shall not be reduced unless all other securities are first entirely excluded from the underwriting.

(b) In connection with any offering involving an underwriting of shares of the Company's capital stock pursuant to Subsection 2.2, the Company shall not be required to include any of the Holders' Registrable Securities in such underwriting unless the Holders accept the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of the offering by the Company. If the total number of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the number of securities to be sold (other than by the Company) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the offering. If the underwriters determine that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be allocated among the selling Holders in proportion (as nearly as practicable to) the number of Registrable Securities owned by each selling Holder or in such other proportions as shall mutually be agreed to by all such selling Holders. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest one hundred (100) shares. Notwithstanding the foregoing, in no event shall the number of Registrable Securities included in the offering be reduced unless all other securities (other than securities to be sold by the Company) are first entirely excluded from the offering. For purposes of the provision in this Subsection 2.3(b) concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and Immediate Family Members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing Persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all Persons included in such "selling Holder," as defined in this sentence.

(c) For purposes of Subsection 2.1, a registration shall not be counted as "effected" if, as a result of an exercise of the underwriter's cutback provisions in Subsection 2.3(a), fewer than fifty percent (50%) of the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

2.4 Obligations of the Company. Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to one hundred twenty (120) days or, if earlier, until the distribution contemplated in the registration statement has been completed; provided, however, that (i) such one hundred twenty (120) day period shall be extended for a period of time equal to the period the Holder refrains, at the request of an underwriter of Common Stock (or other securities) of the Company, from selling any securities included in such registration, and (ii) in the case of any registration of Registrable Securities on Form S-3 that are intended to be offered on a continuous or delayed basis, subject to compliance with applicable SEC rules, such one hundred twenty (120) day period shall be extended for up to one hundred eighty (180) days, if necessary, to keep the registration statement effective until all such Registrable Securities are sold;

(b) prepare and file with the SEC such amendments and supplements to such registration statement, and the prospectus used in connection with such registration statement, as may be necessary to comply with the Securities Act in order to enable the disposition of all securities covered by such registration statement;

(c) furnish to the selling Holders such numbers of copies of a prospectus, including a preliminary prospectus, as required by the Securities Act, and such other documents as the Holders may reasonably request in order to facilitate their disposition of their Registrable Securities;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or blue-sky laws of such jurisdictions as shall be reasonably requested by the selling Holders; provided that the Company shall not be required to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the underwriter(s) of such offering;

(f) use its commercially reasonable efforts to cause all such Registrable Securities covered by such registration statement to be listed on a national securities exchange or trading system and each securities exchange and trading system (if any) on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and provide a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration;

(h) promptly make available for inspection by the selling Holders, any underwriters participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith;

(i) notify each selling Holder, promptly after the Company receives notice thereof, of the time when such registration statement has been declared effective or a supplement to any prospectus forming a part of such registration statement has been filed; and

(j) after such registration statement becomes effective, notify each selling Holder of any request by the SEC that the Company amend or supplement such registration statement or prospectus.

In addition, the Company shall ensure that, at all times after any registration statement covering a public offering of securities of the Company under the Securities Act shall have become effective, its insider trading policy shall provide that the Company's directors may implement a trading program under Rule 10b5-1 of the Exchange Act.

2.5 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as is reasonably required to effect the registration of such Holder's Registrable Securities.

2.6 Expenses of Registration. All expenses (other than Selling Expenses incurred in connection with registrations, filings, or qualifications pursuant to Section 2, including all registration, filing, and qualification fees; printers' and accounting fees; fees and disbursements of counsel for the Company; and the reasonable fees and disbursements of one counsel for the selling Holders ("Selling Holder Counsel"), shall be borne and paid by the Company; provided, however, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Subsection 2.1 if the registration request is subsequently withdrawn at the request of the Holders of a majority of the Registrable Securities to

be registered (in which case all selling Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration), unless the Holders of a majority of the Registrable Securities agree to forfeit their right to one registration pursuant to Subsections 2.1(a) or 2.1(b), as the case may be; provided further that if, at the time of such withdrawal, the Holders shall have learned of a material adverse change in the condition, business, or prospects of the Company from that known to the Holders at the time of their request and have withdrawn the request with reasonable promptness after learning of such information then the Holders shall not be required to pay any of such expenses and shall not forfeit their right to one registration pursuant to Subsections 2.1(a) or 2.1(b). All Selling Expenses relating to Registrable Securities registered pursuant to this Section 2 shall be borne and paid by the Holders pro rata on the basis of the number of Registrable Securities registered on their behalf.

2.7 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.8 Indemnification. If any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each selling Holder, and the managers, partners, members, officers, directors, and stockholders of each such Holder; legal counsel and accountants for each such Holder; any underwriter (as defined in the Securities Act) for each such Holder; and each Person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any Damages, and the Company will pay to each such Holder, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(a) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable for any Damages to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any such Holder, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, and each of its directors, each of its officers who has signed the registration statement, each Person (if any), who controls the Company within the meaning of the Securities Act, legal counsel and accountants for the Company, any underwriter (as defined in the Securities Act), any other Holder selling securities in such registration statement, and any controlling Person of any such underwriter or other

Holder, against any Damages, in each case only to the extent that such Damages arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of such selling Holder expressly for use in connection with such registration; and each such selling Holder will pay to the Company and each other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(b) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and provided further that in no event shall the aggregate amounts payable by any Holder by way of indemnity or contribution under Subsections 2.8(b) and 2.8(d) exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of fraud or willful misconduct by such Holder.

(c) Promptly after receipt by an indemnified party under this Subsection 2.8 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Subsection 2.8, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Subsection 2.8, to the extent that such failure materially prejudices the indemnifying party's ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Subsection 2.8.

(d) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either: (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Subsection 2.8 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Subsection 2.8 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Subsection 2.8, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject (after contribution from others) in such

proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; provided, however, that, in any such case (x) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Subsection 2.8(d), when combined with the amounts paid or payable by such Holder pursuant to Subsection 2.8(b), exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of willful misconduct or fraud by such Holder.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this Subsection 2.8 shall survive the completion of any offering of Registrable Securities in a registration under this Section 2, and otherwise shall survive the termination of this Agreement.

2.9 Reports Under Exchange Act. With a view to making available to the Holders the benefits of SEC Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company shall:

(a) make and keep available adequate current public information, as those terms are understood and defined in SEC Rule 144, at all times after the effective date of the registration statement filed by the Company for the IPO;

(b) use commercially reasonable efforts to file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after the Company has become subject to such reporting requirements); and

(c) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) to the extent accurate, a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety (90) days after the effective date of the registration statement filed by the Company for the IPO), the Securities Act, and the Exchange Act (at any time after the Company has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after the Company so qualifies); and (ii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to Form S-3 (at any time after the Company so qualifies to use such form).

2.10 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of at least fifty percent (50%) of the Registrable Securities then outstanding, enter into any agreement with any holder or prospective holder of any securities of the Company that would (i) provide to such holder the right to include securities in any registration on other than either a pro rata basis with respect to the Registrable Securities or on a subordinate basis after all Holders have had the opportunity to include in the registration and offering all shares of Registrable Securities that they wish to so include; or (ii) allow such holder or prospective holder to initiate a demand for registration of any securities held by such holder or prospective holder.

2.11 "Market Stand-off" Agreement. Each Holder hereby agrees that it will not, without the prior written consent of the managing underwriter, during the period commencing on the date of the final prospectus relating to the registration by the Company of shares of its Common Stock for its IPO or any other equity securities under the Securities Act on a registration statement on Form S-1 or Form S-3 filed within two (2) years after the closing of the Company's IPO, and ending on the date specified by the Company and the managing underwriter (such period not to exceed (x) one hundred eighty (180) days in the case of the IPO, or (y) ninety (90) days in the case of a registration other than the IPO, or such other period in each case as may be requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports, and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2711(f)(4) or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto), (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable (directly or indirectly) for Common Stock held immediately before the effective date of the registration statement for such offering or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise. The foregoing provisions of this Subsection 2.11 shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement, or the transfer of any shares to any trust for the direct or indirect benefit of the Holder or one or more of the Immediate Family Members of the Holder, provided that the trustee of the trust agrees to be bound in writing by the restrictions

set forth herein, and provided further that any such transfer shall not involve a disposition for value, and shall be applicable to the Holders only if all officers and directors are subject to the same restrictions and the Company uses commercially reasonable efforts to obtain a similar agreement from all stockholders individually owning more than one percent (1%) of the Company's outstanding Common Stock (after giving effect to conversion into Common Stock of all outstanding Preferred Stock) are subject to the same restrictions. The underwriters in connection with such registration are intended third-party beneficiaries of this Subsection 2.11 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto. Each Holder further agrees to execute such agreements as may be reasonably requested by the underwriters in connection with such registration that are consistent with this Subsection 2.11 or that are necessary to give further effect thereto. Any discretionary waiver or termination of the restrictions of any or all of such agreements by the Company or the underwriters shall apply pro rata to all Holders subject to such agreements, based on the number of shares subject to such agreements.

2.12 Restrictions on Transfer. The Preferred Stock and the Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize and shall issue stop-transfer instructions to its transfer agent with respect to any such sale, pledge, or transfer, except upon the conditions specified in this Agreement, which conditions are intended to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee, or transferee of the Preferred Stock and the Registrable Securities held by such Holder to agree to take and hold such securities subject to the provisions and upon the conditions specified in this Agreement.

(b) Each certificate, instrument, or book entry representing (i) the Preferred Stock, (ii) the Registrable Securities, and (iii) any other securities issued in respect of the securities referenced in clauses (i) and (ii), upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Subsection 2.12(c)) be notated with a legend substantially in the following form:

> THE SECURITIES REPRESENTED HEREBY HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933. SUCH SHARES MAY NOT BE SOLD, PLEDGED, OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR A VALID EXEMPTION FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SAID ACT.
>
> THE SECURITIES REPRESENTED HEREBY MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF AN AGREEMENT BETWEEN THE COMPANY AND THE STOCKHOLDER, A COPY OF WHICH IS ON FILE WITH THE SECRETARY OF THE COMPANY.

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this Subsection 2.12.

(c) The holder of such Restricted Securities, by acceptance of ownership thereof, agrees to comply in all respects with the provisions of this Section 2. Before any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with SEC Rule 144; or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; provided that each transferee agrees in writing to be subject to the terms of this Subsection 2.12. Each certificate, instrument, or book entry representing the Restricted Securities transferred as above provided shall be notated with, except if such transfer is made pursuant to SEC Rule 144, the appropriate restrictive legend set forth in Subsection 2.12(b), except that such certificate instrument, or book entry shall not be notated with such restrictive legend if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

2.13 Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Subsections 2.1 or 2.2 shall terminate upon the earliest to occur of:

(a) the closing of a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation;

(b) such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of such Holder's shares without limitation during a three-month period without registration; and

(c) the fifth anniversary of the IPO.

3. Information and Inspection Rights.

3.1 Delivery of Financial Statements. The Company shall deliver to each Major Investor:

(a) as soon as practicable, but in any event within one hundred twenty (120) days after the end of each fiscal year of the Company (i) a balance sheet as of the end of such year, (ii) statements of income and of cash flows for such year, and a comparison between (x) the actual amounts as of and for such fiscal year and (y) the comparable amounts for the prior year and as included in the Budget (as defined in Subsection 3.1(d)) for such year, with an explanation of any material differences between such amounts and a schedule as to the sources and applications of funds for such year, and (iii) a statement of stockholders' equity as of the end of such year, all such financial statements, if requested by the holders of at least fifty percent (50%) of the Registrable Securities, shall be audited and certified by independent public accountants selected by the Company and approved by the Board of Directors (including a majority of the Series A Directors);

(b) as soon as practicable, but in any event within forty-five (45) days after the end of each of the first three (3) quarters of each fiscal year of the Company, unaudited statements of income and cash flows for such fiscal quarter, and an unaudited balance sheet and a statement of stockholders' equity as of the end of such fiscal quarter, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments; and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(c) as soon as practicable, but in any event within forty-five (45) days after the end of each fiscal quarter of the Company, an up-to-date capitalization table including, a statement showing the number of shares of each class and series of capital stock and securities convertible into or exercisable for shares of capital stock outstanding at the end of the period, the Common Stock issuable upon conversion or exercise of any outstanding securities convertible or exercisable for Common Stock and the exchange ratio or exercise price applicable thereto, and the number of shares of issued stock options and stock options not yet issued but reserved for issuance, if any, all in sufficient detail as to permit the Major Investors to calculate their respective percentage equity ownership in the Company, and certified by the chief financial officer or chief executive officer of the Company as being true, complete, and correct;

(d) as soon as practicable, but in any event thirty (30) days before the end of each fiscal year, a budget and business plan for the next fiscal year (collectively, the "Budget"), approved by the Board of Directors and prepared on a monthly basis, including balance sheets, income statements, and statements of cash flow for such months and, promptly after prepared, any other budgets or revised budgets prepared by the Company;

(e) in connection with the delivery of the Budget required to be delivered pursuant to Section 3.1(d) above, a schedule setting forth an estimate of the aggregate number of equity awards expected to granted by the Company in such fiscal year; and

(f) such other information relating to the financial condition, business, prospects, or corporate affairs of the Company as any Major Investor may from time to time reasonably request; provided, however, that the Company shall not be obligated under this Subsection 3.1 to provide information (i) that the Company reasonably determines in good faith to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in a form acceptable to the Company); or (ii) the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel.

If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period the financial statements delivered pursuant to the foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

Notwithstanding anything else in this Subsection 3.1 to the contrary, the Company may cease providing the information set forth in this Subsection 3.1 during the period starting with the date thirty (30) days before the Company's good-faith estimate of the date of filing of a registration statement if it reasonably concludes it must do so to comply with the SEC rules applicable to such registration statement and related offering; provided that the Company's covenants under this Subsection 3.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective.

3.2 Inspection. The Company shall permit each Major Investor, at such Major Investor's expense, to visit and inspect the Company's properties; examine its books of account and records; and discuss the Company's affairs, finances, and accounts with its officers, during normal business hours of the Company as may be reasonably requested by the Major Investor; provided, however, that the Company shall not be obligated pursuant to this Subsection 3.2 to provide access to any information that it reasonably and in good faith considers to be a trade secret or confidential information (unless covered by an enforceable confidentiality agreement, in form acceptable to the Company) or the disclosure of which would adversely affect the attorney-client privilege between the Company and its counsel. In addition, at least annually, the management of the Company shall meet in person with AKDL, L.P. to present an update on the Company's business, strategic plans, business development opportunities, intellectual property and other material developments.

3.3 Termination of Information Rights. The covenants set forth in Subsection 3.1 and Subsection 3.2 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation, whichever event occurs first.

3.4 Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor its investment in the Company) any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Subsection 3.4 by such Investor), (b) is or has been independently developed or conceived by the Investor without use of the Company's confidential information, or (c) is or has been made known or disclosed to the Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser is not, in the reasonable judgment of the Board of Directors, a Competitor of the Company and agrees to be bound by the provisions of this Subsection 3.4; (iii) to any Affiliate, partner, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the confidentiality of such information; or (iv) as may otherwise be required by law, provided that the Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure.

4. Rights to Future Stock Issuances.

4.1 Right of First Offer.

(a) Subject to the terms and conditions of this Subsection 4.1 and applicable securities laws, if the Company proposes to offer or sell any New Securities, the Company shall first offer such New Securities to each Major Investor. A Major Investor shall be entitled to apportion the right of first offer hereby granted to it in such proportions as it deems appropriate, among itself and its Affiliates as long as any such Affiliate agrees to enter into this Agreement and each of the Voting Agreement and Right of First Refusal and Co-Sale Agreement of even date herewith among the Company, the Investors and the other parties named therein, as an "**Investor**" under each such agreement.

(b) The Company shall give notice (the "**Offer Notice**") to each Major Investor, stating (i) its bona fide intention to offer such New Securities, (ii) the number of such New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(c) By notification to the Company within twenty (20) days after the Offer Notice is given, each Major Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the proportion that the Common Stock then held by such Major Investor (including all shares of Common Stock then issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held by such Major Investor) bears to the total Common Stock of the Company then outstanding (assuming full conversion and/or exercise, as applicable, of all Preferred Stock and other Derivative Securities). At the expiration of such twenty (20) day period, the Company shall

promptly notify each Major Investor that elects to purchase or acquire all the shares available to it (each, a "**Fully Exercising Investor**") of any other Major Investor's failure to do likewise. During the ten (10) day period commencing after the Company has given such notice, each Fully Exercising Investor may, by giving notice to the Company, elect to purchase or acquire, in addition to the number of shares specified above, up to that portion of the New Securities for which Major Investors were entitled to subscribe but that were not subscribed for by the Major Investors which is equal to the proportion that the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of Preferred Stock and any other Derivative Securities then held, by such Fully Exercising Investor bears to the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held, by all Fully Exercising Investors who wish to purchase such unsubscribed shares. The closing of any sale pursuant to this Subsection 4.1(c) shall occur within the later of ninety (90) days of the date that the Offer Notice is given and the date of initial sale of New Securities pursuant to Subsection 4.1(d).

(d) If all New Securities referred to in the Offer Notice are not elected to be purchased or acquired as provided in Subsection 4.1(c), the Company may, during the ninety (90) day period following the expiration of the periods provided in Subsection 4.1(c), offer and sell the remaining unsubscribed portion of such New Securities to any Person or Persons at a price not less than, and upon terms no more favorable to the offeree than, those specified in the Offer Notice. If the Company does not enter into an agreement for the sale of the New Securities within such period, or if such agreement is not consummated within thirty (30) days of the execution thereof, the right provided hereunder shall be deemed to be revived and such New Securities shall not be offered unless first reoffered to the Major Investors in accordance with this Subsection 4.1.

(e) The right of first offer in this Subsection 4.1 shall not be applicable to (i) Exempted Securities (as defined in the Company's Certificate of Incorporation); and (ii) shares of Common Stock issued in the IPO.

(f) Notwithstanding any provision hereof to the contrary, in lieu of complying with the provisions of this Subsection 4.1, the Company may elect to give notice to the Major Investors within thirty (30) days after the issuance of New Securities. Such notice shall describe the type, price, and terms of the New Securities. Each Major Investor shall have twenty (20) days from the date notice is given to elect to purchase up to the number of New Securities that would, if purchased by such Major Investor, maintain such Major Investor's percentage-ownership position, calculated as set forth in Subsection 4.1(c) before giving effect to the issuance of such New Securities. The closing of such sale shall occur within sixty (60) days of the date notice is given to the Major Investors.

4.2 Termination. The covenants set forth in Subsection 4.1 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act or (iii) upon a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation, whichever event occurs first.

5. Additional Covenants.

5.1 Insurance. The Company shall use its commercially reasonable efforts to obtain, within ninety (90) days of the date hereof, from financially sound and reputable insurers Directors and Officers liability insurance, in an amount and on terms and conditions satisfactory to the Board of Directors, and will use commercially reasonable efforts to cause such insurance policy to be maintained until such time as the Board of Directors determines that such insurance should be discontinued. The policy shall not be cancelable by the Company without prior approval by the Board of Directors including a majority of the Series A Directors. Notwithstanding any other provision of this Section 5.1 to the contrary, for so long as a Series A Director is serving on the Board of Directors, the Company shall not cease to maintain a Directors and Officers liability insurance policy in an amount of at least $3 million unless approved by a majority of the Series A Directors, and the Company shall annually, within one hundred twenty (120) days after the end of each fiscal year of the Company, deliver to the Investors a certification that such a Directors and Officers liability insurance policy remains in effect.

5.2 Employee Agreements. The Company will cause (i) each person now or hereafter employed by it or by any subsidiary (or engaged by the Company or any subsidiary as a consultant/independent contractor) with access to confidential information and/or trade secrets to enter into a nondisclosure and proprietary rights assignment agreement in a form approved by the Board of Directors; and (ii) each Key Employee to enter into a non-solicitation agreement in substantially the form approved by the Board of Directors. In addition, the Company shall not amend, modify, terminate, waive, or otherwise alter, in whole or in part, any of the above-referenced agreements or any restricted stock agreement between the Company and any employee, without the consent of a majority of the Series A Directors.

5.3 Employee Stock. Unless otherwise approved by the Board of Directors, including a majority the Series A Directors, all future employees and consultants of the Company who purchase, receive options to purchase, or receive awards of shares of the Company's capital stock after the date hereof shall be required to execute restricted stock or option agreements, as applicable, providing for (i) vesting of shares over a four (4) year period, with the first twenty-five percent (25%) of such shares vesting following twelve (12) months of continued employment or service, and the remaining shares vesting in equal monthly or quarterly installments over the following thirty-six (36) months, and (ii) a market stand-off provision substantially similar to that in Subsection 2.11. In addition, unless otherwise approved by the Board of Directors, including a majority of the Series A Directors, the Company shall retain a "right of first refusal" on employee transfers until the Company's IPO and shall have the right to repurchase unvested shares at cost upon termination of employment of a holder of restricted stock.

5.4 Matters Requiring Investor Directors Approval. So long as the holders of Series A Preferred Stock are entitled to elect one or more Series A Directors, the Company hereby covenants and agrees with each of the Investors that it shall not, without approval of the Board of Directors, which approval must include the affirmative vote of a majority of the Series A Directors:

(a) make, or permit any subsidiary to make, any loan or advance to, or own any stock or other securities of, any subsidiary or other corporation, partnership, or other entity unless it is wholly owned by the Company;

(b) make, or permit any subsidiary to make, any loan or advance to any Person, including, without limitation, any employee or director of the Company or any subsidiary, except advances and similar expenditures in the ordinary course of business or under the terms of an employee stock or option plan approved by the Board of Directors;

(c) guarantee, directly or indirectly, or permit any subsidiary to guarantee, directly or indirectly, any indebtedness except for trade accounts of the Company or any subsidiary arising in the ordinary course of business;

(d) make any investment inconsistent with any investment policy approved by the Board of Directors;

(e) incur any aggregate indebtedness that is not already included in a budget approved by the Board of Directors, other than trade credit incurred in the ordinary course of business;

(f) otherwise enter into or be a party to any transaction with any director, officer, or employee of the Company or any "associate" (as defined in Rule 12b-2 promulgated under the Exchange Act) of any such Person;

(g) hire, terminate, or change the compensation of the executive officers, including approving any option grants or stock awards to executive officers;

(h) change the principal business of the Company, enter new lines of business, or exit the current line of business;

(i) sell, assign, license, pledge, or encumber material technology or intellectual property, other than licenses granted in the ordinary course of business;

(j) enter into any corporate strategic relationship involving the payment, contribution, or assignment by the Company or to the Company of money or assets exceeding $10,000; or

(k) increase the size of the Board of Directors above ten (10) members.

5.5 Board Matters. Unless otherwise determined by the vote of a majority of the directors then in office, the Board of Directors shall meet at least quarterly in accordance with an agreed-upon schedule. The Company shall reimburse the nonemployee directors for all reasonable out-of-pocket travel expenses incurred (consistent with the Company's travel policy) in connection with attending meetings of the Board of Directors or with respect to the business of the Company. Each Board committee that the Board chooses to establish shall include at least one of the Series A Directors.

5.6 Successor Indemnification. If the Company or any of its successors or assignees consolidates with or merges into any other Person and is not the continuing or surviving corporation or entity of such consolidation or merger, then to the extent necessary, proper provision shall be made so that the successors and assignees of the Company assume the obligations of the Company with respect to indemnification of members of the Board of Directors as in effect immediately before such transaction, whether such obligations are contained in the Company's By-laws, its Certificate of Incorporation, or elsewhere, as the case may be.

5.7 Expenses of Counsel. In the event of a transaction which is a Sale of the Company (as defined in the Voting Agreement of even date herewith among the Investors and the Company), the reasonable fees and disbursements, not to exceed $75,000, of one counsel for the Investors ("**Investor Counsel**"), in their capacities as stockholders, shall be borne and paid by the Company. At the outset of considering a transaction which, if consummated would constitute a Sale of the Company, the Company shall obtain the ability to share with the Investor Counsel (and such counsel's clients) and shall share the confidential information (including, without limitation, the initial and all subsequent drafts of memoranda of understanding, letters of intent and other transaction documents and related noncompete, employment, consulting and other compensation agreements and plans) pertaining to and memorializing any of the transactions which, individually or when aggregated with others would constitute the Sale of the Company. The Company shall be obligated to share (and cause the Company's counsel and investment bankers to share) such materials when distributed to the Company's executives and/or any one or more of the other parties to such transaction(s). In the event that Investor Counsel deems it appropriate, in its reasonable discretion, to enter into a joint defense agreement or other arrangement to enhance the ability of the parties to protect their communications and other reviewed materials under the attorney client privilege, the Company shall, and shall direct its counsel to, execute and deliver to Investor Counsel and its clients such an agreement in form and substance reasonably acceptable to Investor Counsel. In the event that one or more of the other party or parties to such transactions require the clients of Investor Counsel to enter into a confidentiality agreement and/or joint defense agreement in order to receive such information, then the Company shall share whatever information can be shared without entry into such agreement and shall, at the same time, in good faith work expeditiously to enable Investor Counsel and its clients to negotiate and enter into the appropriate agreement(s) without undue burden to the clients of Investor Counsel.

5.8 Indemnification Matters. The Company hereby acknowledges that one (1) or more of the directors nominated to serve on the Board of Directors by the Investors (each a "**Fund Director**") may have certain rights to indemnification, advancement of expenses and/or insurance provided by one or more of the Investors and certain of their affiliates (collectively, the "**Fund Indemnitors**"). The Company hereby agrees (a) that it is the indemnitor of first resort

(*i.e.*, its obligations to any such Fund Director are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by such Fund Director are secondary), (b) that it shall be required to advance the full amount of expenses incurred by such Fund Director and shall be liable for the full amount of all expenses, judgments, penalties, fines and amounts paid in settlement by or on behalf of any such Fund Director to the extent legally permitted and as required by the Company's Certificate of Incorporation or By-laws of the Company (or any agreement between the Company and such Fund Director), without regard to any rights such Fund Director may have against the Fund Indemnitors, and, (c) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of any such Fund Director with respect to any claim for which such Fund Director has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of such Fund Director against the Company.

5.9 Right to Conduct Activities. The Company hereby agrees and acknowledges that certain of the Major Investors and certain of their respective Affiliates are professional venture capital investment funds (collectively, the "**Funds**"), and as such invest in numerous portfolio companies, some of which may be deemed competitive with the Company's business (as currently conducted or as may be conducted in the future). The parties agree that no Fund or any Fund Affiliate investment fund or any of their Affiliates, or any of their or their Affiliates' partners, officers or representatives which manage or advise any such investment funds shall be considered a Competitor of the Company as a result of such investment, management or advisory activities for purposes of this Agreement and the Company agrees that, to the extent permitted under applicable law, neither the Funds nor their Affiliates shall be liable to the Company for any claim arising out of, or based upon, (i) the investment by a Fund or any of their Affiliates in any entity competitive with the Company, or (ii) actions taken by any partner, officer or other representative of a Fund or Fund Affiliate to assist any such competitive company, whether or not such action was taken as a member of the board of directors of such competitive company or otherwise, and whether or not such action has a detrimental effect on the Company; provided, however, that the foregoing shall not relieve (x) any of the Funds from liability associated with the unauthorized disclosure of the Company's confidential information obtained pursuant to this Agreement, or (y) any director or officer of the Company from any liability associated with his or her fiduciary duties to the Company.

5.10 Termination of Covenants. The covenants set forth in this Section 5, except for Subsections 5.6 through 5.9, shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act or (iii) upon a Deemed Liquidation Event, as such term is defined in the Company's Certificate of Incorporation, whichever event occurs first.

6. Miscellaneous.

6.1 Successors and Assigns. The rights under this Agreement may be assigned (but only with all related obligations) by a Holder to a transferee of Registrable Securities that (i) is an Affiliate of a Holder; (ii) is a Holder's Immediate Family Member or trust for the benefit of an individual Holder or one or more of such Holder's Immediate Family Members; or (iii) after such transfer, holds at least 1,000,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations); provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such rights are being transferred; and (y) such transferee agrees in a written instrument delivered to the Company to be bound by and subject to the terms and conditions of this Agreement, including the provisions of Subsection 2.11. For the purposes of determining the number of shares of Registrable Securities held by a transferee, the holdings of a transferee (1) that is an Affiliate or stockholder of a Holder; (2) who is a Holder's Immediate Family Member; or (3) that is a trust for the benefit of an individual Holder or such Holder's Immediate Family Member shall be aggregated together and with those of the transferring Holder; provided further that all transferees who would not qualify individually for assignment of rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Agreement. The terms and conditions of this Agreement inure to the benefit of and are binding upon the respective successors and permitted assignees of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assignees any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided herein.

6.2 Governing Law. This Agreement shall be governed by the internal law of the State of Delaware.

6.3 Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

6.4 Titles and Subtitles. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting this Agreement.

6.5 Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given upon the earlier of actual receipt or (i) personal delivery to the party to be notified; (ii) when sent, if sent by electronic mail or facsimile during the recipient's normal business hours, and if not sent during normal business hours, then on the recipient's next business day; (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid; or (iv) one (1) business day after the business day of deposit with a nationally recognized overnight courier, freight prepaid, specifying next-day delivery, with written verification of receipt. All communications shall be

sent to the respective parties at their addresses as set forth on Schedule A hereto, or to the principal office of the Company and to the attention of the Chief Executive Officer, in the case of the Company, or to such email address, facsimile number, or address as subsequently modified by written notice given in accordance with this Subsection 6.5. If notice is given to the Company, a copy shall also be sent to Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, MA 02109, Attn: Steven D. Singer, Esq.

6.6 Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding; provided that the Company may in its sole discretion waive compliance with Subsection 2.12(c) (and the Company's failure to object promptly in writing after notification of a proposed assignment allegedly in violation of Subsection **2.12(c)** shall be deemed to be a waiver); and provided further that any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party. Notwithstanding the foregoing, this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion (it being agreed that a waiver of the provisions of Section 4 with respect to a particular transaction shall be deemed to apply to all Investors in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Investors may nonetheless, by agreement with the Company, purchase securities in such transaction). The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Subsection 6.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision.

6.7 Severability. In case any one or more of the provisions contained in this Agreement is for any reason held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision of this Agreement, and such invalid, illegal, or unenforceable provision shall be reformed and construed so that it will be valid, legal, and enforceable to the maximum extent permitted by law.

6.8 Aggregation of Stock. All shares of Registrable Securities held or acquired by Affiliates shall be aggregated together for the purpose of determining the availability of any rights under this Agreement and such Affiliated persons may apportion such rights as among themselves in any manner they deem appropriate.

6.9 Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of the Company's Preferred Stock after the date hereof, whether pursuant to the Purchase Agreement or otherwise, any purchaser of such shares of Preferred Stock may become a party to this Agreement by executing and delivering an additional counterpart signature page to this Agreement, and thereafter shall be deemed an "Investor" for all purposes hereunder. No action or consent by the Investors shall be required for such joinder to this Agreement by such additional Investor, so long as such additional Investor has agreed in writing to be bound by all of the obligations as an "Investor" hereunder. In addition, Schedule A hereto may be amended by the Company from time to time in accordance with the Purchase Agreement to add information regarding additional Investors (as defined in the Purchase Agreement) without the consent of the other parties hereto.

6.10 Entire Agreement. This Agreement (including any Schedules and Exhibits hereto) constitutes the full and entire understanding and agreement among the parties with respect to the subject matter hereof, and any other written or oral agreement relating to the subject matter hereof existing between the parties is expressly canceled.

6.11 Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of Delaware and to the jurisdiction of the United States District Court for the District of Delaware for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of Delaware or the United States District Court for the District of Delaware, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court.

WAIVER OF JURY TRIAL: EACH PARTY HEREBY WAIVES ITS RIGHTS TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION BASED UPON OR ARISING OUT OF THIS AGREEMENT, THE OTHER TRANSACTION DOCUMENTS, THE SECURITIES OR THE SUBJECT MATTER HEREOF OR THEREOF. THE SCOPE OF THIS WAIVER IS INTENDED TO BE ALL-ENCOMPASSING OF ANY AND ALL DISPUTES THAT MAY BE FILED IN ANY COURT AND THAT RELATE TO THE SUBJECT MATTER OF THIS TRANSACTION, INCLUDING, WITHOUT LIMITATION, CONTRACT CLAIMS, TORT CLAIMS (INCLUDING NEGLIGENCE), BREACH OF DUTY CLAIMS, AND ALL OTHER COMMON LAW AND STATUTORY CLAIMS. THIS SECTION HAS BEEN FULLY DISCUSSED BY EACH OF THE PARTIES HERETO AND THESE PROVISIONS WILL NOT BE SUBJECT TO ANY EXCEPTIONS. EACH PARTY HERETO HEREBY FURTHER WARRANTS AND REPRESENTS THAT SUCH PARTY HAS REVIEWED THIS WAIVER WITH ITS LEGAL COUNSEL, AND THAT SUCH PARTY KNOWINGLY AND VOLUNTARILY WAIVES ITS JURY TRIAL RIGHTS FOLLOWING CONSULTATION WITH LEGAL COUNSEL.

The prevailing party shall be entitled to reasonable attorney's fees, costs, and necessary disbursements in addition to any other relief to which such party may be entitled. Each of the parties to this Agreement consents to personal jurisdiction for any equitable action sought in the U.S. District Court for the District of Delaware or any court of the State of Delaware having subject matter jurisdiction.

6.12 Delays or Omissions. No delay or omission to exercise any right, power, or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power, or remedy of such nonbreaching or nondefaulting party, nor shall it be construed to be a waiver of or acquiescence to any such breach or default, or to any similar breach or default thereafter occurring, nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. All remedies, whether under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

6.13 Acknowledgment. The Company acknowledges that the Investors are in the business of venture capital investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises which may have products or services which compete directly or indirectly with those of the Company. Nothing in this Agreement shall preclude or in any way restrict the Investors from investing or participating in any particular enterprise whether or not such enterprise has products or services which compete with those of the Company.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first written above.

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P., its General Partner

By: ARCH Venture Partners VIII, LLC, its General Partner

By: /s/ Robert Nelsen
Name: Robert Nelsen
Title: Managing Director

BEACON BIOVENTURES FUND IV LIMITED PARTNERSHIP

By: Beacon Bioventures Advisors Fund IV Limited Partnership, its General Partner

By: Impresa Holdings LLC, its General Partner

By: Impresa Management LLC, its Managing Member

By: /s/ Mary Bevelock Pendergast
Name: Mary Bevelock Pendergast
Title: Vice President

AKDL, L.P.

By: Crestline SI (GP), L.P.,
its General Partner

By: Crestline Investors, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice-President

NEURO LINE PARTNERS, L.P.

By: Bratton Capital Management, L.P.,
its General Partner

By: Bratton Capital, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice President

Flagship Ventures Fund V, L.P.

By its General Partner
Flagship Ventures Fund V General Partner LLC

By: /s/ Noubar B. Afeyan, Ph.D
Noubar B. Afeyan, Ph.D
Its Manager

/s/ Ge Li, Ph.D.

Ge Li, Ph.D.

/s/ Boris Nikolic

Boris Nikolic

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

ABeeC, LLC

By: The Anne Wojcicki Revocable Trust dated 9/2/09

Its: Member

By: /s/ Anne Wojcicki
By: Anne Wojcicki
Its: Trustee

SYMMETRY GROUP LTD

By:/s/ Joseph Cosmai
Name: Joseph Cosmai
Title: Vice President & Treasurer

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

EXPLORE HOLDINGS LLC

By: /s/ Paul Dauber
Name: Paul Dauber
Title: Manager

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

/s/ Vicki Sato

Vicki Sato

FORESITE CAPITAL FUND II, L.P.

By Foresite Capital Management II, LLC
Its: General Partner

By: /s/ Dennis D. Ryan
Name: Dennis D. Ryan
Title: Chief Financial Officer

/s/ Hans Bishop
Hans Bishop

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

THE FLATLEY FAMILY TRUST

By: /s/ Jay Flatley
Name: Jay Flatley
Title: Trustee

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

GYENES & CO., INC. RETIREMENT PLAN

By: /s/ Andrew Gyenes
Name: Andrew Gyenes
Title: Trustee

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

/s/ Akira Matsuno

Akira Matsuno

/s/ Matthew S. McIlwain

Matthew S. McIlwain

/s/ Russell Okung
Russell Okung

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

PARTNERS INNOVATION FUND, LLC

By: /s/ Julius Knowles
Name: Julius Knowles
Title: Partner

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

/s/ Marc Tessier-Lavigne, Ph.D.
Marc Tessier-Lavigne, Ph.D.

THATCHSTONE, LLC

By: /s/ Robert L. Carson
Name: Robert L. Carson
Title: Manager

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

ATWOOD-EDMINSTER TRUST DTD 4/2/00

By: /s/ Brian Atwood
Name: Brian Atwood
Title: Trustee

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

RBC CAPITAL MARKETS LLC CUST FBO KEITH LEONARD ROTH IRA

By: /s/ Keith R. Leonard, Jr.
Name: Keith R. Leonard, Jr.
Title:

/s/ Greg Gottesman

Greg Gottesman

/s/ Yi Shi

Yi Shi

/s/ Peter Pereira Gray

Peter Pereira Gray

1999 FARAH HYDER CHAMPSI REVOCABLE TRUST

By: /s/ Farah Champsi
Name: Farah Champsi
Title: Trustee

DAVID SCHNELL TRUST DTD 5/26/00

By: /s/ David Schnell
Name: David Schnell
Title: Trustee

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

/s/ John Hair III

John Hair III

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

/s/ Steve Harr

Steve Harr

VCVC IV LLC

By: VCVC Management IV LLC, Its Manager

By: Cougar Investment Holdings LLC, Its Manager

By: /s/ Susan Drake
Name: Susan Drake
Title: Vice President

GOOGLE VENTURES 2015, L.P.

By: Google Ventures 2015 GP, L.L.C., its General Partner

By: /s/ Jennifer L. Kercher
Name: Jennifer L. Kercher
Title: Authorized Signatory

TLS BETA PTE LTD.

By: /s/ Fidah Alsagoff
Name: Fidah Alsagoff
Title: Authorized Signatory

DAVID P. SCHENKEIN 2004 REVOCABLE TRUST

By: /s/ David P. Schenkein
Name: David P. Schenkein
Title: Trustee

AMY P. SCHENKEIN 2004 REVOCABLE TRUST

By: /s/ Amy P. Schenkein
Name: Amy P. Schenkein
Title: Trustee

/s/ Bobby Wagner

Bobby Wagner

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

THE BART C. WARNER REVOCABLE TRUST

By: /s/ Bart C. Warner
Name: Bart C. Warner
Title: Trustee

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

THE ELIZABETH A. WARNER REVOCABLE TRUST

By: /s/ Elizabeth A. Warner
Name: Elizabeth A. Warner
Title: Trustee

THE J.W. FAMILY GENERATION SKIPPING TRUST

By: /s/ James N. Warner
Name: James N. Warner
Title: Trustee

/s/ Olaf Schuth
Olaf Schuth

SIGNATURE PAGE TO INVESTORS' RIGHTS AGREEMENT

SCHEDULE A
Investors

ARCH Venture Fund VIII, L.P.

AKDL, L.P.

Beacon Bioventures Fund IV Limited Partnership

Flagship Ventures Fund V, L.P.

Neuro Line Partners, L.P.

SCHEDULE A

Investors after giving effect to the First Additional Closing on May 22, 2015 and Second Additional Closing on July 22, 2015

ARCH Venture Fund VIII, L.P.

AKDL, L.P.

Beacon Bioventures Fund IV Limited Partnership

Flagship Ventures Fund V, L.P.

Neuro Line Partners, L.P.

Ge Li, Ph.D.

Boris Nikolic

ABeeC LLC

Symmetry Group Ltd

Explore Holdings, LLC

Vicki L. Sato

Foresite Capital Fund II, L.P.

Hans Bishop

The Flatley Family Trust

Gyenes & Co., Inc. Retirement Plan

Akira Matsuno

Matthew S McIlwain

Russell Okung

PARTNERS INNOVATION FUND, LLC

Marc Tessier-Lavigne, Ph.D.

ThatchStone, LLC

Atwood-Edminster Trust dtd 4/2/00

RBC Capital Markets LLC Cust FBO Keith Leonard Roth IRA

Gregory Gottesman

Yi Shi

Peter Pereira Gray

1999 Farah Hyder Champsi Revocable Trust

David Schnell Trust dtd 5/26/00

John Hair III

Steven Harr

VCVC IV LLC

Google Ventures 2015, L.P.

TLS Beta Pte Ltd

David P. Schenkein 2004 Revocable Trust

Amy P. Schenkein 2004 Revocable Trust

Bobby Wagner

The Bart C. Warner Revocable Trust

The Elizabeth A. Warner Revocable Trust

The J.W. Family Generation Skipping Trust

Olaf Schuth

DENALI THERAPEUTICS INC.

AMENDMENT NO.1 TO THE
INVESTORS' RIGHTS AGREEMENT

This Amendment No. 1 to the Investors' Rights Agreement (the "**Amendment No. 1**") is made as of June 4, 2015, by and between Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and each of the investors listed on Schedule A to the Investors' Rights Agreement dated as of May 8, 2015 (the "**Agreement**"). Capitalized terms used herein and not otherwise defined shall have the meaning assigned to such term in the Agreement.

RECITALS

WHEREAS, the Investors hold shares of the Company's Preferred Stock and/or shares of Common Stock issued upon conversion thereof and possess registration rights and other rights pursuant to the Agreement; and

WHEREAS, in order to induce the stockholders of Incro Inc. ("**Incro**") (the "**Incro Stockholders**") to approve that certain Merger Agreement by and between the Company and Incro] (the "**Incro Merger Agreement**"), the Company and the Investors have agreed to amend the Agreement so that the Incro Stockholders shall have the registration rights afforded to holders of the Company's Preferred Stock under Section 2.2 of the Agreement in connection with the shares of Common Stock such Incro Stockholders receive pursuant to the Merger Agreement; and

WHEREAS, the Company and the Investors desire that the shares of common stock issued to the stockholders of Incro to be subject to Section 2.11; and

WHEREAS, Section 6.6 of the Agreement provides that any term of the Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding;

WHEREAS, the Investors executing this Amendment are holders of at least a majority of the currently-outstanding Registrable Securities (as defined in the Agreement); and

NOW, THEREFORE, the Company and the Investors hereby agree as follows:

1. Amendment to Section 1.20. Section 1.20 of the Agreement shall be amended and restated in its entirety as follows:

"1.20 "**Registrable Securities**" means (i) the Common Stock issuable or issued upon conversion of the Preferred Stock, excluding any Common Stock issued upon conversion of the Preferred Stock pursuant to Section 5A of Part B of Article FOURTH of the Company's Certificate of Incorporation; (ii) any Common Stock, or any Common Stock issued or issuable (directly or indirectly) upon conversion and/or exercise of any

other securities of the Company, acquired by the Investors after the date hereof; (iii) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares qualified as Registrable Securities pursuant to clause (i) or (ii) above; and (iv) solely with respect to Section 2.2, any Common Stock issued to the Incro Stockholders pursuant to the Incro Merger Agreement; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction in which the applicable rights under this Agreement are not assigned pursuant to Subsection 6.1, and excluding for purposes of Section 2 any shares for which registration rights have terminated pursuant to Subsection 2.13 of this Agreement.

2. Amendment to Section 1. New Sections 1.31 and 1.32 shall be added to the Agreement as follows:

"1.30 **"Incro Merger Agreement**" shall mean the Merger Agreement dated as of June 4, 2015 by and between the Company and Incro Inc., as such may be amended and restated from time to time in accordance with its terms."

"1.31 "**Incro Stockholders**" shall mean those certain stockholders of Incro Inc. ("**Incro**"), whose shares of Incro's capital stock shall be exchanged for shares of the Company's Common Stock pursuant to, or as a consequence of, the Incro Merger Agreement.

3. Statement of Intentions. It is the intent of the Company, the Incro Stockholders and the Investors that the Incro Stockholders be afforded piggy-back registration rights under Section 2.2 of the Agreement, as amended by this Amendment No. 1, to the same extent as the Holders and that pursuant to this Amendment No. 1, the Incro Stockholders shall be deemed added as a party to the Agreement, as amended by this Amendment No.1, but solely with respect to the provisions in Sections 2.2, 2.3(b), 2.4, 2.5, 2.6, 2.7, 2.8, 2.11, 2.13 and Section 6 thereof (and associated definitions) and shall be deemed a "**Holder**" for all purposes of those provisions.

4. Joinder. Each Incro Stockholder shall become a party to the Agreement, as amended by this Amendment No. 1, by executing and delivering a counterpart signature page to the Agreement in substantially the form attached hereto as Exhibit A. No further action or consent by the Investors shall be required for such joinder to this Agreement by such Incro Stockholders. In addition, a new Schedule B shall be added to the Agreement to add information regarding the identities and address information of each Incro Stockholder without the need for further action or consent by the Investors.

5. Miscellaneous.

5.1 Governing Law. This Amendment No. 1 shall be governed by and construed in accordance with the laws of the State of Delaware, without regard to its principles of conflicts of laws.

5.2 Counterparts. This Amendment No. 1 may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Amendment No. 1 may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

5.3 Titles and Subtitles. The titles and subtitles used in this Amendment No. 1 are used for convenience only and are not to be considered in construing or interpreting this Amendment No. 1.

5.4 Amendments and Waivers. This Amendment No. 1 shall be effective upon execution by the Company, the stockholders of Incro and the holders of a majority of Registrable Securities. Upon this Amendment No. 1 becoming effective in accordance with the foregoing, this Amendment No. 1 shall be binding on all parties to the Agreement, even if they do not execute this Amendment No. 1. The Company shall give prompt written notice of this Amendment No. 1 to any party to the Agreement that did not consent in writing to this Amendment No. 1.

5.5 Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

5.6 No Further Changes Effected by this Amendment. Except as set forth in this Amendment No.1, the Agreement, as amended by this Amended No. 1, remains unmodified and in full force and effect.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

COMPANY

DENALI THERAPEUTICS INC.

/s/ Ryan Watts
Ryan Watts
Interim President and Acting CEO

INVESTORS:

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P., its General Partner

By: ARCH Venture Partners VIII, LLC, its General Partner

By: /s/ Robert Nelsen
Name: Robert Nelsen
Title: Managing Director

SIGNATURE PAGE TO AMENDMENT NO. 1 TO THE INVESTORS' RIGHTS AGREEMENT

BEACON BIOVENTURES FUND IV LIMITED PARTNERSHIP

By: Beacon Bioventures Advisors Fund IV Limited Partnership, its General Partner

By: Impresa Holdings LLC, its General Partner

By: Impresa Management LLC, its Managing Member

By: /s/ Mary Bevelock Pendergast
Name: Mary Bevelock Pendergast
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 1 TO THE INVESTORS' RIGHTS AGREEMENT

AKDL, L.P.

By: Crestline SI (GP), L.P.,
its General Partner

By: Crestline Investors, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice-President

SIGNATURE PAGE TO AMENDMENT NO. 1 TO THE INVESTORS' RIGHTS AGREEMENT

NEURO LINE PARTNERS, L.P.

By: Bratton Capital Management, L.P.,
its General Partner

By: Bratton Capital, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title:. Vice-President

SIGNATURE PAGE TO AMENDMENT NO. 1 TO THE INVESTORS' RIGHTS AGREEMENT

Exhibit A

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Gregory D. Cuny

Dated: as of June 3, 2015

By: /s/ Gregory D. Cuny
Name: Gregory D. Cuny
Title:

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Gregory D. Cuny

Dated: as of , 2015

By: _____
Name: Gregory D. Cuny
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Alexei Degterev

Dated: as of June 1, 2015

By: /s/ Alexei Degterev
Name: Alexei Degterev
Title: Associate Professor

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Alexei Degterev

Dated: as of , 2015

By: _____
Name: Alexei Degterev
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Lawrence C. Fritz

Dated: as of May 30, 2015

By: /s/ Lawrence C. Fritz
Name: Lawrence C. Fritz
Title:

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Lawrence C. Fritz

Dated: as of , 2015

By: _____
Name: Lawrence C. Fritz
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Dawei Ma

Dated: as of June 1, 2015

By: /s/ Dawei Ma
Name: Dawei Ma
Title:

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Dawei Ma

Dated: as of , 2015

By: _____
Name: Dawei Ma
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: President and Fellows of Harvard College

Dated: as of June 2, 2015

By: /s/ Isaac T. Kohlberg
Name: Isaac T. Kohlberg
Title: Senior Associate Provost, Chief
Technology Development Officer

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: President and Fellows of Harvard College

Dated: as of , 2015

By: _____
Name:
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: The Brigham & Women's Hospital, Inc.

Dated: as of June 3, 2015

By: /s/ Philip R. Licari
Name: Philip R. Licari
Title: Managing Director of Operations |
Innovation Partners HealthCare

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: The Brigham & Women's Hospital, Inc.

Dated: as of , 2015

By: _____
Name:
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Trustees of Boston University

Dated: as of 6/3/, 2015

By: /s/ Martin J. Howard
Name: Martin J. Howard
Title: Treasurer

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Trustees of Boston University

Dated: as of , 2015

By: _____
Name:
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Tufts University

Dated: as of June 3, 2015

By: /s/ Erik Halvorsen
Name: Erik Halvorsen
Title: Sr. Director, TTIC

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Tufts University

Dated: as of , 2015

By: _____
Name:
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Junying Yuan

Dated: as of May 30, 2015

By: /s/ Junying Yuan
Name: Junying Yuan
Title:

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: _____
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

Counterpart Signature Page

to

Investors' Rights Agreement

By executing and delivering this signature page, the undersigned hereby joins in, becomes a party to and agrees to be bound by that certain Investors' Rights Agreement, dated as of May 8, 2015, by and among the Company and each of the investors listed on Schedule A thereto (the "**Investors' Rights Agreement**") as a "Holder" thereunder, solely with respect to Sections 2.2 and 2.11 (and associated definitions).

The undersigned hereby authorizes this signature page to be attached to the Investors' Rights Agreement or counterparts thereof.

Name: Junying Yuan

Dated: as of , 2015

By: _____
Name:
Title:
Record Address: _____
_____

AGREED TO AND ACCEPTED BY:

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Name: Ryan Watts
Title: Interim President and Acting CEO

Dated: as of , 2015

DENALI THERAPEUTICS INC.

INVESTORS' RIGHTS AGREEMENT

SCHEDULE B

Name and Address

Gregory D. Cuny

Alexei Degterev

Lawrence C. Fritz

Dawei Ma

Junying Yuan

President and Fellows of Harvard College

The Brigham and Women's Hospital, Inc.

Trustees of Boston University

Tufts University

University of Houston System

DENALI THERAPEUTICS INC.

AMENDMENT NO. 2 TO
INVESTORS' RIGHTS AGREEMENT

This Amendment No. 2 to Investors' Rights Agreement (the "**Amendment No. 2**") dated July 22, 2015, amends that certain Investor Rights Agreement dated May 8, 2015, as amended by an Amendment No. 1 to Investors' Rights Agreement dated as of June 4, 2015, by and between Denali Therapeutics Inc., a Delaware corporation (the "**Company**") and the other signatories thereto (the "**Agreement**"). Capitalized terms used herein and not otherwise defined shall have the meaning assigned to such term in the Agreement.

RECITALS

WHEREAS, the Company and the Investors desire that Section 1.16 be amended to reduce the number of Registrable Securities (as defined in the Agreement) required to be a Major Investor (as defined in the Agreement); and

WHEREAS, Section 6.6 of the Agreement provides that any term of the Agreement may be amended and the observance of any term of the Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding;

WHEREAS, the Investors executing this Amendment No. 2 are holders of at least a majority of the currently-outstanding Registrable Securities (as defined in the Agreement); and

NOW, THEREFORE, the Company and the undersigned Investors hereby agree as follows:

1. Amendment to Section 1.16. Section 1.16 of the Agreement shall be amended and restated in its entirety as follows:

   "1.16 "**Major Investor**" means any Investor that, individually or together with such Investor's Affiliates, holds at least 2,000,000 shares of Registrable Securities (as adjusted for any stock split, stock dividend, combination, or other recapitalization or reclassification effected after the date hereof)."

2. Amendment to Section 5.4(k). Section 5.4(k) of the Agreement shall be amended and restated in its entirety as follows:

   "(k) increase the size of the Board of Directors above eleven (11) members."

3. Amendment to Section 6.6. Section 6.6 of the Agreement shall be amended and restated in its entirety as follows:

"6.6 Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding; provided that the Company may in its sole discretion waive compliance with Subsection 2.12(c) (and the Company's failure to object promptly in writing after notification of a proposed assignment allegedly in violation of Subsection 2.12(c) shall be deemed to be a waiver); and provided, further that any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party; provided, further, that no Major Investor that purchases any New Securities pursuant to Section 4 may consent to any waiver of the provisions of Section 4 with respect to the issuance of such New Securities. Notwithstanding the foregoing, this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion. The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Subsection 6.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision."

4. Miscellaneous.

4.1 Governing Law. This Amendment No. 2 shall be governed by and construed in accordance with the laws of the State of Delaware, without regard to its principles of conflicts of laws.

4.2 Counterparts. This Amendment No. 2 may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Amendment No. 2 may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

4.3 Titles and Subtitles. The titles and subtitles used in this Amendment No. 2 are used for convenience only and are not to be considered in construing or interpreting this Amendment No. 2.

4.4 Amendments and Waivers. This Amendment No. 2 shall be effective upon execution by the Company and the holders of a majority of the currently-outstanding Registrable Securities. Upon this Amendment No. 2 becoming effective in accordance with the foregoing, this Amendment No. 2 shall be binding on all parties to the Agreement, even if they do not execute this Amendment No. 2. The Company shall give prompt written notice of this Amendment No. 2 to any party to the Agreement that did not consent in writing to this Amendment No. 2.

4.5 Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

4.6 No Further Changes Effected by this Amendment No. 2. Except as set forth in this Amendment No. 2, the Agreement remains unmodified and in full force and effect.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

COMPANY

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Ryan Watts
Interim President and Acting CEO

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P., its General Partner

By: ARCH Venture Partners VIII, LLC, its General Partner

By: /s/ Keith Crandell
Name: Keith Crandell
Title: Managing Director

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

BEACON BIOVENTURES FUND IV
LIMITED PARTNERSHIP

By: Beacon Bioventures Advisors Fund IV
Limited Partnership, its General Partner

By: Impresa Holdings LLC, its General Partner

By: Impresa Management LLC, its Managing Member

By: /s/ Mary Bevelock Pendergast
Name: Mary Bevelock Pendergast
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

AKDL, L.P.

By: Crestline SI (GP), L.P.,
its General Partner

By: Crestline Investors, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice-President

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

NEURO LINE PARTNERS, L.P.

By: Bratton Capital Management, L.P.,
its General Partner

By: Bratton Capital, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice-President

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

FLAGSHIP VENTURES FUND V, L.P.

By: Flagship Ventures Fund V General Partner LLC, its General Partner

By: /s/ Noubar B. Afeyan
Name: Noubar B. Afeyan, Ph.D.
Title: Its Manager

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

/s/ Ge Li, Ph.D.

Ge Li, Ph.D.

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

EXPLORE HOLDINGS LLC

By: /s/ Paul Dauber
Name: Paul Dauber
Title: Manager

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

/s/ Marc Tessier-Lavigne
Marc Tessier-Lavigne, Ph.D.

SIGNATURE PAGE TO AMENDMENT NO. 2 TO THE INVESTORS' RIGHTS AGREEMENT

DENALI THERAPEUTICS INC.

AMENDMENT NO. 3 TO
INVESTORS' RIGHTS AGREEMENT

This Amendment No. 3 to Investors' Rights Agreement (the "**Amendment No. 3**") dated June 22, 2016, amends that certain Investors' Rights Agreement dated May 8, 2015, as amended on June 4, 2015 and July 22, 2015, by and between Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and the Investors party thereto (the "**Agreement**"). Capitalized terms used herein and not otherwise defined shall have the meaning assigned to such term in the Agreement.

RECITALS

WHEREAS, the Company and the Investors are entering into an amendment to the Preferred Stock Purchase Agreement, dated as of May 8, 2015, as amended, to permit the sale of shares of Series B-1 Preferred Stock and Series B-2 Preferred Stock of the Company, and desire that such shares be covered by the Agreement; and

WHEREAS, Section 6.6 of the Agreement provides that any term of the Agreement may be amended with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding;

NOW, THEREFORE, the Company and the undersigned Investors, comprising holders of a majority of the Registrable Securities currently outstanding, hereby agree as follows:

1. Amendment. Section 1.30 of the Agreement shall be amended and restated in its entirety as follows:

"1.30 "**Series B Preferred Stock**" means, collectively, shares of the Company's Series B-1 Preferred Stock, par value $0.01 per share, and Series B-2 Preferred Stock, par value $0.01 per share."

2. Miscellaneous.

2.1 Governing Law. This Amendment No. 3 shall be governed by and construed in accordance with the laws of the State of Delaware, without regard to its principles of conflicts of laws.

2.2 Counterparts. This Amendment No. 3 may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Amendment No. 3 may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

2.3 Titles and Subtitles. The titles and subtitles used in this Amendment No. 3 are used for convenience only and are not to be considered in construing or interpreting this Amendment No. 3.

2.4 Amendments and Waivers. This Amendment No. 3 shall be effective upon execution by the Company and the holders of a majority of the currently-outstanding Registrable Securities. Upon this Amendment No. 3 becoming effective in accordance with the foregoing, this Amendment No. 3 shall be binding on all parties to the Agreement, even if they do not execute this Amendment No. 3. The Company shall give prompt written notice of this Amendment No. 3 to any party to the Agreement that did not consent in writing to this Amendment No. 3.

2.5 Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

2.6 No Further Changes Effected by this Amendment No. 3. Except as set forth in this Amendment No. 3, the Agreement remains unmodified and in full force and effect.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Amendment No. 3 as of the date first above written.

COMPANY

DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts
Ryan Watts
President and CEO

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

ARCH VENTURE FUND VIII, L.P.

By: ARCH Venture Partners VIII, L.P., its General Partner

By: ARCH Venture Partners VIII, LLC, its General Partner

By: /s/ Mark McDonnell
Name: Mark McDonnell
Title: Managing Director

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

AKDL, L.P.

By: Crestline SI (GP), L.P.,
its General Partner

By: Crestline Investors, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

NEURO LINE PARTNERS, L.P.

By: Bratton Capital Management, L.P.,
its General Partner

By: Bratton Capital, Inc.,
its General Partner

By: /s/ John S. Cochran
Name: John S. Cochran
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

F-PRIME CAPITAL PARTNERS HEALTHCARE FUND IV LP

By: F-Prime Capital Partners Healthcare Advisors Fund IV LP, its General Partner

By: Impresa Holdings LLC, its General Partner

By: Impresa Management LLC, its Managing Member

By: /s/ Mary Bevelock Pendergast
Name: Mary Bevelock Pendergast
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

ASIA VENTURES III L.P.

By: Asia Partners III, L.P., its General Partner

By: FIL Capital Management Ltd., as General Partner

By: /s/ Allan Pelvang
Name: Allan Pelvang
Title: Director

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

JAPAN VENTURES I L.P.

By: Japan Partners I L.P., its General Partner

By: FIL Capital Management, its General Partner

By: /s/ Andrew Knights
Name: Andrew Knights
Title: Director

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

FIL CAPITAL INVESTMENTS (MAURITIUS) II LIMITED

By: /s/ Rooksana Shahabally-Coowar
Name: Rooksana Shahabally-Coowar
Title: Director

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Flagship Ventures Fund V, L.P.
by Flagship Ventures Fund V General Partner LLC
its General Partner

Printed Name of Stockholder

/s/ Douglas Cole

Signature

Douglas Cole

Printed Name of Signatory

Manager

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

VCVC IV LLC
By: VCVC Management IV LLC, its Manager
By: Cougar Investment Holdings LLC, Its Manager

By: /s/ Barbara J. Bennett
Name: Barbara J. Bennett
Title: Vice President

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

1999 Farah Hyder Champsi Revocable Trust
Printed Name of Stockholder

/s/ Farah Champsi
Signature

Farah Champsi
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

ABeeC, LLC
Printed Name of Stockholder

/s/ Rebecca Maguire
Signature

Rebecca Maguire
Printed Name of Signatory

Officer
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Atwood-Edminster Trust DTD 4/2/00
Printed Name of Stockholder

/s/ Brian Atwood
Signature

Brian Atwood
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Bart C. Warner Revocable Trust
Printed Name of Stockholder

/s/ Bart C. Warner
Signature

Bart C. Warner
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Hans Bishop
Printed Name of Stockholder

/s/ Hans Bishop
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

EcoR1 Capital Fund, LP
Printed Name of Stockholder

/s/ Oleg Nodelman
Signature

Oleg Nodelman
Printed Name of Signatory

Manager, EcoR1 Capital LLC, as GP
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

EcoR1 Capital Fund Qualified, LP
Printed Name of Stockholder

/s/ Oleg Nodelman
Signature

Oleg Nodelman
Printed Name of Signatory

Manager, EcoR1 Capital LLC, as GP
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Elizabeth A. Warner Revocable Trust
Printed Name of Stockholder

/s/ Elizabeth A. Warner
Signature

Elizabeth A. Warner
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Explore Holdings LLC
Printed Name of Stockholder

/s/ Paul Dauber
Signature

Paul Dauber
Printed Name of Signatory

Manager
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Foresite Capital Fund II, L.P.
Printed Name of Stockholder

/s/ Dennis D. Ryan
Signature

Dennis D. Ryan, CFO of
Foresite Capital Management II, LLC
Printed Name of Signatory

General Partner
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Greg Gottesman
Printed Name of Stockholder

/s/ Greg Gottesman
Signature

Greg Gottesman
Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Peter John Pereira Gray
Printed Name of Stockholder

/s/ Peter John Pereira Gray
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

GV 2015, L.P.
By: GV 2015 GP, L.L.C., its General Partner
Printed Name of Stockholder

/s/ Jennifer L. Kercher
Signature

Jennifer L. Kercher
Printed Name of Signatory

Authorized Signatory
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

John Hair III
Printed Name of Stockholder

/s/ John Hair III
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Steve Harr
Printed Name of Stockholder

/s/ Steve Harr
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Ge Li, Ph.D.
Printed Name of Stockholder

/s/ Ge Li, Ph.D.
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Akira Matsuno

Printed Name of Stockholder

/s/ Akira Matsuno

Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Matthew S. McIlwain
Printed Name of Stockholder

/s/ Matthew S. McIlwain
Signature

Matthew S. McIlwain
Printed Name of Signatory

Partner
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Russell Okung
Printed Name of Stockholder

/s/ Russell Okung
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Partners Innovation Fund
Printed Name of Stockholder

/s/ J. Knowles
Signature

Julius Knowles
Printed Name of Signatory

Partner
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

RBC Capital Markets, LLC Cust
FBO Keith Leonard Roth IRA
Printed Name of Stockholder

/s/ Keith R. Leonard, Jr.
Signature

Keith R. Leonard, Jr.
Printed Name of Signatory

Account Owner
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

David Schenkein
Printed Name of Stockholder

/s/ David Schenkein
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

David Schnell

Printed Name of Stockholder

/s/ David Schnell

Signature

David Schnell

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Alexander Schuth

Printed Name of Stockholder

/s/ Alexander Schuth

Signature

Alexander Schuth

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Olaf Schuth

Printed Name of Stockholder

/s/ Olaf Schuth

Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Yi Shi

Printed Name of Stockholder

/s/ Yi Shi

Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Symmetry Group Ltd.
Printed Name of Stockholder

/s/ Joseph Cosmai
Signature

Joseph Cosmai
Printed Name of Signatory

Vice President & Treasurer
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Marc Tessier-Lavigne
Printed Name of Stockholder

/s/ Marc Tessier-Lavigne
Signature

Printed Name of Signatory

Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

The Flatley Family Trust
Printed Name of Stockholder

/s/ Jay Flatley
Signature

Jay Flatley
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

The JW Family Gen. Skipping Trust
Printed Name of Stockholder

/s/ James N. Warner
Signature

James N. Warner
Printed Name of Signatory

Trustee
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

TLS Beta Pte Ltd
Printed Name of Stockholder

/s/ Christina Choo
Signature

Christina Choo
Printed Name of Signatory

Authorised Signatory
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

INVESTORS:

Bobby J. Wagner
Printed Name of Stockholder

/s/ Bobby J. Wagner
Signature

Bobby J. Wagner
Printed Name of Signatory

Self
Title of Signatory

SIGNATURE PAGE TO AMENDMENT NO. 3 TO THE INVESTORS' RIGHTS AGREEMENT

Exhibit 10.2

2015 STOCK INCENTIVE PLAN

OF

DENALI THERAPEUTICS INC.

(as amended through December 13, 2016)

TABLE OF CONTENTS

2015 STOCK INCENTIVE PLAN

OF

DENALI THERAPEUTICS INC.

(as amended through December 13, 2016)

1. Purpose

The purpose of this 2015 Stock Incentive Plan (the "**Plan**") of Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), is to advance the interests of the Company's stockholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company's stockholders. Except where the context otherwise requires, the term "**Company**" shall include any of the Company's present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the "**Code**") and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the "**Board**"); *provided*, *however*, that such other business ventures shall be limited to entities that, where required by Section 409A of the Code, are eligible issuers of service recipient stock (as defined in Treas. Reg. Section 1.409A-1(b)(5)(iii)(E), or applicable successor regulation).

2. Eligibility

All of the Company's employees, officers and directors, as well as consultants and advisors to the Company (as such terms consultants and advisors are defined and interpreted for purposes of Rule 701 under the Securities Act of 1933, as amended (the "**Securities Act**") (or any successor rule)) are eligible to be granted Awards under the Plan. Each person who is granted an Award under the Plan is deemed a "**Participant**." "**Award**" means Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), Restricted Stock Units (as defined in Section 7) and Other Stock-Based Awards (as defined in Section 8).

3. Administration and Delegation

(a) Administration by the Board. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board's sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (each, a "**Committee**"). All references in the Plan to the "**Board**" shall mean the Board or a Committee of the Board to the extent that the Board's powers or authority under the Plan have been delegated to such Committee.

4. Stock Available for Awards

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 33,300,000 shares of common stock, $0.01 par value per share, of the Company (the "**Common Stock**"), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award or to satisfy tax withholding obligations arising with respect to an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an "**Option**") and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an "incentive stock option" as defined in Section 422 of the Code (an "**Incentive Stock Option**") shall only be granted to employees of Denali Therapeutics Inc., any of Denali Therapeutics Inc.'s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be designated a "**Nonstatutory**

Stock Option." The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable Option agreement. The exercise price shall be not less than 100% of the fair market value per share of Common Stock, as determined by (or in a manner approved by) the Board ("**Fair Market Value**"), on the date the Option is granted. "**Fair Market Value**" of a share of Common Stock for purposes of the Plan will be determined as follows:

(1) if the Common Stock is not publicly traded, the Board will determine the Fair Market Value for purposes of the Plan using any measure of value it determines to be appropriate (including, as it considers appropriate, relying on appraisals) in a manner consistent with the valuation principles under Code Section 409A, except as the Board may expressly determine otherwise;

(2) if the Common Stock trades on a national securities exchange, the closing sale price (for the primary trading session) on the date of grant; or

(3) if the Common Stock does not trade on any such exchange, the average of the closing bid and asked prices as reported by an authorized OTCBB market data vendor as listed on the OTCBB website (otcbb.com) on the date of grant.

For any date that is not a trading day, the Fair Market Value of a share of Common Stock for such date will be determined by using the closing sale price or average of the bid and asked prices, as appropriate, for the immediately preceding trading day and with the timing in the formulas above adjusted accordingly. The Board can substitute a particular time of day or other measure of "closing sale price" or "bid and asked prices" if appropriate because of exchange or market procedures or can, in its sole discretion, use weighted averages either on a daily basis or such longer period as complies with Code Section 409A.

The Board has sole discretion to determine the Fair Market Value for purposes of the Plan, and all Awards are conditioned on the participants' agreement that the Administrator's determination is conclusive and binding even though others might make a different determination.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement; *provided*, *however*, that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options.

(1) Options may be exercised by delivery to the Company of a notice of exercise in a form of notice (which may be electronic) approved by the Company, together with payment in full (in a manner specified in Section 5(f)) of the exercise price for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(2) Unless a Participant's employment is terminated for cause (as defined by applicable law, the terms of the Plan or option grant or a contract of employment), in the event of termination of employment of such Participant, such Participant shall have the right to exercise an Option, to the extent that such Participant is entitled to exercise such Option on the date employment terminated, until the earlier of: (i) at least six (6) months from the date of termination, if termination was caused by such Participant's death or disability, (ii) at least thirty (30) days from the date of termination, if termination was caused other than by such Participant's death or disability and (iii) the Option expiration date.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) when the Common Stock is registered under the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), except as may otherwise be provided in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) when the Common Stock is registered under the Exchange Act and to the extent provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their Fair Market Value, *provided* (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board in its sole discretion, by delivery of a notice of "net exercise" to the Company, as a result of which the Participant would pay the exercise price for the portion of the Option being exercised by cancelling a portion of the Option for such number of shares as is equal to the exercise price divided by the excess of the Fair Market Value on the date of exercise over the Option exercise price per share.

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of a promissory note of the Participant to the Company on terms determined by the Board, or (ii) payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights ("**SARs**") entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the Fair Market Value of a share of Common Stock over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Fair Market Value on the date the SAR is granted.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; provided, *however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

7. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock ("**Restricted Stock**"), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests ("**Restricted Stock Units**") (Restricted Stock and Restricted Stock Units are each referred to herein as a "**Restricted Stock Award**").

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Unless otherwise provided in the applicable Award agreement, any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock ("**Accrued Dividends**") shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Accrued Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to Participant's Designated Beneficiary. "**Designated Beneficiary**" means (i) the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death or (ii) in the absence of an effective designation by a Participant, "**Designated Beneficiary**" the Participant's estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions (i.e., settlement) with respect to each Restricted Stock Unit, the Participant shall be entitled to receive from the Company one share of Common Stock or (if so provided in the applicable Award agreement) an amount of cash equal to the Fair Market Value of one share of Common Stock. The Board may, in its discretion, provide that settlement of Restricted Stock Units shall be deferred, on a mandatory basis or at the election of the Participant in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units.

(3) Dividend Equivalents. The Award agreement for Restricted Stock Units may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock ("**Dividend Equivalents**"). Dividend Equivalents may be paid currently or credited to an account for the Participants, may be settled in cash and/or shares of Common Stock and may be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which paid, in each case to the extent provided in the applicable Award agreement.

8. Other Stock-Based Awards

(a) General. Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants ("**Other Stock-Based-Awards**"). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine.

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price applicable thereto.

(c) Additional Limitations for Other Stock-Based Awards. The terms of all Awards granted to a Participant under this Section 8 shall comply, to the extent applicable, with Sections 260.140.42, 260.140.45 and 260.140.46 of the California Code of Regulations.

9. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the number and class of securities and exercise price per share of each outstanding Option, (iii) the share and per-share provisions and the measurement price of each outstanding SAR, (iv) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award and (v) the share and per-share-related provisions and the purchase price, if any, of each outstanding Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A "**Reorganization Event**" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock.

(i) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant): (i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that all of the Participant's unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such

notice, (iii) provide that outstanding Awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "**Acquisition Price**"), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of Common Stock subject to the vested portion of the Award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such Reorganization Event) multiplied by (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such Award and any applicable tax withholdings, in exchange for the termination of such Award, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 9(b)(2), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(ii) Notwithstanding the terms of Section 9(b)(2)(i), in the case of outstanding Restricted Stock Units that are subject to Section 409A of the Code: (i) if the applicable Restricted Stock Unit agreement provides that the Restricted Stock Units shall be settled upon a "change in control event" within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a "change in control event", then no assumption or substitution shall be permitted pursuant to Section 9(b)(2)(i)(i) and the Restricted Stock Units shall instead be settled in accordance with the terms of the applicable Restricted Stock Unit agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 9(b)(2)(i) if the Reorganization Event constitutes a "change in control event" as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A of the Code; if the Reorganization Event is not a "change in control event" as so defined or such action is not permitted or required by Section 409A of the Code, and the acquiring or succeeding corporation does not assume or substitute the Restricted Stock Units pursuant to clause (i) of Section 9(b)(2)(i), then the unvested Restricted Stock Units shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(iii) For purposes of Section 9(b)(2)(i)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided*, *however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or

succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding Restricted Stock shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to such Restricted Stock; provided, however, that the Board may provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, either initially or by amendment. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

(c) Additional Restriction Regarding Recapitalizations, Stock Splits, Etc. For purposes of this Section 9, in the event of a stock split, reverse stock split, stock dividend, recapitalization, combination, reclassification or other distribution of the Company's securities underlying the Award without the receipt of consideration by the Company, the number of securities purchasable, and in the case of Options, the exercise price of such Options, must be proportionately adjusted.

10. General Provisions Applicable to Awards.

(a) Transferability of Awards. Awards (or any interest in an Award, including, prior to exercise, any interest in shares of Common Stock issuable upon exercise of an Option or SAR) shall not be sold, assigned, transferred (including by establishing any short position, put equivalent position (as defined in Rule 16a-1 issued under the Exchange Act) or call equivalent position (as defined in Rule 16a-1 issued under the Exchange Act)), pledged, hypothecated or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, and, during the life of the Participant, shall be exercisable only by the Participant; except that Awards, other than Awards subject to Section 409A of the Code, may be transferred to family members (as defined in Rule 701(c)(3) under the Securities Act) through gifts or (other than Incentive Stock Options) domestic relations orders or to an executor or guardian upon the death of the Participant. The Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall deliver to the Company a written instrument, as a condition to such transfer, in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 10(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or release from forfeiture of an Award or at the same time as payment of the exercise or purchase price unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; provided, however, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award.

(1) The Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or realization, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 9.

(2) The Board may, without stockholder approval, amend any outstanding Award granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Award. The Board may also, without stockholder

approval, cancel any outstanding award (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled award.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

(i) Additional Limitations on Timing of Awards. No Award granted to a Participant shall become exercisable, vested or realizable, as applicable to such Award, unless the Plan has been approved by the holders of a majority of the Company's outstanding voting securities by the later of (i) within twelve (12) months before or after the date the Plan was adopted by the Board, or (ii) prior to or within twelve (12) months of the granting of any Award to a Participant.

11. Miscellaneous.

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date on which it is adopted by the Board. No Awards shall be granted under the Plan after the expiration of 10 years from the earlier of (i) the date on which the Plan was adopted by the Board or (ii) the date the Plan was approved by the Company's stockholders, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time; provided that if at any time the approval of the Company's stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 11(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan.

(e) Authorization of Sub-Plans (including Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A of the Code. Except as provided in individual Award agreements initially or by amendment, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to the Plan in connection with Participant's employment termination constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that the Participant is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A of the Code) (the "**New Payment Date**"), except as Section 409A of the Code may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A of the Code but do not to satisfy the conditions of that section.

(g) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, other employee, or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument such individual executes in

such individual's capacity as a director, officer, other employee, or agent of the Company. The Company will indemnify and hold harmless each director, officer, other employee, or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Board's approval) arising out of any act or omission to act concerning the Plan unless arising out of such person's own fraud or bad faith.

(h) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

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DENALI THERAPEUTICS INC.

INCENTIVE STOCK OPTION AGREEMENT
GRANTED UNDER 2015 STOCK INCENTIVE PLAN

1. Grant of Option.

This Incentive Stock Option Agreement (the "**Agreement**") evidences the grant by Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), on [, 20] (the "**Grant Date**") to [ ], an employee of the Company (the "**Participant**"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2015 Stock Incentive Plan (the "**Plan**"), a total of [ ] shares (the "**Shares**") of common stock, $0.01 par value per share, of the Company ("**Common Stock**") at $[ ] per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [, 20] [date is ten years minus one day from grant date] (the "**Final Exercise Da**te").

It is intended that the option evidenced by this Agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "**Code**"). Except as otherwise indicated by the context, the term "**Participant**", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("**vest**") as to 25% of the original number of Shares on the first anniversary of the Vesting Commencement Date (as defined below) and as to an additional 2.0833% of the original number of Shares at the end of each successive month following the first anniversary of the Vesting Commencement Date until the fourth anniversary of the Vesting Commencement Date. On the fourth anniversary of the Vesting Commencement Date, this option will be exercisable as to all Shares. For purposes of this Agreement, "**Vesting Commencement Date**" shall mean [ ].

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this Agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee or officer of, or consultant or advisor to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an "**Eligible Participant**").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant's employment shall be considered to have been terminated for Cause if the Company determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "**Transfer Notice**") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "**Offered Shares**"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "**Securities Act**"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 75% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

> "The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b) Disqualifying Disposition. If the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company's initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first above written. The Participant hereby accepts the foregoing option and agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2015 Stock Incentive Plan.

COMPANY:

DENALI THERAPEUTICS INC.

By: _____
Name: _____
Title: _____

PARTICIPANT:

By: _____
[Name]

Address: [_____]
[_____]

SPOUSAL CONSENT: [1]

By: _____
Name: _____

Address: [_____]
[_____]

1 If the Participant resides in a community property state, it is desirable to have the Participant's spouse also accept the option. The following are community property states: Arizona, California, Idaho, Louisiana, Nevada, New Mexico, Texas, and Washington. Although Wisconsin is not formally a community property state, it has laws governing the division of marital property similar to community property states and it may be desirable to have a Wisconsin Participant's spouse accept the option.

EXHIBIT A

NOTICE OF STOCK OPTION EXERCISE

[DATE][1]

Denali Therapeutics Inc.
[Address]
[Address]

Attention: Treasurer

Dear Sir or Madam:

I am the holder of an Incentive Stock Option granted to me under the Denali Therapeutics Inc. (the "**Company**") 2015 Stock Incentive Plan on [ ][2] for the purchase of [ ][3] shares of Common Stock of the Company at a purchase price of $[ ][4] per share.

I hereby exercise my option to purchase [ ][5] shares of Common Stock (the "**Shares**"), for which I have enclosed [ ][6] in the amount of [ ][7]. Please register my stock certificate as follows:

Name(s): _____[8]

_____

Address: _____

_____

I represent, warrant and covenant as follows:

---

1 Enter date of exercise.
2 Enter the date of grant.
3 Enter the total number of shares of Common Stock for which the option was granted.
4 Enter the option exercise price per share of Common Stock.
5 Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.
6 Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".
7 Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.
8 Enter name(s) to appear on stock certificate in one of the following formats: (a) your name only (i.e., John Doe); (b) your name and other name (i.e., John Doe and Jane Doe, Joint Tenants with Right to Survivorship); or for Nonstatutory Stock Options only, (c) a child's name, with you as custodian (i.e. Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences for registering shares in a child's name.

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the "**Securities Act**"), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are "restricted securities" within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

_____

[Name]

DENALI THERAPEUTICS INC.

NONSTATUTORY STOCK OPTION AGREEMENT
GRANTED UNDER 2015 STOCK INCENTIVE PLAN

1. Grant of Option.

This Nonstatutory Stock Option Agreement (the "**Agreement**") evidences the grant by Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), on [, 20] (the "**Grant Date**") to [ ], an employee, consultant or director of the Company (the "**Participant**"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2015 Stock Incentive Plan (the "**Plan**"), a total of [ ] shares (the "**Shares**") of common stock, $0.01 par value per share, of the Company ("**Common Stock**") at $[ ] per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on [, 20] [date is ten years minus one day from grant date] (the "**Final Exercise Date**").

It is intended that the option evidenced by this Agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "**Code**"). Except as otherwise indicated by the context, the term "**Participant**", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("**vest**") as to 25% of the original number of Shares on the first anniversary of the Vesting Commencement Date (as defined below) and as to an additional 2.0833% of the original number of Shares at the end of each successive month following the first anniversary of the Vesting Commencement Date until the fourth anniversary of the Vesting Commencement Date. On the fourth anniversary of the Vesting Commencement Date, this option will be exercisable as to all Shares. For purposes of this Agreement, "**Vesting Commencement Date**" shall mean [ ].

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this Agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of Shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "**Eligible Participant**").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment or other relationship. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment or other relationship by the Company for Cause, and the effective date of such employment or other termination is subsequent to the date of the delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment or other relationship shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment or other relationship (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate immediately upon the effective date of such termination of employment or other relationship). If the Participant is party to an employment, consulting or severance agreement with the Company that contains a definition of "cause" for termination of employment or other relationship, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant's employment or other relationship shall be considered to have been terminated for "Cause" if the Company determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "**Transfer Notice**") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "**Offered Shares**"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "**Securities Act**"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 75% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

> "The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any other securities of the Company or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock or other securities of the Company, whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

7. Transfer Restrictions.

(a) This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) The Participant agrees that he or she will not transfer any Shares issued pursuant to the exercise of this option unless the transferee, as a condition to such transfer, delivers to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of Section 4 and Section 5; provided that such a written confirmation shall not be required with respect to (1) Section 4 after such provision has terminated in accordance with Section 4(g) or (2) Section 5 after the completion of the lock-up period in connection with the Company's initial underwritten public offering.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the day and year first above written. The Participant hereby accepts the foregoing option and agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2015 Stock Incentive Plan.

COMPANY:

DENALI THERAPEUTICS INC.

By: _____
Name: _____
Title: _____

PARTICIPANT:

By: _____
[Name]

Address: [_____]
[_____]

SPOUSAL CONSENT: [1]

By: _____
Name: _____

Address: [_____]
[_____]

1 If the Participant resides in a community property state, it is desirable to have the Participant's spouse also accept the option. The following are community property states: Arizona, California, Idaho, Louisiana, Nevada, New Mexico, Texas, and Washington. Although Wisconsin is not formally a community property state, it has laws governing the division of marital property similar to community property states and it may be desirable to have a Wisconsin Participant's spouse accept the option.

EXHIBIT A

NOTICE OF STOCK OPTION EXERCISE

[DATE][1]

Denali Therapeutics Inc.
[Address]
[Address]

Attention: Treasurer

Dear Sir or Madam:

I am the holder of a Nonstatutory Stock Option granted to me under the Denali Therapeutics Inc. (the "**Company**") 2015 Stock Incentive Plan on [ ][2] for the purchase of [ ][3] shares of Common Stock of the Company at a purchase price of $[ ][4] per share.

I hereby exercise my option to purchase [ ][5] shares of Common Stock (the "**Shares**"), for which I have enclosed [ ][6] in the amount of [ ][7]. Please register my stock certificate as follows:

Name(s): _____[8]

_____

Address: _____

_____

1 Enter date of exercise.
2 Enter the date of grant.
3 Enter the total number of shares of Common Stock for which the option was granted.
4 Enter the option exercise price per share of Common Stock.
5 Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.
6 Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".
7 Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.
8 Enter name(s) to appear on stock certificate in one of the following formats: (a) your name only (i.e., John Doe); (b) your name and other name (i.e., John Doe and Jane Doe, Joint Tenants with Right to Survivorship); or for Nonstatutory Stock Options only, (c) a child's name, with you as custodian (i.e. Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences for registering shares in a child's name.

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the "**Securities Act**"), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are "restricted securities" within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

_____

[Name]

DENALI THERAPEUTICS INC.

RESTRICTED STOCK AGREEMENT
GRANTED UNDER 2015 STOCK INCENTIVE PLAN

This Restricted Stock Agreement (the "**Agreement**") is made this [ ] day of [ ], 20[ ] between Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and [ ] (the "**Participant**").

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Purchase of Shares.

The Company shall issue and sell to the Participant, and the Participant shall purchase from the Company, subject to the terms and conditions set forth in this Agreement and in the Company's 2015 Stock Incentive Plan (the "**Plan**"), [ ] shares (the "**Shares**") of common stock, $0.01 par value, of the Company ("**Common Stock**"), at a purchase price of $[ ] per share. The aggregate purchase price for the Shares shall be paid by the Participant by check payable to the order of the Company or such other method as may be acceptable to the Company. Upon receipt by the Company of payment for the Shares, the Company shall issue to the Participant one or more certificates in the name of the Participant for that number of Shares purchased by the Participant. The Participant agrees that the Shares shall be subject to the purchase options set forth in Sections 3 and 6 of this Agreement and the restrictions on transfer set forth in Section 5 of this Agreement.

2. Certain Definitions.

(a) "**Service**" shall mean employment by or the provision of services to the Company or a parent or subsidiary thereof as an advisor, officer, consultant or member of the Board of Directors.

(b) "**Vesting Commencement Date**" shall mean [ ]

3. Purchase Option.

(a) In the event that the Participant ceases to provide Service for any reason or no reason, with or without cause, prior to the fourth (4th) anniversary of the Vesting Commencement Date, the Company shall have the right and option (the "**Purchase Option**") to purchase from the Participant, for a sum of $0.01 per share (the "**Option Price**"), some or all of the Shares as set forth herein.

(b) All of the Shares shall initially be subject to the Purchase Option. The Participant shall acquire a vested interest in, and the Company's Purchase Option shall accordingly lapse with respect to, (i) twenty-five percent (25%) of the Shares upon Participant's completion of one (1) year of Service measured from the Vesting Commencement Date and (ii) the balance of the Shares in a series of successive equal monthly installments of 1/36th of the remaining Shares upon Participant's completion of each additional month of Service over the thirty-six (36)-month period measured from the first anniversary of the Vesting Commencement Date.

4. Exercise of Purchase Option and Closing.

(a) The Company may exercise the Purchase Option by delivering or mailing to the Participant (or the Participant's estate), within 180 days after the termination of the Service of the Participant, a written notice of exercise of the Purchase Option. Such notice shall specify the number of Shares to be purchased. If and to the extent the Purchase Option is not so exercised by the giving of such a notice within such 180-day period, the Purchase Option shall automatically expire and terminate effective upon the expiration of such180-day period.

(b) Within ten (10) days after delivery to the Participant of the Company's notice of the exercise of the Purchase Option pursuant to subsection (a) above, the Participant (or the Participant's estate) shall, pursuant to the provisions of the Joint Escrow Instructions referred to in Section 8 below, tender to the Company at its principal offices the certificate or certificates representing the Shares that the Company has elected to purchase in accordance with the terms of this Agreement, duly endorsed in blank or with duly endorsed stock powers attached thereto, all in form suitable for the transfer of such Shares to the Company. Promptly following its receipt of such certificate or certificates, the Company shall pay to the Participant the aggregate Option Price for such Shares (provided that any delay in making such payment shall not invalidate the Company's exercise of the Purchase Option with respect to such Shares).

(c) After the time at which any Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Shares, but shall, in so far as permitted by law, treat the Company as the owner of such Shares.

(d) The Option Price may be payable, at the option of the Company, in cancellation of all or a portion of any outstanding indebtedness of the Participant to the Company or in cash (by check) or both.

(e) The Company shall not purchase any fraction of a Share upon exercise of the Purchase Option, and any fraction of a Share resulting from a computation made pursuant to Section 3 of this Agreement shall be rounded to the nearest whole Share (with any one-half Share being rounded upward).

(f) The Company may assign its Purchase Option to one or more persons or entities.

5. Restrictions on Transfer.

(a) The Participant shall not sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively "**transfer**") any Shares, or any interest therein, that are subject to the Purchase Option, except that the Participant may transfer such Shares (i) to or for the benefit of any spouse, children, parents, uncles, aunts, siblings, grandchildren and any other relatives approved by the Board of Directors (collectively, "**Approved Relatives**") or to a trust established solely for the benefit of the Participant and/or Approved Relatives, provided that such Shares shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in this Section 5, the Purchase Option and the right of first refusal set forth in Section 6) and such permitted transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement or (ii) as part of the sale of all or substantially all of the shares of capital stock of the Company (including pursuant to a merger or consolidation), provided that, in accordance with the Plan, the securities or other property received by the Participant in connection with such transaction shall remain subject to this Agreement.

(b) The Participant shall not transfer any Shares, or any interest therein, that are no longer subject to the Purchase Option, except in accordance with Section 6 below.

6. Right of First Refusal.

(a) If the Participant proposes to transfer any Shares that are no longer subject to the Purchase Option (either because they are free from the Purchase Option pursuant to Section 3 or because the Purchase Option expired unexercised pursuant to Section 4), then the Participant shall first give written notice of the proposed transfer (the "**Transfer Notice**") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "**Offered Shares**"), the price per share and all other material terms and conditions of the transfer.

(b) For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after the Participant's receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 6 shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in Section 5 and the right of first refusal set forth in this Section 6) and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(d) After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) The following transactions shall be exempt from the provisions of this Section 6:

(1) a transfer of Shares to or for the benefit of any Approved Relatives, or to a trust established solely for the benefit of the Participant and/or Approved Relatives;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "**Securities Act**"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to this Agreement (including without limitation the restrictions on transfer set forth in Section 5 and the right of first refusal set forth in this Section 6) and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Agreement.

(f) The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 6 to one or more persons or entities.

(g) The provisions of this Section 6 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) a Change in Control.

(h) The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Agreement, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

7. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock, whether any transaction described in clause (a) or (b) is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days from the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f)(4) or NYSE Rule 472(f)(4) or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

8. Escrow.

The Participant shall, upon the execution of this Agreement, execute Joint Escrow Instructions in the form attached to this Agreement as Exhibit A. The Joint Escrow Instructions shall be delivered to the Secretary of the Company, as escrow agent thereunder. The Participant shall deliver to such escrow agent a stock assignment duly endorsed in blank, in the form attached to this Agreement as Exhibit B, and hereby instructs the Company to deliver to such escrow agent, on behalf of the Participant, the certificate(s) evidencing the Shares issued hereunder. Such materials shall be held by such escrow agent pursuant to the terms of such Joint Escrow Instructions.

9. Restrictive Legends.

All certificates representing Shares shall have affixed thereto legends in substantially the following form, in addition to any other legends that may be required under federal or state securities laws:

> "The shares of stock represented by this certificate are subject to restrictions on transfer and an option to purchase set forth in a certain Restricted Stock Agreement between the corporation and the registered owner of these shares (or such owner's predecessor in interest), and such Agreement is available for inspection without charge at the office of the Secretary of the corporation."
>
> "The shares represented by this certificate have not been registered under the Securities Act of 1933, as amended, and may not be sold, transferred or otherwise disposed of in the absence of an effective registration statement under such Act or an opinion of counsel satisfactory to the corporation to the effect that such registration is not required."

10. Provisions of the Plan.

This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

11. Investment Representations.

The Participant represents, warrants and covenants as follows:

(a) The Participant is purchasing the Shares for Participant's own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act, or any rule or regulation under the Securities Act.

(b) The Participant has had such opportunity as Participant has deemed adequate to obtain from representatives of the Company such information as is necessary to permit him to evaluate the merits and risks of Participant's investment in the Company.

(c) The Participant has sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

(d) The Participant can afford a complete loss of the value of the Shares and is able to bear the economic risk of holding such Shares for an indefinite period.

(e) The Participant understands that (i) the Shares have not been registered under the Securities Act and are "restricted securities" within the meaning of Rule 144 under the Securities Act; (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

12. Withholding Taxes; Section 83(b) Election.

(a) The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state or local taxes of any kind required by law to be withheld with respect to the purchase of the Shares by the Participant or the lapse of the Purchase Option.

(b) The Participant has reviewed with the Participant's own tax advisors the federal, state, local and foreign tax consequences of this investment and the transactions contemplated by this Agreement. The Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's own tax liability that may arise as a result of this investment or the transactions contemplated by this Agreement. The Participant understands that it may be beneficial in many circumstances to elect to be taxed at the time the Shares are granted by the Company rather than when and as the Company's Purchase Option expires by filing an election under Section 83(b) of the Internal Revenue Code of 1986 with the I.E. within 30 days from the date of grant by the Company.

THE PARTICIPANT ACKNOWLEDGES THAT IT IS SOLELY THE PARTICIPANT'S RESPONSIBILITY AND NOT THE COMPANY'S TO FILE TIMELY THE ELECTION UNDER SECTION 83(b), EVEN IF THE PARTICIPANT REQUESTS THE COMPANY OR ITS REPRESENTATIVES TO MAKE THIS FILING ON THE PARTICIPANT'S BEHALF.

13. Miscellaneous.

(a) No Rights to Employment. The Participant acknowledges and agrees that the vesting of the Shares pursuant to Section 3 hereof is earned only by the Participant's continuous Service (not through the act of being hired or purchasing the Shares hereunder). The Participant further acknowledges and agrees that the transactions contemplated hereunder and the vesting schedule set forth herein do not constitute an express or implied promise of continued engagement as an employee or consultant for the vesting period, for any period, or at all.

(b) Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, and each other provision of this Agreement shall be severable and enforceable to the extent permitted by law.

(c) Waiver. Any provision for the benefit of the Company contained in this Agreement may be waived, either generally or in any particular instance, by the Board of Directors of the Company.

(d) Binding Effect. This Agreement shall be binding upon and inure to the benefit of the Company and the Participant and their respective heirs, executors, administrators, legal representatives, successors and assigns, subject to the restrictions on transfer set forth in Sections 5 and 6 of this Agreement.

(e) Notice. All notices required or permitted hereunder shall be in writing and deemed effectively given upon personal delivery or five days after deposit in the United States Post Office, by registered or certified mail, postage prepaid, addressed to the other party hereto at the address shown beneath his or her or its respective signature to this Agreement, or at such other address or addresses as either party shall designate to the other in accordance with this Section 13(e).

(f) Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa.

(g) Entire Agreement. This Agreement and the Plan constitute the entire agreement between the parties, and supersedes all prior agreements and understandings, relating to the subject matter of this Agreement.

(h) Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Participant.

(i) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflict of law principles.

(j) Participant's Acknowledgments. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation, and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) understands that the law firm of Wilmer ale is acting as counsel to the Company in connection with the transactions contemplated by the Agreement, and is not acting as counsel for the Participant.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed the Restricted Stock Agreement as of the date and year first above written. The Participant hereby agrees to the terms and conditions thereof. The Participant hereby acknowledges receipt of a copy of the Company's 2015 Stock Incentive Plan.

COMPANY:

DENALI THERAPEUTICS INC.

By: _____
Name: _____
Title: _____

Address: [_____]
[_____]

PARTICIPANT:

By: _____
Name: _____
Title: _____

Address: [_____]
[_____]

SPOUSAL CONSENT:

By: _____
Name: _____
Title: _____

Address: [_____]
[_____]

EXHIBIT A

JOINT ESCROW INSTRUCTIONS

40

DENALI THERAPEUTICS INC.

JOINT ESCROW INSTRUCTIONS

[_____, 20__]

Denali Therapeutics Inc.
[Address]
[Address]

Attention: Secretary

Dear Secretary:

As Escrow Agent for Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and its successors in interest under the Restricted Stock Agreement (the "**Agreement**") of even date herewith, to which a copy of these Joint Escrow Instructions is attached, and the undersigned person ("**Holder**"), you are hereby authorized and directed to hold the documents delivered to you pursuant to the terms of the Agreement in accordance with the following instructions:

1. Appointment. Holder irrevocably authorizes the Company to deposit with you any certificates evidencing Shares (as defined in the Agreement) to be held by you hereunder and any additions and substitutions to said Shares. For purposes of these Joint Escrow Instructions, "**Shares**" shall be deemed to include any additional or substitute property. Holder does hereby irrevocably constitute and appoint you as his or her attorney-in-fact and agent for the term of this escrow to execute with respect to such Shares all documents necessary or appropriate to make such Shares negotiable and to complete any transaction herein contemplated. Subject to the provisions of this Section 1 and the terms of the Agreement, Holder shall exercise all rights and privileges of a stockholder of the Company while the Shares are held by you.

2. Closing of Purchase.

(a) Upon any purchase by the Company of the Shares pursuant to the Agreement, the Company shall give to Holder and you a written notice specifying the number of Shares to be purchased, the purchase price for the Shares, as determined pursuant to the Agreement, and the time for a closing hereunder (the "**Closing**") at the principal office of the Company. Holder and the Company hereby irrevocably authorize and direct you to close the transaction contemplated by such notice in accordance with the terms of said notice.

(b) Al the Closing, you are directed (i) to date the stock assignment form or forms necessary for the transfer of the Shares, (ii) to fill in on such form or forms the number of Shares being transferred, and (iii) to deliver the same, together with the certificate or certificates evidencing the Shares to be transferred, to the Company against the simultaneous delivery to you of the purchase price for the Shares being purchased pursuant to the Agreement.

3. Withdrawal. The Holder shall have the right to withdraw from this escrow any Shares as to which the Purchase Option (as defined in the Agreement) has terminated or expired.

4. Duties of Escrow Agent.

(a) Your duties hereunder may be altered, amended, modified or revoked only by a writing signed by all of the parties hereto.

(b) You shall be obligated only for the performance of such duties as are specifically set forth herein and may rely and shall be protected in relying or refraining from acting on any instrument reasonably believed by you to be genuine and to have been signed or presented by the proper party or parties. You shall not be personally liable for any act you may do or omit to do hereunder as Escrow Agent or as attorney-in-fact of Holder while acting in good faith and in the exercise of your own good judgment, and any act done or omitted by you pursuant to the advice of your own attorneys shall be conclusive evidence of such good faith.

(c) You are hereby expressly authorized to disregard any and all warnings given by any of the parties hereto or by any other person or entity, excepting only orders or process of courts of law, and are hereby expressly authorized to comply with and obey orders, judgments or decrees of any court. If you are uncertain of any actions to be taken or instructions to be followed, you may refuse to act in the absence of an order, judgment or decrees of a court. In case you obey or comply with any such order, judgment or decree of any court, you shall not be liable to any of the parties hereto or to any other person or entity, by reason of such compliance, notwithstanding any such order, judgment or decree being subsequently reversed, modified, annulled, set aside, vacated or found to have been entered without jurisdiction.

(d) You shall not be liable in any respect on account of the identity, authority or rights of the parties executing or delivering or purporting to execute or deliver the Agreement or any documents or papers deposited or called for hereunder.

(e) You shall be entitled to employ such legal counsel and other experts as you may deem necessary properly to advise you in connection with your obligations hereunder and may rely upon the advice of such counsel.

(f) Your rights and responsibilities as Escrow Agent hereunder shall terminate if (i) you cease to be Secretary of the Company or (ii) you resign by written notice to each party. In the event of a termination under clause (i), your successor as Secretary shall become Escrow Agent hereunder; in the event of a termination under clause (ii), the Company shall appoint a successor Escrow Agent hereunder.

(g) If you reasonably require other or further instruments in connection with these Joint Escrow Instructions or obligations in respect hereto, the necessary parties hereto shall join in furnishing such instruments.

(h) It is understood and agreed that if you believe a dispute has arisen with respect to the delivery and/or ownership or right of possession of the securities held by you hereunder, you are authorized and directed to retain in your possession without liability to anyone all or any part of said securities until such dispute shall have been settled either by mutual written agreement of the parties concerned or by a final order, decree or judgment of a court of competent jurisdiction after the time for appeal has expired and no appeal has been perfected, but you shall be under no duty whatsoever to institute or defend any such proceedings.

(i) These Joint Escrow Instructions set forth your sole duties with respect to any and all matters pertinent hereto and no implied duties or obligations shall be read into these Joint Escrow Instructions against you.

(j) The Company shall indemnify you and hold you harmless against any and all damages, losses, liabilities, costs, and expenses, including attorneys' fees and disbursements, (including without limitation the fees of counsel retained pursuant to Section 4(e) above, for anything done or omitted to be done by you as Escrow Agent in connection with this Agreement or the performance of your duties hereunder, except such as shall result from your gross negligence or willful misconduct.

5. Notice. Any notice required or permitted hereunder shall be given in writing and shall be deemed effectively given upon personal delivery or upon deposit in the United States Post Office, by registered or certified mail with postage and fees prepaid, addressed to each of the other parties thereunto entitled at the following addresses, or at such other addresses as a party may designate by ten days' advance written notice to each of the other parties hereto

COMPANY:	Notices to the Company shall be sent to the address set forth in the salutation hereto, Attn: President
HOLDER:	Notices to Holder shall be sent to the address set forth below Holder's signature below.
ESCROW AGENT:	Notices to the Escrow Agent shall be sent to the address set forth in the salutation hereto.

6. Miscellaneous

(a) By signing these Joint Escrow Instructions, you become a party hereto only for the purpose of said Joint Escrow Instructions, and you do not become a party to the Agreement.

(b) This instrument shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed these Joint Escrow Instructions as of the day and year first above written.

Very truly yours,

COMPANY:

DENALI THERAPEUTICS INC.

By: _____
Name: _____
Title: _____

HOLDER

By: _____
Name: _____

Address: [_____]
[_____]

ESCROW AGENT:

By: _____
Name: _____
Title: Secretary

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

EXHIBIT B

STOCK ASSIGNMENT SEPARATE FROM CERTIFICATE

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

STOCK ASSIGNMENT SEPARATE FROM CERTIFICATE

FOR VALUE RECEIVED, I hereby sell, assign and transfer unto ( ) shares of Common Stock, $0.01 par value per share, of Denali Therapeutics Inc. (the "**Corporation**") standing in my name on the books of the Corporation represented by Certificate(s) Number herewith, and do hereby irrevocably constitute and appoint Wilmer Cutler Pickering Hale and Dorr LLP attorney to transfer the said stock on the books of the Corporation with full power of substitution in the premises.

Dated:

PARTICIPANT:

[Name]

Name of Spouse (if any):

Instructions to Participant: Please do not fill in any blanks other than the signature line(s). The purpose of the Stock Assignment Separate from Certificate is to enable the Company to acquire the Shares upon exercise of its Right of First Refusal and/or Purchase Option without requiring additional signatures on the part of the Participant or Participant's spouse, if any. The signature(s) to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration, enlargement, or any change whatever.

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

NOTICE ON 83(B) ELECTIONS

IF YOU WISH TO MAKE A SECTION 83(B) ELECTION, THE FILING OF SUCH ELECTION IS YOUR RESPONSIBILITY.

THE FORM FOR MAKING THIS SECTION 83(B) ELECTION IS ATTACHED TO THIS AGREEMENT. YOU MUST FILE THIS FORM WITHIN 30 DAYS OF THE GRANT DATE.

YOU (AND NOT THE COMPANY, ANY OF ITS AGENTS OR ANY OTHER PERSON) SHALL BE SOLELY RESPONSIBLE FOR FILING SUCH FORM WITH THE IRS, EVEN IF YOU REQUEST THE COMPANY, ITS AGENTS OR ANY OTHER PERSON TO MAKE THIS FILING ON YOUR BEHALF AND EVEN IF THE COMPANY, ANY OF ITS AGENTS OR ANY OTHER PERSON HAS PREVIOUSLY MADE THIS FILING ON YOUR BEHALF.

The 83(b) election should be filed by mailing a signed election form by certified mail, return receipt requested to the IRS Service Center where you file your tax returns. See www.irs.gov.

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

SECTION 83(B) ELECTION

The undersigned hereby makes an election pursuant to Section 83(b) of the Internal Revenue Code of 1986, as amended, with respect to the property described below and supplies the following information in accordance with Treas. Reg.§ 1.83-2:

1. The name, address, and taxpayer identification number of the undersigned are:

   Name]
   [Address]
   [City, State Zip]

   Taxpayer Identification Number: _____

2. The property with respect to which this election is being made is [ ] shares of common stock, $0.01 par value per share, of Denali Therapeutics Inc., a Delaware corporation (the "**Company**").

3. The date on which the property was transferred or the date on which the restrictions on such property were imposed, whichever is later, is , 20[ ] and the taxable year for which this election is being made is the calendar year 20[ ].

4. The property is subject to vesting provisions and may be forfeited under the terms of a stock restriction agreement executed between the undersigned and the Company.

5. The fair market value of the property at the time of the transfer or the date on which the restrictions on such property were imposed, whichever is later, (determined without regard to any lapse restriction, as defined in Treas. Reg.§ 1.83-3(i)) is $[ ], equal to a fair market value of $[ ] per share.

6. The amount paid for the property by the undersigned is $[ ][19] [20] equal to a purchase price of $[ ] per share.

7. This statement is executed on ,20[ ]

In accordance with Treas. Reg.§ 1.83-2(d) & (e)(7), a copy of this statement has been furnished to the Company.

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19 If restrictions are being added to previously unrestricted stock, the following language is to be used: "[ ] shares of the Company, having a fair market price of $[ ],"

20 If the shares were issued in exchange for an assignment of intellectual property rights, the following language is to be used: "Intellectual Property having a fair market value of $[ ],"

Signature of Taxpayer

Signature of Spouse (if any)

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

SECTION 83(B) ELECTION

BACKGROUND INFORMATION

Section 83(b) of the Internal Revenue Code permits persons who receive restricted property, such as restricted stock, in connection with the performance of services to include the value of such property in their gross income for the year the property is received. Such persons who purchase stock of the company subject to a stock restriction agreement providing for the vesting of such stock over a period of time are entitled to make this election. Any person who makes a timely Section 83(b) election will recognize compensation income on the date of grant (the date listed in item 3 of the election form) equal to the difference, if any, between the fair market value of the stock and the amount paid for the stock. A person who pays taxes in connection with an election and subsequently forfeits the stock, however, will not receive a refund or other tax benefit for the taxes previously paid.

Any person who does not make the election will be required to include the value of the stock in gross income in the year in which the stock vests. In particular, when the stock vests, the person will recognize compensation income in an amount equal to the difference between the fair market value of the stock on the vesting date and the amount paid for the stock. As a result, if the value of the stock increases, a person who does not make a timely Section 83(b) election will have compensation income at the time each installment of stock vests.

Each person should consult with his or her tax or legal advisor regarding the advisability and timing of filing the election. **The original, signed and dated Section 83(b) election must be filed within 30 days of the grant date but may be filed prior to the grant date.** The election should be filed by certified mail, return receipt requested, with the Internal Revenue Service at the service center where the electing person ordinarily files his or her annual tax return. A copy of the Section 83(b) election, as filed, must be returned to the company. A copy of the Section 83(b) election must also be included with the person's federal income tax return for the year of grant (each person should check with his or her tax preparer regarding this and any state, local, foreign or other filing requirements).

Please also note that the certified mailing receipt for the Section 83(b) election should be retained. This receipt is essential if the Internal Revenue Service does not receive the Section 83(b) election and challenges the election.

SIGNATURE PAGE TO JOINT ESCROW INSTRUCTIONS

Exhibit 10.9

LEASE

THE COVE AT OYSTER POINT

HCP OYSTER POINT III LLC,

a Delaware limited liability company

as Landlord,

and

DENALI THERAPEUTICS INC.,

a Delaware corporation,

as Tenant.

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THE COVE AT OYSTER POINT

LEASE

This Lease (the "**Lease**"), dated as of the date set forth in Section 1 of the Summary of Basic Lease Information (the "**Summary**"), below, is made by and between HCP OYSTER POINT III LLC, a Delaware limited liability company ("**Landlord**"), and DENALI THERAPEUTICS INC., a Delaware corporation ("**Tenant**").

SUMMARY OF BASIC LEASE INFORMATION

TERMS OF LEASE		DESCRIPTION
1. Date:		September 24, 2015
2. Premises (Article 1)		
2.1	Building:	That certain four-story building containing approximately 153,047 rentable square feet of space ("**RSF**") located at: 151 Oyster Point Boulevard South San Francisco, California 94080
2.2	Premises:	Approximately 38,109 RSF on the second (2nd) floor of the Building, as further set forth in **Exhibit A** to the Lease.
3. Lease Term (Article 2)		
3.1	Length of Term:	Eight (8) years.
3.2	Lease Commencement Date:	The date that is the later of (i) the date the Premises are "Ready for Occupancy" as defined in the Tenant Work Letter attached hereto as **Exhibit B**, and (ii) August 1, 2016.
3.3	Lease Expiration Date:	The day prior to the eighth (8th) anniversary of the Lease Commencement Date.

4. Base Rent (Article 3):

Lease Year	Annualized Base Rent	Monthly Installment of Base Rent	Monthly Base Rent per RSF
1 (months 1 – 9)*	$1,063,241.10	$ 88,603.43	$ 4.65
1 (months 10 – 12)	$2,126,482.20	$177,206.85	$ 4.65
2	$2,199,651.48	$183,304.29	$ 4.81

3	$2,276,639.28	$189,719.94	$4.98
4	$2,356,321.66	$196,360.14	$5.16
5	$2,438,792.91	$203,232.74	$5.34
6	$2,524,150.67	$210,345.89	$5.52
7	$2,612,495.94	$217,707.99	$5.72
8	$2,703,933.30	$225,327.77	$5.92

* Note that for the first nine (9) months of the Lease Term, Tenant's Base Rent obligation has been calculated as if the Premises contained only 50% of the rentable square feet of the Premises. Such calculation shall not affect Tenant's right to use the entire Premises, or Tenant's obligations under this Lease with respect to the entire Premises, including without limitation, Tenant's obligation to pay Tenant's Share of Direct Expenses with respect to the Premises which shall be as provided in Section 6 of this Summary, all in accordance with the terms and conditions of this Lease.

Address for Payment of Rent:

If by check, remittances should be mailed to:
HCP Life Sciences REIT

If by ACH, remit to:
HCP Life Sciences REIT Bank of America

If by Wire, remit to:
HCP Life Sciences REIT Bank of America

If by overnight mail, remit to:
Bank of America Lockbox Services

5.	Tenant Improvement Allowance (**Exhibit B**):	$145.00 per RSF of the Premises (i.e., $5,525,805.00)
6.	Tenant's Share (Article 4):	24.90%
7.	Permitted Use (Article 5):	The Premises shall be used only for general office, research and development, engineering, and laboratory and vivarium uses, including, but not limited to, administrative offices and other lawful uses reasonably related to or incidental to such specified uses, all (i) consistent with first class life sciences projects in South San Francisco, California ("**First Class Life Sciences Projects**"), and (ii) in compliance with, and subject to, applicable laws and the terms of this Lease.
8.	Letter of Credit (Article 21):	$450,913.20.

9.	Parking (Article 28):	97 unreserved parking spaces, subject to the terms of Article 28 of the Lease.
10.	Address of Tenant (Section 29.18):	Before commencement of the Lease: Denali Therapeutics Inc. 201 Gateway Boulevard South San Francisco, California 94080 Attention: Chief Operating Officer After the commencement of the Lease: Denali Therapeutics Inc. 151 Oyster Point Boulevard South San Francisco, California 94080 Attention: Chief Operating Officer
11.	Address of Landlord (Section 29.18):	See Section 29.18 of the Lease.
12.	Broker(s) (Section 29.18):	Kidder Mathews and CBRE, Inc.

1. PREMISES, BUILDING, PROJECT, AND COMMON AREAS.

1.1 **Premises, Building, Project and Common Areas**.

1.1.1 **The Premises**. Landlord hereby leases to Tenant and Tenant hereby leases from Landlord the premises set forth in Section 2.2 of the Summary (the "**Premises**"). The outline of the Premises is set forth in **Exhibit A** attached hereto. The outline of the "Building" and the "Project," as those terms are defined in Section 1.1.2 below, are further depicted on the Site Plan attached hereto as **Exhibit A**. The parties hereto agree that the lease of the Premises is upon and subject to the terms, covenants and conditions herein set forth, and Tenant covenants as a material part of the consideration for this Lease to keep and perform each and all of such terms, covenants and conditions by it to be kept and performed. The parties hereto hereby acknowledge that the purpose of **Exhibit A** is to show the approximate location of the Premises only, and such Exhibit is not meant to constitute an agreement, representation or warranty as to the construction of the Premises, the precise area thereof or the specific location of the "Common Areas," as that term is defined in Section 1.1.3, below, or the elements thereof or of the accessways to the Premises or the "Project," as that term is defined in Section 1.1.2, below, and that the square footage of the Premises shall be as set forth in Section 2.1 of the Summary of Basic Lease Information. Except as specifically set forth in this Lease and in the Tenant Work Letter attached hereto as **Exhibit B** (the "**Tenant Work Letter**"), Landlord shall not be obligated to provide or pay for any improvement work or services related to the improvement of the Premises. Tenant also acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty regarding the condition of the Premises, the Building or the Project or with respect to the suitability of any of the foregoing for the conduct of Tenant's business, except as specifically set forth in this Lease and the Tenant Work Letter. For purposes of Section 1938 of the California Civil Code, Landlord hereby discloses to Tenant, and Tenant hereby acknowledges, that the Building and Premises have not undergone inspection by a Certified Access Specialist (CASp). Landlord shall deliver the Premises to Tenant in good, vacant, broom clean condition, in compliance with all laws, with the roof water-tight and shall cause the plumbing, electrical systems, fire sprinkler system, lighting, and all other building systems serving the Premises in good operating condition and repair on or before the Lease Commencement Date, or such earlier date as Landlord and Tenant mutually agree. Landlord will be responsible for causing the exterior of the Building, the existing Building entrances, and all exterior Common Areas (including required striping and handicapped spaces in the parking areas) to be in compliance with ADA and parking requirements, to the extent required to allow the legal occupancy of the Premises or completion of the Tenant Improvements.

1.1.2 **The Building and The Project**. The Premises constitutes the space set forth in Section 2.1 of the Summary (the "**Building**"). The Building is part of an office/laboratory project currently known as "The Cove at Oyster Point." The term "**Project**," as used in this Lease, shall mean (i) the Building and the Common Areas, (ii) the land (which is improved with landscaping, parking facilities and other improvements) upon which the Building and the Common Areas are located, (iii) the other office/laboratory buildings located at The Cove at Oyster Point, and the land upon which such adjacent office/laboratory buildings are located, and (iv) at Landlord's discretion, any additional real property, areas, land, buildings or other improvements added thereto outside of the Project (provided that any such additions do not increase Tenant's obligations under this Lease).

1.1.3 **Common Areas**. Tenant shall have the non-exclusive right to use in common with other tenants in the Project, and subject to the rules and regulations referred to in Article 5 of this Lease, those portions of the Project which are provided, from time to time, for use in common by Landlord, Tenant and any other tenants of the Project, which shall include the shipping and receiving area in the Building (such areas, together with such other portions of the Project designated by Landlord, in its discretion, are collectively referred to herein as the "**Common Areas**"). Landlord shall maintain and operate the Common Areas, including all sprinkler and other systems serving the Common Areas, in a first class manner, and the use thereof shall be subject to such rules, regulations and restrictions as Landlord may reasonably make from time to time. Landlord reserves the right to close temporarily, make alterations or additions to, or change the location of elements of the Project and the Common Areas, provided that in connection therewith Landlord will use commercially reasonable efforts to minimize any interference with Tenant's use of and access to the Premises and parking areas. Landlord hereby acknowledges that as of the date of this Lease Landlord is planning to construct and operate an amenities center in the Building for use by the tenants of the Project during the Lease Term, and in connection therewith Landlord agrees to utilize commercially reasonable efforts to operate and maintain such amenities center (which amenities center shall include a café) throughout the

Lease Term (provided that Tenant acknowledges that the amenities center is currently anticipated to begin operations after the Lease Commencement Date); provided, however, Tenant nevertheless acknowledges herby that if despite such commercially reasonable efforts Landlord is unable for any reason to maintain continuous operation of the amenities center during the Lease Term, in no event shall such failure be deemed a default of the Lease, nor shall such failure impact the validity of this Lease and Landlord shall not be subject to any liability for such failure, provided that in such event Landlord shall utilize commercially reasonable efforts to provide replacement food services to Tenant (e.g., an on-site café in a different location or the routine scheduling of food trucks to the Project).

1.2 **Rentable Square Feet of Premises**. Tenant hereby acknowledges and agrees that Landlord shall have the one-time right during the Lease Term to remeasure the rentable square footage of the Premises and/or Building in accordance with the terms of this Section 1.2. Any such remeasurement shall be determined in accordance with the standards set forth in ANSI Z65.1-2010, as promulgated by the Building Owners and Managers Association (the "**BOMA Standard**"), and subject to related guidelines applicable thereto. Landlord's space planner/architect shall certify any such remeasurement and shall provide reasonable documentation to Tenant for Tenant's review following such remeasurement. In the event that Landlord's space planner/architect determines that the rentable square footage of the Premises and/or Building are different from those set forth in this Lease, all amounts, percentages and figures appearing or referred to in this Lease based upon such amounts (including, without limitation, the amount of the Base Rent, Tenant Improvement Allowance, Additional Tenant Improvement Allowance, and Tenant's Share) shall be modified in accordance with such determination, provided that Landlord and Tenant hereby acknowledge and agree that the rentable square footage of the Premises shall not increase by more than one percent (1%) from the rentable square footage set forth in Section 2.2 of the Summary. If such determination is made, it will be confirmed in writing by Landlord to Tenant.

1.3 **Right of First Offer**.

1.3.1 **Right of First Offer**. Subject to the terms and conditions of this Section 1.3, Landlord hereby grants to Tenant an on-going right of first offer during the initial Lease Term with respect to any space on the third (3rd) or fourth (4th) floors of the Building (the "**First Offer Space**"). Notwithstanding the foregoing, such first offer right of Tenant shall commence only following the expiration of the first (1st) Lease Year (the "**ROFO Commencement Date**") (and Landlord shall have the right to enter into leases in the building prior to the ROFO Commencement Date (the "**Initial Leases**") without providing Tenant with notice or any opportunity to lease such space), and shall terminate at the end of the initial Lease Term (and shall not be effective during any Option Term). Such right of first offer shall be subordinate to all rights granted in any Initial Leases, which rights relate to the First Offer Space and are set forth in the Initial Leases upon execution thereof, including, without limitation, any renewal, expansion, first offer, first refusal, first negotiation and other rights, regardless of whether such rights are executed strictly in accordance with their respective terms or pursuant to a lease amendment or a new lease (the "**Superior Rights**"). Further, such right of first offer shall be subject and subordinate to the terms of any renewal right contained in any lease of the First Offer Space entered into by Landlord with a third party after Tenant's failure to exercise its right of first offer as provided in this Section 1.3 (the "**Intervening Leases**"). All such tenants under Initial Leases or Intervening Leases, are collectively referred to as the "**Superior Right Holders**".

1.3.2 **Procedure for Lease**.

1.3.2.1 **Procedure for Offer**. Subject to the terms hereof, Landlord shall notify Tenant (the "**First Offer Notice**") prior to entering into any lease with a third party for the First Offer Space, which notice shall outline the base rent, allowance amounts if any, length of term, and other economic terms on which Landlord would be willing to lease the First Offer Space (as set forth in such proposal) to Tenant (the "**Fundamental Terms**"). Pursuant to such First Offer Notice, Landlord shall offer to lease to Tenant the applicable First Offer Space on the Fundamental Terms.

1.3.2.2 **Procedure for Acceptance**. If Tenant wishes to exercise Tenant's right of first offer with respect to the First Offer Space described in the First Offer Notice, then within five (5) business days after delivery of the First Offer Notice to Tenant, Tenant shall deliver notice to Landlord of Tenant's irrevocable exercise of its right of first offer with respect to all of the First Offer Space described in the First Offer Notice on the Fundamental Terms provided for therein. If Tenant does not so notify Landlord within such five (5) business day period of Tenant's exercise of its first offer right, then Landlord shall be free to negotiate and enter into a lease for

the First Offer Space to anyone whom it desires on any terms that Landlord desires, provided that, if Landlord has not entered into any such lease within ninety (90) days after the date of delivery of the First Offer Notice, then, prior to entering into any lease of such First Offer Space, Landlord shall first again offer such space to Tenant in accordance with the terms of this Section 1.3, provided that, prior to the entering into a lease of such space on terms that are more than 10% more favorable to the tenant than those set forth in the First Offer Notice (as determined on a net effective basis), Landlord shall first deliver any other First Officer Notice to Tenant offering such space to Tenant on such reduced terms. Tenant shall respond to any such "re-offer" within five (5) days after delivery of such "re-offer" notice.

1.3.2.3 **Construction In First Offer Space**. Unless the Fundamental Terms provided to Tenant for the First Offer Space otherwise specify, Tenant shall take the First Offer Space in its "as is" condition, and Landlord shall not be obligated to provide or pay for any improvement of the First Offer Space. For the avoidance of doubt, if the Fundamental Terms include a tenant improvement allowance or a turn-key build out, Tenant shall receive the same allowance or turn-key build out, as applicable.

1.3.2.4 **Lease of First Offer Space**. If Tenant timely exercises Tenant's right of first offer to lease First Offer Space as set forth herein, Tenant shall within fifteen (15) days after receipt of Landlord's first draft of an amendment accurately setting forth the Fundamental Terms and not containing any new material terms, enter an amendment to this Lease (the "**First Offer Space Amendment**") for such First Offer Space pursuant to this Section 1.3. Tenant's lease of such First Offer Space shall be upon the express terms set forth in the First Offer Notice, but otherwise upon the same general terms and conditions set forth in this Lease and this Section 1.3. The First Offer Space Lease shall not contain the rights set forth in Section 2.2, below, unless such rights were set forth in the First Offer Notice. The term of Tenant's lease of the First Offer Space shall commence on the date set forth in the First Offer Notice (provided that such commencement date shall in no event be earlier than the date of Landlord's delivery of the applicable First Offer Space to Tenant), and shall expire on the applicable date set forth in the First Offer Notice (the "**First Offer Space Expiration Date**").

1.3.2.5 **Limitation of Exercise of First Offer Right**. The right to lease First Offer Space as provided in this Section 1.3 may not be exercised if, as of the date of the attempted exercise of the expansion option by Tenant, Tenant is in default under this Lease, beyond any applicable notice and cure period. The terms of this Section 1.3 shall be personal to the originally named Tenant hereunder (the "**Original Tenant**") or a Permitted Transferee, and may not be exercised by any assignee, subtenant, or other Transferee of Original Tenant's interest in this Lease other than a Permitted Transferee. Tenant's right of first offer shall be continuous during the initial Lease Term. Tenant's rejection of any particular offer shall not relieve Landlord of its obligation to again offer the First Offer Space to Tenant any time the First Offer Space subsequently becomes available (provided that Tenant's rights under this Section 1.3 shall be subject and subordinate to the renewal rights of any tenant under a lease entered into by Landlord after Tenant has declined or failed to respond to a First Offer Notice).

2. LEASE TERM; OPTION TERM.

2.1 **Lease Term**. The terms and provisions of this Lease shall be effective as of the date of this Lease. The term of this Lease (the "**Lease Term**") shall be as set forth in Section 3.1 of the Summary, shall commence on the date set forth in Section 3.2 of the Summary (the "**Lease Commencement Date**"), and shall terminate on the date set forth in Section 3.3 of the Summary (the "**Lease Expiration Date**") unless this Lease is sooner terminated as hereinafter provided. For purposes of this Lease, the term "**Lease Year**" shall mean each consecutive twelve (12) month period during the Lease Term. At any time during the Lease Term, Landlord may deliver to Tenant a notice in the form as set forth in **Exhibit C**, attached hereto, as a confirmation only of the information set forth therein, which Tenant shall execute and return to Landlord within five (5) days of receipt thereof. Notwithstanding the foregoing, if Landlord has not delivered possession of the Premises in the condition required by Section 1.1.1, above, (1) on or before December 1, 2016, then, as Tenant's sole remedy for such delay, the date Tenant is otherwise obligated to commence payment of rent shall be delayed by one day for each day that the delivery date is delayed beyond such date, or (2) April 1, 2017, then, Tenant shall also have the right to terminate this Lease by written notice thereof to Landlord, whereupon any monies previously paid by Tenant to Landlord shall be reimbursed to Tenant. The foregoing dates shall be extended to the extent of any delays in delivery of possession caused by Tenant Delay, as provided in Section 1(j) of the Tenant Work Letter, war, terrorism, acts of God, natural disaster, civil unrest, governmental strike or area-wide of industry-wide labor disputes, inability to obtain services, labor, or materials or reasonable substitutes therefor, or delays due to utility companies that are not the result of any action or inaction of Landlord (provided that such delay shall not extend any such date by more than ninety (90) days).

2.2 **Option Term**.

2.2.1 **Option Right**. Landlord hereby grants to the Original Tenant, and its "Permitted Assignees", as that term is defined in Section 14.8, below, one (1) option to extend the Lease Term for a period of five (5) years (the "**Option Term**"), which option shall be irrevocably exercised only by written notice delivered by Tenant to Landlord not more than twelve (12) months nor less than nine (9) months prior to the expiration of the initial Lease Term, provided that the following conditions **(**the "**Option Conditions**") are satisfied: (i) as of the date of delivery of such notice, Tenant is not in default under this Lease, after the expiration of any applicable notice and cure period; (ii) Tenant has not previously been in default under this Lease, after the expiration of any applicable notice and cure period, more than twice in the twelve (12) month period prior to the date of Tenant's attempted exercise; and (iii) the Lease then remains in full force and effect. Landlord may, at Landlord's option, exercised in Landlord's sole and absolute discretion, waive any of the Option Conditions in which case the option, if otherwise properly exercised by Tenant, shall remain in full force and effect. Upon the proper exercise of such option to extend, and provided that Tenant satisfies all of the Option Conditions (except those, if any, which are waived by Landlord), the Lease Term, as it applies to the Premises, shall be extended for a period of five (5) years. The rights contained in this Section 2.2 shall be personal to Original Tenant and any Permitted Assignees, and may be exercised by Original Tenant or such Permitted Assignees (and not by any assignee, sublessee or other "Transferee," as that term is defined in Section 14.1 of this Lease, of Tenant's interest in this Lease).

2.2.2 **Option Rent**. The annual Rent payable by Tenant during the Option Term (the "**Option Rent**") shall be equal to the "Fair Rental Value," as that term is defined below, for the Premises as of the commencement date of the Option Term. The "**Fair Rental Value**," as used in this Lease, shall be equal to the annual rent per rentable square foot (including additional rent and considering any "base year" or "expense stop" applicable thereto), including all escalations, at which tenants (pursuant to leases consummated within the twelve (12) month period preceding the first day of the Option Term), are leasing non-sublease, non-encumbered, non-equity space which is not significantly greater or smaller in size than the subject space, with a comparable level of improvements (excluding any property that Tenant would be allowed to remove from the Premises at the termination of the Lease), for a comparable lease term, in an arm's length transaction, which comparable space is located in the "Comparable Buildings," as that term is defined in this Section 2.2.2, below (transactions satisfying the foregoing criteria shall be known as the "**Comparable Transactions**"), taking into consideration the following concessions (the "**Concessions**"): (a) rental abatement concessions, if any, being granted such tenants in connection with such comparable space; (b) tenant improvements or allowances provided or to be provided for such comparable space, and taking into account the value, if any, of the existing improvements in the subject space, such value to be based upon the age, condition, design, quality of finishes and layout of the improvements and the extent to which the same can be utilized by a general office/lab user other than Tenant; and (c) other reasonable monetary concessions being granted such tenants in connection with such comparable space; provided, however, that in calculating the Fair Rental Value, no consideration shall be given to the fact that Landlord is or is not required to pay a real estate brokerage commission in connection with Tenant's exercise of its right to extend the Lease Term, or the fact that landlords are or are not paying real estate brokerage commissions in connection with such comparable space. The Concessions shall be reflected in the effective rental rate (which effective rental rate shall take into consideration the total dollar value of such Concessions as amortized on a straight-line basis over the applicable term of the Comparable Transaction (in which case such Concessions evidenced in the effective rental rate shall not be granted to Tenant)) payable by Tenant. The term "**Comparable Buildings**" shall mean the Building and those other life sciences buildings which are comparable to the Building in terms of age (based upon the date of completion of construction or major renovation of to the building), quality of construction, level of services and amenities, size and appearance, and are located in South San Francisco, California and the surrounding commercial area.

2.2.3 **Determination of Option Rent**. In the event Tenant timely and appropriately exercises an option to extend the Lease Term, Landlord shall notify Tenant of Landlord's determination of the Option Rent within thirty (30) days thereafter. If Tenant, on or before the date which is ten (10) days following the date upon which Tenant receives Landlord's determination of the Option Rent, in good faith objects to Landlord's determination of the Option Rent, then Landlord and Tenant shall attempt to agree upon the Option Rent using their best good-faith efforts. If Landlord and Tenant fail to reach agreement within ten (10) days following Tenant's

objection to the Option Rent (the "**Outside Agreement Date**"), then Tenant shall have the right to withdraw its exercise of the option by delivering written notice thereof to Landlord within five (5) days thereafter, in which event Tenant's right to extend the Lease pursuant to this Section 2.2 shall be of no further force or effect. If Tenant does not withdraw its exercise of the extension option, each party shall make a separate determination of the Option Rent, as the case may be, within ten (10) days after the Outside Agreement Date, and such determinations shall be submitted to arbitration in accordance with Sections 2.2.3.1 through 2.2.3.7, below. If Tenant fails to object to Landlord's determination of the Option Rent within the time period set forth herein, then Tenant shall be deemed to have objected to Landlord's determination of Option Rent.

2.2.3.1 Landlord and Tenant shall each appoint one arbitrator who shall be a real estate appraiser who shall have been active over the five (5) year period ending on the date of such appointment in the appraisal of other class A life sciences buildings located in the South San Francisco market area. The determination of the arbitrators shall be limited solely to the issue of whether Landlord's or Tenant's submitted Option Rent is the closest to the actual Option Rent, taking into account the requirements of Section 2.2.2 of this Lease, as determined by the arbitrators. Each such arbitrator shall be appointed within fifteen (15) days after the Outside Agreement Date. Landlord and Tenant may consult with their selected arbitrators prior to appointment and may select an arbitrator who is favorable to their respective positions. The arbitrators so selected by Landlord and Tenant shall be deemed "**Advocate Arbitrators**."

2.2.3.2 The two (2) Advocate Arbitrators so appointed shall be specifically required pursuant to an engagement letter within ten (10) days of the date of the appointment of the last appointed Advocate Arbitrator to agree upon and appoint a third arbitrator ("**Neutral Arbitrator**") who shall be qualified under the same criteria set forth hereinabove for qualification of the two Advocate Arbitrators, except that neither the Landlord or Tenant or either parties' Advocate Arbitrator may, directly or indirectly, consult with the Neutral Arbitrator prior or subsequent to his or her appearance. The Neutral Arbitrator shall be retained via an engagement letter jointly prepared by Landlord's counsel and Tenant's counsel.

2.2.3.3 The three arbitrators shall, within thirty (30) days of the appointment of the Neutral Arbitrator, reach a decision as to whether the parties shall use Landlord's or Tenant's submitted Option Rent, and shall notify Landlord and Tenant thereof.

2.2.3.4 The decision of the majority of the three arbitrators shall be binding upon Landlord and Tenant.

2.2.3.5 If either Landlord or Tenant fails to appoint an Advocate Arbitrator within fifteen (15) days after the Outside Agreement Date, then either party may petition the presiding judge of the Superior Court of San Mateo County to appoint such Advocate Arbitrator subject to the criteria in Section 2.2.3.1 of this Lease, or if he or she refuses to act, either party may petition any judge having jurisdiction over the parties to appoint such Advocate Arbitrator.

2.2.3.6 If the two (2) Advocate Arbitrators fail to agree upon and appoint the Neutral Arbitrator, then either party may petition the presiding judge of the Superior Court of San Mateo County to appoint the Neutral Arbitrator, subject to criteria in Section 2.2.3.1 of this Lease, or if he or she refuses to act, either party may petition any judge having jurisdiction over the parties to appoint such arbitrator.

2.2.3.7 The cost of the arbitration shall be paid by Landlord and Tenant equally.

2.2.3.8 In the event that the Option Rent shall not have been determined pursuant to the terms hereof prior to the commencement of the Option Term, Tenant shall be required to pay the Option Rent initially provided by Landlord to Tenant, and upon the final determination of the Option Rent, the payments made by Tenant shall be reconciled with the actual amounts of Option Rent due, and the appropriate party shall make any corresponding payment to the other party.

2.3 **Early Termination Right**. In the event that Landlord and Tenant fully execute and deliver a new lease agreement (the "**New Lease**") for other space in the Project during the Lease Term (or other space in a project owned by an affiliate of Landlord) which satisfies the following conditions: (i) a term for such New Lease which extends beyond the Lease Expiration Date of this Lease as set forth in Section 3.4 of the Summary, and (ii) the premises under such New Lease containing no less than the number of rentable square feet of the Premises as set forth in Section 2.2 of the Summary (i.e., contains more than 38,109 rentable square feet), and provided that Tenant is not then in default of this Lease beyond any applicable notice and cure period, then Tenant shall have the right to terminate this Lease without the payment of any penalty or termination fee by delivering written notice (the "**Tenant Termination Notice**") to Landlord not less than thirty (30) days prior to the commencement date under such New Lease, and in the event such Tenant Termination Notice is timely delivered by Tenant to Landlord, then this Lease shall terminate effective as of the date which is five (5) business days following the commencement date under such New Lease (the "**Tenant Early Termination Date**"). To the extent Tenant exercises its right to terminate this Lease, pursuant to the terms of this Section 2.3, then this Lease shall terminate effective as of the Tenant Early Termination Date with the same force and effect as if the Lease were scheduled to expire in accordance with its terms as of such Tenant Early Termination Date, subject to the provisions of this Lease which expressly survive the expiration or earlier termination of this Lease.

3. BASE RENT. Tenant shall pay, without prior notice or demand, to Landlord at the address set forth in Section 4 of the Summary, or, at Landlord's option, at such other place as Landlord may from time to time designate in writing, by a check for currency which, at the time of payment, is legal tender for private or public debts in the United States of America, base rent ("**Base Rent**") as set forth in Section 4 of the Summary, payable in equal monthly installments as set forth in Section 4 of the Summary in advance on or before the first day of each and every calendar month during the Lease Term, without any setoff or deduction whatsoever. The Base Rent for the first full month of the Lease Term shall be paid at the time of Tenant's execution of this Lease. If any Rent payment date (including the Lease Commencement Date) falls on a day of the month other than the first day of such month or if any payment of Rent is for a period which is shorter than one month, the Rent for any fractional month shall accrue on a daily basis for the period from the date such payment is due to the end of such calendar month or to the end of the Lease Term at a rate per day which is equal to 1/365 of the applicable annual Rent. All other payments or adjustments required to be made under the terms of this Lease that require proration on a time basis shall be prorated on the same basis.

4. ADDITIONAL RENT.

4.1 **General Terms**.

4.1.1 **Direct Expenses; Additional Rent**. In addition to paying the Base Rent specified in Article 3 of this Lease, Tenant shall pay "**Tenant's Share**" of the annual "**Direct Expenses**," as those terms are defined in Sections 4.2.6 and 4.2.2 of this Lease, respectively, allocable to the Building as described in Section 4.3. Such payments by Tenant, together with any and all other amounts payable by Tenant to Landlord pursuant to the terms of this Lease, are hereinafter collectively referred to as the "**Additional Rent**", and the Base Rent and the Additional Rent are herein collectively referred to as "**Rent**." All amounts due under this Article 4 as Additional Rent shall be payable for the same periods and in the same manner as the Base Rent. Without limitation on other obligations of Tenant which survive the expiration of the Lease Term, the obligations of Tenant to pay the Additional Rent provided for in this Article 4 shall survive the expiration of the Lease Term.

4.1.2 **Triple Net Lease**. Landlord and Tenant acknowledge that, to the extent provided in this Lease, it is their intent and agreement that this Lease be a "**TRIPLE NET**" lease and that as such, the provisions contained in this Lease are intended to pass on to Tenant or reimburse Landlord for the costs and expenses reasonably associated with this Lease, the Building and the Project, and Tenant's operation therefrom to the extent provided in this Lease. To the extent such costs and expenses payable by Tenant cannot be charged directly to, and paid by, Tenant, such costs and expenses shall be paid by Landlord but reimbursed by Tenant as Additional Rent.

4.2 **Definitions of Key Terms Relating to Additional Rent** . As used in this Article 4, the following terms shall have the meanings hereinafter set forth:

4.2.1 Intentionally Deleted.

4.2.2 "**Direct Expenses**" shall mean "**Operating Expenses**" and "**Tax Expenses**."

4.2.3 "**Expense Year**" shall mean each calendar year in which any portion of the Lease Term falls, through and including the calendar year in which the Lease Term expires, provided that Landlord, upon notice to Tenant, may change the Expense Year from time to time to any other twelve (12) consecutive month period, and, in the event of any such change, Tenant's Share of Direct Expenses shall be equitably adjusted for any Expense Year involved in any such change.

4.2.4 "**Operating Expenses**" shall mean all expenses, costs and amounts of every kind and nature which Landlord pays or accrues during any Expense Year because of or in connection with the ownership, management, maintenance, security, repair, replacement, restoration or operation of the Project, or any portion thereof. Without limiting the generality of the foregoing, Operating Expenses shall specifically include any and all of the following: (i) the cost of supplying all utilities, the cost of operating, repairing and maintaining the utility, telephone, mechanical, sanitary, storm drainage, and elevator systems, and the cost of maintenance and service contracts in connection therewith; (ii) the cost of licenses, certificates, permits and inspections and the cost of contesting any governmental enactments which are reasonably likely to increase Operating Expenses during the Lease Term, and the costs incurred in connection with a governmentally mandated transportation system management program or similar program; (iii) the cost of all insurance carried by Landlord in connection with the Project and Premises as reasonably determined by Landlord; (iv) the cost of landscaping, relamping, and all supplies, tools, equipment and materials used in the operation, repair and maintenance of the Project, or any portion thereof; (v) the cost of parking area operation, repair, restoration, and maintenance; (vi) management and/or incentive fees, consulting fees, legal fees and accounting fees, of all contractors and consultants in connection with the management, operation, maintenance and repair of the Project; (vii) payments under any equipment rental agreements; (viii) subject to item (f), below, wages, salaries and other compensation and benefits, including taxes levied thereon, of all persons engaged in the operation, maintenance and security of the Project; (ix) costs under any easement pertaining to the sharing of costs by the Project; (x) operation, repair, maintenance and replacement of all systems and equipment and components thereof of the Project; (xi) the cost of janitorial, alarm, security and other services, replacement of wall and floor coverings, ceiling tiles and fixtures in Common Areas, maintenance and replacement of curbs and walkways, repair to roofs and re-roofing; (xii) amortization (including interest on the unamortized cost) over such period of time as Landlord shall reasonably determine, of the cost of acquiring or the rental expense of personal property used in the maintenance, operation and repair of the Project, or any portion thereof; (xiii) the cost of capital improvements or other costs incurred in connection with the Project (A) which are intended to effect economies in the operation or maintenance of the Project, or any portion thereof, or to reduce current or future Operating Expenses or to enhance the safety or security of the Project or its occupants, (B) which are required to comply with present or anticipated conservation programs, (C) which are replacements or modifications of nonstructural items located in the Common Areas required to keep the Common Areas in good order or condition, or (D) which are required under any governmental law or regulation; provided, however, that any capital expenditure shall be amortized (including reasonable interest on the amortized cost) over the reasonable useful life of such capital item; and (xiv) costs, fees, charges or assessments imposed by, or resulting from any mandate imposed on Landlord by, any federal, state or local government for fire and police protection, trash removal, community services, or other services which do not constitute "Tax Expenses" as that term is defined in Section 4.2.5, below, and (xv) payments under any easement, license, operating agreement, declaration, restrictive covenant, or instrument pertaining to the sharing of costs by the Building, including, without limitation, any covenants, conditions and restrictions affecting the property, and reciprocal easement agreements affecting the property, any parking licenses, and any agreements with transit agencies affecting the Property (collectively, "**Underlying Documents**"). Notwithstanding the foregoing, for purposes of this Lease, Operating Expenses shall not, however, include:

(a) costs, including legal fees, space planners' fees, advertising and promotional expenses (except as otherwise set forth above), and brokerage fees incurred in connection with the original construction or development, or original or future leasing of the Project, and costs, including permit, license and inspection costs, incurred with respect to the installation of tenant improvements made for new tenants initially occupying space in the Project after the Lease Commencement Date or incurred in renovating or otherwise improving, decorating, painting or redecorating vacant space for tenants or other occupants of the Project (excluding, however, such costs relating to any common areas of the Project or parking facilities);

(b) except as set forth in items (xii), (xiii), and (xiv) above, depreciation, interest and principal payments on mortgages and other debt costs, if any, penalties and interest;

(c) costs for which the Landlord is reimbursed by any tenant or occupant of the Project or by insurance by its carrier or any tenant's carrier or by anyone else, electric power costs for which any tenant directly contracts with the local public service company and costs of utilities and services provided to other tenants that are not provided to Tenant;

(d) any bad debt loss, rent loss, or reserves for bad debts or rent loss or other reserves to the extent not used in the same year;

(e) costs associated with the operation of the business of the partnership or entity which constitutes the Landlord, as the same are distinguished from the costs of operation of the Project (which shall specifically include, but not be limited to, accounting costs associated with the operation of the Project). Costs associated with the operation of the business of the partnership or entity which constitutes the Landlord include costs of partnership accounting and legal matters, costs of defending any lawsuits with any mortgagee (except as the actions of the Tenant may be in issue), costs of selling, syndicating, financing, mortgaging or hypothecating any of the Landlord's interest in the Project, and costs incurred in connection with any disputes between Landlord and its employees, between Landlord and Project management, or between Landlord and other tenants or occupants;

(f) the wages and benefits of any employee who does not devote substantially all of his or her employed time to the Project unless such wages and benefits are prorated to reflect time spent on operating and managing the Project vis-a-vis time spent on matters unrelated to operating and managing the Project; provided, that in no event shall Operating Expenses for purposes of this Lease include wages and/or benefits attributable to personnel above the level of Project manager;

(g) amount paid as ground rental for the Project by the Landlord;

(h) except for a property management fee not to exceed three percent (3%) of gross revenues, overhead and profit increment paid to the Landlord, and any amounts paid to the Landlord or to subsidiaries or affiliates of the Landlord for services in the Project to the extent the same exceeds the costs of such services rendered by qualified, first-class unaffiliated third parties on a competitive basis;

(i) any compensation paid to clerks, attendants or other persons in commercial concessions operated by the Landlord (other than as direct reimbursement for costs which, if incurred directly by Landlord, would properly be included in Operating Expenses);

(j) rentals and other related expenses incurred in leasing air conditioning systems, elevators or other equipment which if purchased the cost of which would be excluded from Operating Expenses as a capital cost, except equipment not affixed to the Project which is used in providing engineering, janitorial or similar services and, further excepting from this exclusion such equipment rented or leased to remedy or ameliorate an emergency condition in the Project;

(k) all items and services for which Tenant or any other tenant in the Project reimburses Landlord or which Landlord provides selectively to one or more tenants (other than Tenant) without reimbursement;

(l) any costs expressly excluded from Operating Expenses elsewhere in this Lease;

(m) rent for any office space occupied by Project management personnel;

(n) costs arising from the gross negligence or willful misconduct of Landlord or its agents, employees or contractors in connection with this Lease;

(o) costs incurred to comply with laws relating to the removal or remediation of hazardous material (as defined under applicable law), and any costs of fines or penalties relating to the presence of hazardous material, in each case to the extent not brought into the Building or Premises by Tenant or any Tenant Parties;

(p) costs to correct any construction defect in the Project or to remedy any violation of a covenant, condition, restriction, underwriter's requirement or law that exists as of the Lease Commencement Date;

(q) capital costs occasioned by casualties or condemnation.

(r) legal fees, accountants' fees (other than normal bookkeeping expenses) and other expenses incurred in connection with disputes of tenants or other occupants of the Project or associated with the enforcement of the terms of any leases with tenants or the defense of Landlord's title to or interest in the Project or any part thereof;

(s) costs incurred due to a violation by Landlord or any other tenant of the Project of the terms and conditions of a lease; and

(t) self-insurance retentions

4.2.5 **Taxes**.

4.2.5.1 "**Tax Expenses**" shall mean all federal, state, county, or local governmental or municipal taxes, fees, charges or other impositions of every kind and nature, whether general, special, ordinary or extraordinary (including, without limitation, real estate taxes, general and special assessments, transit taxes, leasehold taxes or taxes based upon the receipt of rent, including gross receipts or sales taxes applicable to the receipt of rent, unless required to be paid by Tenant, personal property taxes imposed upon the fixtures, machinery, equipment, apparatus, systems and equipment, appurtenances, furniture and other personal property used in connection with the Project, or any portion thereof), which shall be paid or accrued during any Expense Year (without regard to any different fiscal year used by such governmental or municipal authority) because of or in connection with the ownership, leasing and operation of the Project, or any portion thereof.

4.2.5.2 Tax Expenses shall include, without limitation: (i) Any tax on the rent, right to rent or other income from the Project, or any portion thereof, or as against the business of leasing the Project, or any portion thereof; (ii) Any assessment, tax, fee, levy or charge in addition to, or in substitution, partially or totally, of any assessment, tax, fee, levy or charge previously included within the definition of real property tax; (iii) Any assessment, tax, fee, levy, or charge allocable to or measured by the area of the Premises or the Rent payable hereunder, including, without limitation, any business or gross income tax or excise tax with respect to the receipt of such rent, or upon or with respect to the possession, leasing, operating, management, maintenance, alteration, repair, use or occupancy by Tenant of the Premises, or any portion thereof; and (iv) Any assessment, tax, fee, levy or charge, upon this transaction or any document to which Tenant is a party, creating or transferring an interest or an estate in the Premises or the improvements thereon.

4.2.5.3 Any costs and expenses (including, without limitation, reasonable attorneys' and consultants' fees) incurred in attempting to protest, reduce or minimize Tax Expenses shall be included in Tax Expenses in the Expense Year such expenses are incurred. Tax refunds shall be credited against Tax Expenses and refunded to Tenant regardless of when received, based on the Expense Year to which the refund is applicable, provided that in no event shall the amount to be refunded to Tenant for any such Expense Year exceed the total amount paid by Tenant as Additional Rent under this Article 4 for such Expense Year. If Tax Expenses for any period during the Lease Term or any extension thereof are increased after payment thereof for any reason, including, without limitation, error or reassessment by applicable governmental or municipal authorities, Tenant shall pay Landlord upon demand Tenant's Share of any such increased Tax Expenses. Notwithstanding anything to the contrary contained in this Section 4.2.5, there shall be excluded from Tax Expenses (i) all excess profits taxes, franchise taxes, gift taxes, capital stock taxes, inheritance and succession taxes, transfer taxes, estate taxes, federal and state income taxes, and other

taxes to the extent applicable to Landlord's net income (as opposed to rents, receipts or income attributable to operations at the Project), (ii) any items included as Operating Expenses, (iii) any items paid by Tenant under Section 4.5 of this Lease, (iv) assessments in excess of the amount which would be payable if such assessment expense were paid in installments over the longest permitted term; (v) taxes imposed on land and improvements other than the Project; and (vi) tax increases resulting from the improvement of any of the Project for the sole use of other occupants.

4.2.6 "**Tenant's Share**" shall mean the percentage set forth in Section 6 of the Summary.

4.3 **Allocation of Direct Expenses**. The parties acknowledge that the Building is a part of a multi-building project and that the costs and expenses incurred in connection with the Project (i.e., the Direct Expenses) should be shared between the Building and the other buildings in the Project. Accordingly, as set forth in Section 4.2 above, Direct Expenses (which consist of Operating Expenses and Tax Expenses) are determined annually for the Project as a whole, and a portion of the Direct Expenses, which portion shall be determined by Landlord on an equitable basis, shall be allocated to the Building (as opposed to other buildings in the Project). Such portion of Direct Expenses allocated to the Building shall include all Direct Expenses attributable solely to the Building and a pro rata portion of the Direct Expenses attributable to the Project as a whole, and shall not include Direct Expenses attributable solely to other buildings in the Project.

4.4 **Calculation and Payment of Additional Rent**. Tenant shall pay to Landlord, in the manner set forth in Section 4.4.1, below, and as Additional Rent, Tenant's Share of Direct Expenses for each Expense Year.

4.4.1 **Statement of Actual Direct Expenses and Payment by Tenant**. Landlord shall give to Tenant within five (5) months following the end of each Expense Year, a statement (the "**Statement**") which shall state the Direct Expenses incurred or accrued for such preceding Expense Year, and which shall indicate the amount of Tenant's Share of Direct Expenses. Upon receipt of the Statement for each Expense Year commencing or ending during the Lease Term, Tenant shall pay, with its next installment of Base Rent due that is at least thirty (30) days thereafter, the full amount of Tenant's Share of Direct Expenses for such Expense Year, less the amounts, if any, paid during such Expense Year as "**Estimated Direct Expenses**," as that term is defined in Section 4.4.2, below, and if Tenant paid more as Estimated Direct Expenses than the actual Tenant's Share of Direct Expenses, Tenant shall receive a credit in the amount of Tenant's overpayment against Rent next due under this Lease. The failure of Landlord to timely furnish the Statement for any Expense Year shall not prejudice Landlord or Tenant from enforcing its rights under this Article 4. Even though the Lease Term has expired and Tenant has vacated the Premises, when the final determination is made of Tenant's Share of Direct Expenses for the Expense Year in which this Lease terminates, Tenant shall immediately pay to Landlord such amount, and if Tenant paid more as Estimated Direct Expenses than the actual Tenant's Share of Direct Expenses, Landlord shall, within thirty (30) days, deliver a check payable to Tenant in the amount of the overpayment. The provisions of this Section 4.4.1 shall survive the expiration or earlier termination of the Lease Term. Notwithstanding the immediately preceding sentence, Tenant shall not be responsible for Tenant's Share of any Direct Expenses attributable to any Expense Year which are first billed to Tenant more than two (2) calendar years after the earlier of the expiration of the applicable Expense Year or the Lease Expiration Date, provided that in any event Tenant shall be responsible for Tenant's Share of Direct Expenses levied by any governmental authority or by any public utility companies at any time following the Lease Expiration Date which are attributable to any Expense Year (provided that Landlord delivers Tenant a bill for such amounts within two (2) years following Landlord's receipt of the bill therefor).

4.4.2 **Statement of Estimated Direct Expenses**. In addition, Landlord shall give Tenant a yearly expense estimate statement (the "**Estimate Statement**") which shall set forth Landlord's reasonable estimate (the "**Estimate**") of what the total amount of Direct Expenses for the then-current Expense Year shall be and the estimated Tenant's Share of Direct Expenses (the "**Estimated Direct Expenses**"). The failure of Landlord to timely furnish the Estimate Statement for any Expense Year shall not preclude Landlord from enforcing its rights to collect any Estimated Direct Expenses under this Article 4, nor shall Landlord be prohibited from revising any Estimate Statement or Estimated Direct Expenses theretofore delivered to the extent necessary. Thereafter, Tenant shall pay, with its next installment of Base Rent due that is at least thirty (30) days thereafter, a fraction of the Estimated

Direct Expenses for the then-current Expense Year (reduced by any amounts paid pursuant to the last sentence of this Section 4.4.2). Such fraction shall have as its numerator the number of months which have elapsed in such current Expense Year, including the month of such payment, and twelve (12) as its denominator. Until a new Estimate Statement is furnished (which Landlord shall have the right to deliver to Tenant at any time), Tenant shall pay monthly, with the monthly Base Rent installments, an amount equal to one-twelfth (1/12) of the total Estimated Direct Expenses set forth in the previous Estimate Statement delivered by Landlord to Tenant.

4.5 **Taxes and Other Charges for Which Tenant Is Directly Responsible**. Tenant shall be liable for and shall pay ten (10) days before delinquency, taxes levied against Tenant's equipment, furniture, fixtures and any other personal property located in or about the Premises. If any such taxes on Tenant's equipment, furniture, fixtures and any other personal property are levied against Landlord or Landlord's property or if the assessed value of Landlord's property is increased by the inclusion therein of a value placed upon such equipment, furniture, fixtures or any other personal property and if Landlord pays the taxes based upon such increased assessment, which Landlord shall have the right to do regardless of the validity thereof but only under proper protest if requested by Tenant, Tenant shall upon demand repay to Landlord the taxes so levied against Landlord or the proportion of such taxes resulting from such increase in the assessment, as the case may be.

4.6 **Landlord's Books and Records**. Within one hundred twenty (120) days after receipt by Tenant of a Statement, if Tenant disputes the amount of Additional Rent set forth in the Statement, a member of Tenant's finance department, or an independent certified public accountant (which accountant is a member of a nationally recognized accounting firm and is not working on a contingency fee basis) ("**Tenant's Accountant**"), designated and paid for by Tenant, may, after reasonable notice to Landlord and at reasonable times, inspect Landlord's records with respect to the Statement at Landlord's offices, provided that there is no existing Event of Default and Tenant has paid all amounts required to be paid under the applicable Estimate Statement and Statement, as the case may be. In connection with such inspection, Tenant and Tenant's agents must agree in advance to follow Landlord's reasonable rules and procedures regarding inspections of Landlord's records, and shall execute a commercially reasonable confidentiality agreement regarding such inspection. Tenant's failure to dispute the amount of Additional Rent set forth in any Statement within one hundred twenty (120) days of Tenant's receipt of such Statement shall be deemed to be Tenant's approval of such Statement and Tenant, thereafter, waives the right or ability to dispute the amounts set forth in such Statement. If after such inspection, Tenant still disputes such Additional Rent, a determination as to the proper amount shall be made, at Tenant's expense, by an independent certified public accountant (the "**Accountant**") selected by Landlord and subject to Tenant's reasonable approval; provided that if such Accountant determines that Direct Expenses were overstated by more than five percent (5%), then the cost of the Accountant and the cost of such determination shall be paid for by Landlord, and Landlord shall reimburse Tenant's the cost of the Tenant's Accountant (provided that such cost shall be a reasonable market cost for such services). Tenant hereby acknowledges that Tenant's sole right to inspect Landlord's books and records and to contest the amount of Direct Expenses payable by Tenant shall be as set forth in this Section 4.6, and Tenant hereby waives any and all other rights pursuant to applicable law to inspect such books and records and/or to contest the amount of Direct Expenses payable by Tenant.

5. USE OF PREMISES.

5.1 **Permitted Use**. Tenant shall use the Premises solely for the Permitted Use set forth in Section 7 of the Summary and Tenant shall not use or permit the Premises or the Project to be used for any other purpose or purposes whatsoever without the prior written consent of Landlord, which may be withheld in Landlord's sole discretion.

5.2 **Prohibited Uses**. Tenant further covenants and agrees that Tenant shall not use or permit any person or persons to use, the Premises or any part thereof for any use or purpose in violation of the laws of the United States of America, the State of California, or the ordinances, regulations or requirements of the local municipal or county governing body or other lawful authorities having jurisdiction over the Project) including, without limitation, any such laws, ordinances, regulations or requirements relating to hazardous materials or substances, as those terms are defined by applicable laws now or hereafter in effect. Landlord shall have the right to impose reasonable, nondiscriminatory and customary rules and regulations regarding the use of the Project that do not unreasonably interfere with Tenant's use of the Premises, as reasonably deemed necessary by Landlord with respect to the orderly operation of the Project, and Tenant shall comply with such reasonable rules and regulations.

Tenant shall not do or permit anything to be done in or about the Premises which will in any way obstruct or interfere with the rights of other tenants or occupants of the Building, or injure or annoy them or use or allow the Premises to be used for any improper, unlawful or objectionable purpose, nor shall Tenant cause, maintain or permit any nuisance in, on or about the Premises. Tenant shall comply with, and Tenant's rights and obligations under the Lease and Tenant's use of the Premises shall be subject and subordinate to, all recorded easements, covenants, conditions, and restrictions now or hereafter affecting the Project, so long as the same do not unreasonably interfere with Tenant's use of the Premises or parking rights or materially increase Tenant's obligations or decrease Tenant's rights under this Lease.

5.3 **Hazardous Materials**.

5.3.1 **Tenant's Obligations**.

5.3.1.1 **Prohibitions**. As a material inducement to Landlord to enter into this Lease with Tenant, Tenant has fully and accurately completed Landlord's Pre-Leasing Environmental Exposure Questionnaire (the "**Environmental Questionnaire**"), which is attached as **Exhibit E**. Tenant agrees that except for those chemicals or materials, and their respective quantities, specifically listed on the Environmental Questionnaire (as the same may be updated from time to time as provided below), neither Tenant nor Tenant's employees, contractors and subcontractors of any tier, entities with a contractual relationship with Tenant (other than Landlord), or any entity acting as an agent or sub-agent of Tenant (collectively, "**Tenant's Agents**") will produce, use, store or generate any "Hazardous Materials," as that term is defined below, on, under or about the Premises, nor cause any Hazardous Material to be brought upon, placed, stored, manufactured, generated, blended, handled, recycled, used or "Released," as that term is defined below, on, in, under or about the Premises. If any information provided to Landlord by Tenant on the Environmental Questionnaire, or otherwise relating to information concerning Hazardous Materials is intentionally false, incomplete, or misleading in any material respect, the same shall be deemed a default by Tenant under this Lease. Upon Landlord's request, or in the event of any material change in Tenant's use of Hazardous Materials in the Premises, Tenant shall deliver to Landlord an updated Environmental Questionnaire at least once a year. Tenant shall notify Landlord prior to using any Hazardous Materials in the Premises not described on the initial Environmental Questionnaire, and, to the extent such use would, in Landlord's reasonable judgment, cause a material increase in the risk of liability compared to the uses previously allowed in the Premises, such additional use shall be subject to Landlord's prior consent, which may be withheld in Landlord's reasonable discretion. Tenant shall not install or permit Tenant's Agents to install any underground storage tank on the Premises. For purposes of this Lease, "**Hazardous Materials**" means all flammable explosives, petroleum and petroleum products, waste oil, radon, radioactive materials, toxic pollutants, asbestos, polychlorinated biphenyls ("**PCBs**"), medical waste, chemicals known to cause cancer or reproductive toxicity, pollutants, contaminants, hazardous wastes, toxic substances or related materials, including without limitation any chemical, element, compound, mixture, solution, substance, object, waste or any combination thereof, which is or may be hazardous to human health, safety or to the environment due to its radioactivity, ignitability, corrosiveness, reactivity, explosiveness, toxicity, carcinogenicity, infectiousness or other harmful or potentially harmful properties or effects, or defined as, regulated as or included in, the definition of "hazardous substances," "hazardous wastes," "hazardous materials," or "toxic substances" under any Environmental Laws. For purposes of this Lease, "**Release**" or "**Released**" or "**Releases**" shall mean any release, deposit, discharge, emission, leaking, spilling, seeping, migrating, injecting, pumping, pouring, emptying, escaping, dumping, disposing, or other movement of Hazardous Materials into the environment. Landlord acknowledges that Tenant will be installing and using fume hoods in the Premises and that emissions of Hazardous Materials into the air in compliance with all Environmental Laws shall not be considered Releases.

5.3.1.2 **Notices to Landlord**. Tenant shall notify Landlord in writing as soon as possible but in no event later than five (5) days after (i) the occurrence of any actual, alleged or threatened Release of any Hazardous Material in, on, under, from, about or in the vicinity of the Premises (whether past or present), regardless of the source or quantity of any such Release, or (ii) Tenant becomes aware of any regulatory actions, inquiries, inspections, investigations, directives, or any cleanup, compliance, enforcement or abatement proceedings (including any threatened or contemplated investigations or proceedings) relating to or potentially affecting the Premises, or (iii) Tenant becomes aware of any claims by any person or entity relating to any Hazardous Materials in, on, under, from, about or in the vicinity of the Premises, whether relating to damage, contribution, cost recovery, compensation, loss or injury. Collectively, the matters set forth in clauses (i), (ii) and (iii) above are hereinafter

referred to as "**Hazardous Materials Claims**". Tenant shall promptly forward to Landlord copies of all orders, notices, permits, applications and other communications and reports in connection with any Hazardous Materials Claims. Additionally, Tenant shall promptly advise Landlord in writing of Tenant's discovery of any occurrence or condition on, in, under or about the Premises that could subject Tenant or Landlord to any liability, or restrictions on ownership, occupancy, transferability or use of the Premises under any "Environmental Laws," as that term is defined below. Tenant shall not enter into any legal proceeding or other action, settlement, consent decree or other compromise with respect to any Hazardous Materials Claims without first notifying Landlord of Tenant's intention to do so and affording Landlord the opportunity to join and participate, as a party if Landlord so elects, in such proceedings and in no event shall Tenant enter into any agreements which are binding on Landlord or the Premises without Landlord's prior written consent. Landlord shall have the right to appear at and participate in, any and all legal or other administrative proceedings concerning any Hazardous Materials Claim. For purposes of this Lease, "**Environmental Laws**" means all applicable present and future laws relating to the protection of human health, safety, wildlife or the environment, including, without limitation, (i) all requirements pertaining to reporting, licensing, permitting, investigation and/or remediation of emissions, discharges, Releases, or threatened Releases of Hazardous Materials, whether solid, liquid, or gaseous in nature, into the air, surface water, groundwater, or land, or relating to the manufacture, processing, distribution, use, treatment, storage, disposal, transport, or handling of Hazardous Materials; and (ii) all requirements pertaining to the health and safety of employees or the public. Environmental Laws include, but are not limited to, the Comprehensive Environmental Response, Compensation and Liability Act of 1980, 42 USC § 9601, et seq., the Hazardous Materials Transportation Authorization Act of 1994, 49 USC § 5101, et seq., the Solid Waste Disposal Act, as amended by the Resource Conservation and Recovery Act of 1976, and Hazardous and Solid Waste Amendments of 1984, 42 USC § 6901, et seq., the Federal Water Pollution Control Act, as amended by the Clean Water Act of 1977, 33 USC § 1251, et seq., the Clean Air Act of 1966, 42 USC § 7401, et seq., the Toxic Substances Control Act of 1976, 15 USC § 2601, et seq., the Safe Drinking Water Act of 1974, 42 USC §§ 300f through 300j, the Occupational Safety and Health Act of 1970, as amended, 29 USC § 651 et seq., the Oil Pollution Act of 1990, 33 USC § 2701 et seq., the Emergency Planning and Community Right-To-Know Act of 1986, 42 USC § 11001 et seq., the National Environmental Policy Act of 1969, 42 USC § 4321 et seq., the Federal Insecticide, Fungicide and Rodenticide Act of 1947, 7 USC § 136 et seq., California Carpenter-Presley-Tanner Hazardous Substance Account Act, California Health & Safety Code §§ 25300 et seq., Hazardous Materials Release Response Plans and Inventory Act, California Health & Safety Code, §§ 25500 et seq., Underground Storage of Hazardous Substances provisions, California Health & Safety Code, §§ 25280 et seq., California Hazardous Waste Control Law, California Health & Safety Code, §§ 25100 et seq., and any other state or local law counterparts, as amended, as such applicable laws, are in effect as of the Lease Commencement Date, or thereafter adopted, published, or promulgated.

5.3.1.3 **Releases of Hazardous Materials**. If any Release of any Hazardous Material in, on, under, from or about the Premises shall occur at any time during the Lease by Tenant or Tenant's Agents, in addition to notifying Landlord as specified above, Tenant, at its own sole cost and expense, shall (i) immediately comply with any and all reporting requirements imposed pursuant to any and all Environmental Laws, (ii) provide a written certification to Landlord indicating that Tenant has complied with all applicable reporting requirements, (iii) take any and all necessary investigation, corrective and remedial action in accordance with any and all applicable Environmental Laws, utilizing an environmental consultant approved by Landlord, all in accordance with the provisions and requirements of this **Section 5.3**, including, without limitation, **Section 5.3.4**, and (iv) take any such additional investigative, remedial and corrective actions as Landlord shall in its reasonable discretion deem necessary such that the Premises are remediated to the condition existing prior to such Release.

5.3.1.4 **Indemnification**.

5.3.1.4.1 **In General**. Without limiting in any way Tenant's obligations under any other provision of this Lease, Tenant shall be solely responsible for and shall protect, defend, indemnify and hold the Landlord Parties harmless from and against any and all claims, judgments, losses, damages, costs, expenses, penalties, enforcement actions, taxes, fines, remedial actions, liabilities (including, without limitation, actual attorneys' fees, litigation, arbitration and administrative proceeding costs, expert and consultant fees and laboratory costs) including, without limitation, consequential damages and sums paid in settlement of claims, which arise during or after the Lease Term, whether foreseeable or unforeseeable, that arise during or after the Lease Term in whole or in part, foreseeable or unforeseeable, directly or indirectly arising out of or attributable to the Release of Hazardous Materials in, on, under or about the Premises by Tenant or Tenant's Agents.

5.3.1.4.2 **Limitations**. Notwithstanding anything in **Section 5.3.1.4**, above, to the contrary, Tenant's indemnity of Landlord as set forth in **Section 5.3.1.4**, above, shall not be applicable to claims based upon Hazardous Materials not Released by Tenant or Tenant's Agents.

5.3.1.4.3 **Landlord Indemnity**. Under no circumstance shall Tenant be liable for, and Landlord shall indemnify, defend, protect and hold harmless Tenant and Tenant's Agents from and against, all losses, costs, claims, liabilities and damages (including attorneys' and consultants' fees) arising out of any Hazardous Materials that exist in, on or about the Project as of the date hereof, or Hazardous Material Released by Landlord or any Landlord Parties. Landlord will provide Tenant with any Hazardous Material reports relating to the Building that Landlord has in its immediate possession. The provision of such reports shall be for informational purposes only, and Landlord does not make any representation or warranty as to the correctness or completeness of any such reports.

5.3.1.5 **Compliance with Environmental Laws**. Without limiting the generality of Tenant's obligation to comply with applicable laws as otherwise provided in this Lease, Tenant shall, at its sole cost and expense, comply with all Environmental Laws related to the use of Hazardous Materials by Tenant and Tenant's Agents. Tenant shall obtain and maintain any and all necessary permits, licenses, certifications and approvals appropriate or required for the use, handling, storage, and disposal of any Hazardous Materials used, stored, generated, transported, handled, blended, or recycled by Tenant on the Premises. Landlord shall have a continuing right, without obligation, to require Tenant to obtain, and to review and inspect any and all such permits, licenses, certifications and approvals, together with copies of any and all Hazardous Materials management plans and programs, any and all Hazardous Materials risk management and pollution prevention programs, and any and all Hazardous Materials emergency response and employee training programs respecting Tenant's use of Hazardous Materials. Upon request of Landlord, Tenant shall deliver to Landlord a narrative description explaining the nature and scope of Tenant's activities involving Hazardous Materials and showing to Landlord's satisfaction compliance with all Environmental Laws and the terms of this Lease.

5.3.2 **Assurance of Performance**.

5.3.2.1 **Environmental Assessments In General**. Landlord may, but shall not be required to, engage from time to time such contractors as Landlord determines to be appropriate (and which are reasonably acceptable to Tenant) to perform environmental assessments of a scope reasonably determined by Landlord (an "**Environmental Assessment**") to ensure Tenant's compliance with the requirements of this Lease with respect to Hazardous Materials.

5.3.2.2 **Costs of Environmental Assessments**. All costs and expenses incurred by Landlord in connection with any such Environmental Assessment initially shall be paid by Landlord; provided that if any such Environmental Assessment shows that Tenant has failed to comply with the provisions of this **Section 5.3**, then all of the costs and expenses of such Environmental Assessment shall be reimbursed by Tenant as Additional Rent within thirty (30) days after receipt of written demand therefor.

5.3.3 **Tenant's Obligations upon Surrender**. At the expiration or earlier termination of the Lease Term, Tenant, at Tenant's sole cost and expense, shall: (i) cause an Environmental Assessment of the Premises to be conducted in accordance with **Section 15.3**; (ii) cause all Hazardous Materials brought onto the Premises by Tenant or Tenant's Agents to be removed from the Premises and disposed of in accordance with all Environmental Laws and as necessary to allow the Premises to be used for the purposes allowed as of the date of this Lease; and (iii) cause to be removed all containers installed or used by Tenant or Tenant's Agents to store any Hazardous Materials on the Premises, and cause to be repaired any damage to the Premises caused by such removal.

5.3.4 **Clean-up**.

5.3.4.1 **Environmental Reports; Clean-Up**. If any written report, including any report containing results of any Environmental Assessment (an "**Environmental Report**") shall indicate (i) the presence of any Hazardous Materials as to which Tenant has a removal or remediation obligation under this **Section 5.3**, and (ii) that as a result of same, the investigation, characterization, monitoring, assessment, repair, closure, remediation, removal, or other clean-up (the "**Clean-up**") of any Hazardous Materials is required, Tenant shall immediately prepare and submit to Landlord within thirty (30) days after receipt of the Environmental Report a comprehensive plan, subject to Landlord's written approval, specifying the actions to be taken by Tenant to perform the Clean-up so that the Premises are restored to the conditions required by this Lease. Upon Landlord's approval of the Clean-up plan, Tenant shall, at Tenant's sole cost and expense, without limitation on any rights and remedies of Landlord under this Lease, immediately implement such plan with a consultant reasonably acceptable to Landlord and proceed to Clean-Up Hazardous Materials in accordance with all applicable laws. If, within thirty (30) days after receiving a copy of such Environmental Report, Tenant fails either (a) to complete such Clean-up, or (b) with respect to any Clean-up that cannot be completed within such thirty-day period, fails to proceed with diligence to prepare the Clean-up plan and complete the Clean-up as promptly as practicable, then Landlord shall have the right, but not the obligation, and without waiving any other rights under this Lease, to carry out any Clean-up recommended by the Environmental Report or required by any governmental authority having jurisdiction over the Premises, and recover all of the costs and expenses thereof from Tenant as Additional Rent, payable within ten (10) days after receipt of written demand therefor.

5.3.4.2 **No Rent Abatement**. Tenant shall continue to pay all Rent due or accruing under this Lease during any Clean-up, and shall not be entitled to any reduction, offset or deferral of any Base Rent or Additional Rent due or accruing under this Lease during any such Clean-up.

5.3.4.3 **Surrender of Premises**. Tenant shall complete any Clean-up prior to surrender of the Premises upon the expiration or earlier termination of this Lease. Tenant shall obtain and deliver to Landlord a letter or other written determination from the overseeing governmental authority confirming that the Clean-up has been completed in accordance with all requirements of such governmental authority and that no further response action of any kind is required for the unrestricted use of the Premises ("**Closure Letter**"). Upon the expiration or earlier termination of this Lease, Tenant shall also be obligated to close all permits obtained in connection with Hazardous Materials used by Tenant or Tenant's Agents in accordance with applicable laws.

5.3.4.4 **Failure to Timely Clean-Up**. Should any Clean-up for which Tenant is responsible not be completed, or should Tenant not receive the Closure Letter and any governmental approvals required under Environmental Laws in conjunction with such Clean-up prior to the expiration or earlier termination of this Lease, then, commencing on the later of the termination of this Lease and three (3) business days after Landlord's delivery of notice of such failure and that it elects to treat such failure as a holdover, Tenant shall be liable to Landlord as a holdover tenant (as more particularly provided in **Article 16**) until Tenant has fully complied with its obligations under this **Section 5.3**.

5.3.5 **Confidentiality**. Unless compelled to do so by applicable law, Tenant agrees that Tenant shall not disclose, discuss, disseminate or copy any information, data, findings, communications, conclusions and reports regarding the environmental condition of the Premises to any Person (other than Tenant's consultants, attorneys, property managers, employees, shareholders and potential and actual investors, lenders, business and merger partners, subtenants and assignees that have a need to know such information), including any governmental authority, without the prior written consent of Landlord. In the event Tenant reasonably believes that disclosure is compelled by applicable law, it shall provide Landlord ten (10) days' advance notice of disclosure of confidential information so that Landlord may attempt to obtain a protective order. Tenant may additionally release such information to bona fide prospective purchasers or lenders, subject to any such parties' written agreement to be bound by the terms of this **Section 5.3**.

5.3.6 **Copies of Environmental Reports**. Within thirty (30) days of receipt thereof, Tenant shall provide Landlord with a copy of any and all environmental assessments, audits, studies and reports regarding Tenant's activities with respect to the Premises, or ground water beneath the Land, or the environmental condition or Clean-up thereof. Tenant shall be obligated to provide Landlord with a copy of such materials without regard to whether such materials are generated by Tenant or prepared for Tenant, or how Tenant comes into possession of such materials.

5.3.7 **Signs, Response Plans, Etc**. Tenant shall be responsible for posting on the Premises any signs required under applicable Environmental Laws with respect to the use of Hazardous Materials by Tenant or Tenant's Agents. Tenant shall also complete and file any business response plans or inventories required by any applicable laws. Tenant shall concurrently file a copy of any such business response plan or inventory with Landlord.

5.3.8 **Survival**. Each covenant, agreement, representation, warranty and indemnification made by Tenant set forth in this **Section 5.3** shall survive the expiration or earlier termination of this Lease and shall remain effective until all of Tenant's obligations under this **Section 5.3** have been completely performed and satisfied.

6. SERVICES AND UTILITIES.

6.1 **In General**. Landlord will be responsible, at Tenant's sole cost and expense (subject to the terms of Section 4.2.4, above), for the furnishing of heating, ventilation and air-conditioning, electricity, water, and interior Building security services to the Premises. Landlord shall not provide janitorial or telephone services for the Premises. Tenant shall be solely responsible for performing all janitorial services and other cleaning of the Premises, all in compliance with applicable laws. The janitorial and cleaning of the Premises shall be adequate to maintain the Premises in a manner consistent with First Class Life Sciences Projects.

Tenant shall cooperate fully with Landlord at all times and abide by all reasonable regulations and requirements that Landlord may reasonably prescribe for the proper functioning and protection of the HVAC, electrical, mechanical and plumbing systems. Provided that Landlord agrees to provide and maintain and keep in continuous service utility connections to the Project, including electricity, water and sewage connections, Landlord shall have no obligation to provide any services or utilities to the Building, including, but not limited to heating, ventilation and air-conditioning, electricity, water, telephone, janitorial and interior Building security services, except as set forth in this Section 6.1, above.

6.2 **Tenant Payment of Utilities Costs**. To the extent that any utilities (including without limitation, electricity, gas, sewer and water) to the Building are separately metered or sub-metered to the Premises, such utilities shall either be contracted for and paid directly by Tenant to the applicable utility provider, or reimbursed by Tenant to Landlord within thirty (30) days after billing. To the extent that any utilities (including without limitation, electricity, gas, sewer and water) to the Building are not separately metered to the Premises, then Tenant shall pay to Landlord, within thirty (30) days after billing, an equitable portion of the Building utility costs, based on Tenant's proportionate use thereof.

6.3 **Interruption of Use**. Tenant agrees that Landlord shall not be liable for damages, by abatement of Rent or otherwise, for failure to furnish or delay in furnishing any service or utility (including, without limitation, telephone and telecommunication services, UPS services, or other laboratory services or utilities), or for any diminution in the quality or quantity thereof, when such failure or delay or diminution is occasioned, in whole or in part, by breakage, repairs, replacements, or improvements, by any strike, lockout or other labor trouble, by inability to secure electricity, gas, water, or other fuel at the Building or Project after reasonable effort to do so, by any riot or other dangerous condition, emergency, accident or casualty whatsoever, by act or default of Tenant or other parties, or by any other cause; and such failures or delays or diminution shall never be deemed to constitute an eviction or disturbance of Tenant's use and possession of the Premises or relieve Tenant from paying Rent or performing any of its obligations under this Lease. Notwithstanding the foregoing, Landlord may be liable for damages to the extent caused by the negligence or willful misconduct of Landlord or the Landlord Parties, provided that Landlord shall not be liable under any circumstances for injury to, or interference with, Tenant's business, including, without limitation, loss of profits, however occurring, through or in connection with or incidental to a failure to furnish any of the services or utilities as set forth in this Article 6.

6.4 **Energy Performance Disclosure Information**. Tenant hereby acknowledges that Landlord may be required to disclose certain information concerning the energy performance of the Building pursuant to California Public Resources Code Section 25402.10 and the regulations adopted pursuant thereto (collectively the "**Energy Disclosure Requirements**"). Tenant hereby acknowledges prior receipt of the Data Verification Checklist, as defined in the Energy Disclosure Requirements (the "**Energy Disclosure Information**"), and agrees that Landlord has timely complied in full with Landlord's obligations under the Energy Disclosure Requirements. Tenant acknowledges and agrees that (i) Landlord makes no representation or warranty regarding the energy performance of the Building or the accuracy or completeness of the Energy Disclosure Information, (ii) the Energy Disclosure Information is for the current occupancy and use of the Building and that the energy performance of the Building may vary depending on future occupancy and/or use of the Building, and (iii) Landlord shall have no liability to Tenant for any errors or omissions in the Energy Disclosure Information. If and to the extent not prohibited by applicable laws, Tenant hereby waives any right Tenant may have to receive the Energy Disclosure Information, including, without limitation, any right Tenant may have to terminate this Lease as a result of Landlord's failure to disclose such information. Further, Tenant hereby releases Landlord from any and all losses, costs, damages, expenses and/or liabilities relating to, arising out of and/or resulting from the Energy Disclosure Requirements, including, without limitation, any liabilities arising as a result of Landlord's failure to disclose the Energy Disclosure Information to Tenant prior to the execution of this Lease. Tenant's acknowledgment of the AS-IS condition of the Premises pursuant to the terms of this Lease shall be deemed to include the energy performance of the Building. Tenant further acknowledges that pursuant to the Energy Disclosure Requirements, Landlord may be required in the future to disclose information concerning Tenant's energy usage to certain third parties, including, without limitation, prospective purchasers, lenders and tenants of the Building (the "**Tenant Energy Use Disclosure**"). Tenant hereby (A) consents to all such Tenant Energy Use Disclosures, and (B) acknowledges that Landlord shall not be required to notify Tenant of any Tenant Energy Use Disclosure. Further, Tenant hereby releases Landlord from any and all losses, costs, damages, expenses and liabilities relating to, arising out of and/or resulting from any Tenant Energy Use Disclosure. The terms of this Section 6.3 shall survive the expiration or earlier termination of this Lease.

6.5 **Existing Generator**. Commencing on the Lease Commencement Date, Tenant shall have the right to connect to the Building back-up generator, which Landlord shall install as part of Landlord's Work (the "**Generator**"), for Tenant's Share of the Generator's capacity to provide back-up generator services to the Premises. During the Lease Term, Landlord shall maintain the Generator in good condition and repair, and Tenant shall be responsible for a share of the costs of such maintenance and repair based on the proportion of the Generator capacity allocated to the Premises. Notwithstanding the foregoing, Landlord shall not be liable for any damages whatsoever resulting from any failure in operation of the Generator, or the failure of the Generator to provide suitable or adequate back-up power to the Premises, including but not limited to, loss of profits, loss of rents or other revenues, loss of business opportunity, loss of goodwill or loss of use, in each case, however occurring, or loss to inventory, scientific research, scientific experiments, laboratory animals, products, specimens, samples, and/or scientific, business, accounting and other records of every kind and description kept at the Premises and any and all income derived or derivable therefrom.

6.6 **Chemical Storage Room**. Tenant shall have the right to utilize storage space in the chemical storage room to be constructed by Landlord in the Building pursuant to **Schedule 1 to Exhibit B** (the "**Chemical Storage Room**"), for up to Tenant's Share of the Chemical Storage Room's storage capacity. During the Lease Term, Landlord shall maintain the Chemical Storage Room in good condition and repair, and Tenant shall be responsible for a share of the costs of such maintenance and repair based on the proportion of the capacity of the Chemical Storage Room allocated to Tenant's use (subject to the provisions of Section 4.2.4 above). Notwithstanding the foregoing, Landlord shall not be liable for any damages whatsoever resulting from any failure in operation of the Chemical Storage Room, or the failure of the Chemical Storage Room to provide suitable or adequate storage of Tenant's chemicals, including but not limited to, loss of profits, loss of rents or other revenues, loss of business opportunity, loss of goodwill or loss of use, in each case, however occurring, or loss to inventory, scientific research, scientific experiments, laboratory animals, products, specimens, samples, and/or scientific, business, accounting and other records of every kind and description kept at the Chemical Storage Room or the Premises and any and all income derived or derivable therefrom.

7. REPAIRS.

7.1 **Tenant Repair Obligations**. Tenant shall, throughout the Term, at its sole cost and expense, maintain, repair or replace as required, the Premises in a good standard of maintenance, repair and replacement as required, and in good and sanitary condition, all in accordance with the standards of First Class Life Sciences Projects, except for the Landlord Repair Obligations, whether or not such maintenance, repair, replacement or improvement is required in order to comply with applicable Laws ("**Tenant's Repair Obligations**"), including without limitation, all electrical facilities and equipment, including lighting fixtures, lamps, fans and any exhaust equipment and systems, electrical motors and all other appliances and equipment of every kind and nature located in the Premises; all communications systems serving the Premises; all of Tenant's security systems in or about or serving the Premises; Tenant's signage; interior demising walls and partitions (including painting and wall coverings), equipment, floors. Tenant shall additionally be responsible, at Tenant's sole cost and expense, to furnish all expendables, including light bulbs, paper goods and soaps, used in the Premises.

7.2 **Landlord Repair Obligations**. Landlord shall be responsible, as a part of Operating Expenses, for repairs to and routine maintenance of the Building including without limitation: (1) exterior windows, window frames, window casements (including the repairing, resealing, cleaning and replacing of exterior windows); (2) exterior doors, door frames and door closers; (3) the Building (as opposed to the Premises) and Project plumbing, sewer, drainage, electrical, fire protection, life safety and security systems and equipment, existing heating, ventilation and air-conditioning systems, and all other mechanical and HVAC systems and equipment (collectively, the "**Building Systems**"), (4) the exterior glass, exterior walls, foundation and roof of the Building, the structural portions of the floors of the Building, including, without limitation, any painting, sealing, patching and waterproofing of exterior walls, and (5) repairs to the elevator in the Building and underground utilities, except to the extent that any such repairs are required due to the negligence or willful misconduct of Tenant (the "**Landlord Repair Obligations**"); provided, however, that if such repairs are due to the negligence or willful misconduct of Tenant, Landlord shall nevertheless make such repairs at Tenant's expense, or, if covered by Landlord's insurance, Tenant shall only be obligated to pay any deductible in connection therewith. Costs expended by Landlord in connection with the Landlord Repair Obligations shall be included in Operating Expenses to the extent allowed pursuant to the terms of Article 4, above. Landlord shall cooperate with Tenant to enforce any warranties that Landlord holds that could reduce Tenant's maintenance obligations under this Lease.

7.3 **Tenant's Right to Make Repairs**. Notwithstanding any provision to the contrary contained in this Lease, if Tenant provides written notice to Landlord of an event or circumstance which requires the action of Landlord under this Lease with respect to repair and/or maintenance required in the Premises, including repairs to the portions of the Building located within the Premises that are Landlord's responsibility under Section 7.4 (the "**Base Building**"), which event or circumstance with respect to the Base Building materially and adversely affects the conduct of Tenant's business from the Premises, and Landlord fails to commence corrective action within a reasonable period of time, given the circumstances, after the receipt of such notice, but in any event not later than thirty (30) days after receipt of said notice (unless Landlord's obligation cannot reasonably be performed within thirty (30) days, in which event Landlord shall be allowed additional time as is reasonably necessary to perform the obligation so long as Landlord begins performance within the initial thirty (30) days and diligently pursues performance to completion), or, in the event of an Emergency (as defined below), not later than five (5) business days after receipt of such notice, then Tenant shall have the right to undertake such actions as may be reasonably necessary to make such repairs if Landlord thereafter fails to commence corrective action within five (5) business days following Landlord's receipt of a second written notice from Tenant specifying that Tenant will undertake such actions if Landlord fails to timely do so (provided that such notice shall include the following language in bold, capitalized text: "**IF LANDLORD FAILS TO COMMENCE THE REPAIRS DESCRIBED IN THIS LETTER WITHIN FIVE (5) BUSINESS DAYS FROM LANDLORD'S RECEIPT OF THIS LETTER, TENANT WILL PERFORM SUCH REPAIRS AT LANDLORD'S EXPENSE**"; provided, however, that in no event shall Tenant undertake any actions that could materially or adversely affect the Base Building. Notwithstanding the foregoing, in the event of an Emergency, no second written notice shall be required as long as Tenant advises Landlord in the first written notice of Tenant's intent to perform such Emergency repairs if Landlord does not commence the same within such five (5) business day period, utilizing the language required in second notices. If such action was required under the terms of this Lease to be taken by Landlord and was not commenced by Landlord within such five (5) business day period and thereafter diligently pursued to completion, then Tenant shall be entitled to prompt reimbursement by Landlord of the reasonable out-of-pocket third-party costs and expenses actually incurred by Tenant in taking such action. If Tenant undertakes such corrective actions pursuant to this Section 7.3, then (a) the insurance and indemnity provisions set forth in this Lease shall apply to Tenant's performance of such corrective actions, (b) Tenant shall proceed in accordance with all applicable laws, (c) Tenant shall retain to perform such corrective actions only such reputable contractors and suppliers as are duly licensed and

qualified, (d) Tenant shall effect such repairs in a good and workmanlike and commercially reasonable manner, (e) Tenant shall use new or like new materials, and (f) Tenant shall take reasonable efforts to minimize any material interference or impact on the other tenants and occupants of the Building. Promptly following completion of any work taken by Tenant pursuant to the terms of this Section 7.5, Tenant shall deliver a detailed invoice of the work completed, the materials used and the costs relating thereto, and Landlord shall reimburse Tenant the amounts expended by Tenant in connection with such work, provided that Landlord shall have the right to object if Landlord claims that such action did not have to be taken by Landlord pursuant to the terms of this Lease or that the charges are excessive (in which case Landlord shall pay the amount it contends would not have been excessive). For purposes of this Section 7.5, an "**Emergency**" shall mean an event threatening immediate and material danger to people located in the Building or immediate, material damage to the Building, Base Building, or creating a realistic possibility of an immediate and material interference with, or immediate and material interruption of a material aspect of Tenant's business operations.

8. ADDITIONS AND ALTERATIONS.

8.1 **Landlord's Consent to Alterations**. Tenant may not make any improvements, alterations, additions or changes to the Premises or any mechanical, plumbing or HVAC facilities or systems pertaining to the Premises (collectively, the "**Alterations**") without first procuring the prior written consent of Landlord to such Alterations, which consent shall be requested by Tenant not less than ten (10) business days prior to the commencement thereof, and which consent shall not be unreasonably withheld by Landlord, provided it shall be deemed reasonable for Landlord to withhold its consent to any Alteration which adversely affects the structural portions or the systems or equipment of the Building or is visible from the exterior of the Building. Notwithstanding the foregoing, Tenant shall be permitted to make Alterations following ten (10) business days' notice to Landlord (as to Alterations costing more than $10,000 only), but without Landlord's prior consent, to the extent that such Alterations (i) do not affect the building systems or equipment (other than minor changes such as adding or relocating electrical outlets and thermostats), (ii) are not visible from the exterior of the Building, and (iii) cost less than $50,000.00 for a particular job of work. The construction of the Tenant Improvements to the Premises shall be governed by the terms of the Tenant Work Letter and not the terms of this Article 8.

8.2 **Manner of Construction**. Landlord may impose, as a condition of its consent to any and all Alterations or repairs of the Premises or about the Premises, such requirements as Landlord in its reasonable discretion may deem desirable, including, but not limited to, the requirement that upon Landlord's request, Tenant shall, at Tenant's expense, remove such Alterations upon the expiration or any early termination of the Lease Term. Tenant shall construct such Alterations and perform such repairs in a good and workmanlike manner, in conformance with any and all applicable federal, state, county or municipal laws, rules and regulations and pursuant to a valid building permit, issued by the city in which the Building is located (or other applicable governmental authority). Tenant shall not use (and upon notice from Landlord shall cease using) contractors, services, workmen, labor, materials or equipment that, in Landlord's reasonable judgment, would disturb labor harmony with the workforce or trades engaged in performing other work, labor or services in or about the Building or the Common Areas. Upon completion of any Alterations, Tenant shall deliver to Landlord final lien waivers from all contractors, subcontractors and materialmen who performed such work. In addition to Tenant's obligations under Article 9 of this Lease, upon completion of any Alterations, Tenant agrees to cause a Notice of Completion to be recorded in the office of the Recorder of the County of San Mateo in accordance with Section 3093 of the Civil Code of the State of California or any successor statute, and Tenant shall deliver to the Project construction manager a reproducible copy of the "**as built**" drawings of the Alterations as well as all permits, approvals and other documents issued by any governmental agency in connection with the Alterations.

8.3 **Payment for Improvements**. In connection with any Alterations that affect the Building systems (other than minor changes such as adding or relocating electrical outlets and thermostats), or which have a cost in excess of $100,000, Tenant shall reimburse Landlord for Landlord's reasonable, actual, out-of-pocket costs and expenses actually incurred in connection with Landlord's review of such work.

8.4 **Construction Insurance**. In addition to the requirements of Article 10 of this Lease, in the event that Tenant makes any Alterations, prior to the commencement of such Alterations, Tenant shall provide Landlord with evidence that Tenant or Tenant's contractor carries "**Builder's All Risk**" insurance (to the extent that the cost of such work shall exceed $50,000) in an amount approved by Landlord covering the construction of such Alterations,

and such other insurance as Landlord may reasonably require, it being understood and agreed that all of such Alterations shall be insured by Landlord pursuant to Article 10 of this Lease immediately upon completion thereof. In addition, Tenant's contractors and subcontractors shall be required to carry Commercial General Liability Insurance in an amount approved by Landlord and otherwise in accordance with the requirements of Article 10 of this Lease. In connection with Alterations with a cost in excess of $250,000, Landlord may, in its reasonable discretion, require Tenant to obtain a lien and completion bond or some alternate form of security satisfactory to Landlord in an amount sufficient to ensure the lien-free completion of such Alterations and naming Landlord as a co-obligee.

8.5 **Landlord's Property**. All Alterations, improvements, fixtures, equipment and/or appurtenances which may be installed or placed in or about the Premises, from time to time, shall be at the sole cost of Tenant and all Alterations and improvements, shall be and become the property of Landlord and remain in place at the Premises following the expiration or earlier termination of this Lease. Notwithstanding the foregoing, Landlord may, by written notice to Tenant given at the time it consents to an Alteration, require Tenant, at Tenant's expense, to remove any Alterations within the Premises and to repair any damage to the Premises and Building caused by such removal. If Tenant fails to complete such removal and/or to repair any damage caused by the removal of any Alterations, Landlord may do so and may charge the cost thereof to Tenant. Tenant hereby protects, defends, indemnifies and holds Landlord harmless from any liability, cost, obligation, expense or claim of lien in any manner relating to the installation, placement, removal or financing of any such Alterations, improvements, fixtures and/or equipment in, on or about the Premises, which obligations of Tenant shall survive the expiration or earlier termination of this Lease. Notwithstanding the foregoing, except to the extent the same are paid for by the Tenant Improvement Allowance, the items set forth in **Exhibit F** attached hereto (the "**Tenant's Property**") shall at all times be and remain Tenant's property. **Exhibit F** may be updated from time to time by agreement of the parties. Tenant may remove the Tenant's Property from the Premises at any time, provided that Tenant repairs all damage caused by such removal. Landlord shall have no lien or other interest in the Tenant's Property.

9. **COVENANT AGAINST LIENS**. Tenant shall keep the Project and Premises free from any liens or encumbrances arising out of the work performed, materials furnished or obligations incurred by or on behalf of Tenant, and shall protect, defend, indemnify and hold Landlord harmless from and against any claims, liabilities, judgments or costs (including, without limitation, reasonable attorneys' fees and costs) arising out of same or in connection therewith. Except as to Alterations as to which no notice is required under the second sentence of Section 8.1, Tenant shall give Landlord notice at least ten (10) business days prior to the commencement of any such work on the Premises (or such additional time as may be necessary under applicable laws) to afford Landlord the opportunity of posting and recording appropriate notices of non-responsibility (to the extent applicable pursuant to then applicable laws). Tenant shall remove any such lien or encumbrance by bond or otherwise within ten (10) business days after notice by Landlord, and if Tenant shall fail to do so, Landlord may pay the amount necessary to remove such lien or encumbrance, without being responsible for investigating the validity thereof.

10. INSURANCE.

10.1 **Indemnification and Waiver**. Except as provided in Section 10.5 or to the extent due to the negligence, willful misconduct or violation of this Lease by Landlord or the Landlord Parties, Tenant hereby assumes all risk of damage to property in, upon or about the Premises from any cause whatsoever (including, but not limited to, any personal injuries resulting from a slip and fall in, upon or about the Premises) and agrees that Landlord, its partners, subpartners and their respective officers, agents, servants, employees, and independent contractors (collectively, "**Landlord Parties**") shall not be liable for, and are hereby released from any responsibility for, any damage either to person or property or resulting from the loss of use thereof, which damage is sustained by Tenant or by other persons claiming through Tenant. Tenant shall indemnify, defend, protect, and hold harmless the Landlord Parties from any and all loss, cost, damage, expense and liability (including without limitation court costs and reasonable attorneys' fees) incurred in connection with or arising from any cause in, on or about the Premises (including, but not limited to, a slip and fall), any acts, omissions or negligence of Tenant or of any person claiming by, through or under Tenant, or of the contractors, agents, servants, employees, invitees, guests or licensees of Tenant or any such person, in, on or about the Project or any breach of the terms of this Lease, either prior to, during, or after the expiration of the Lease Term, provided that the terms of the foregoing indemnity and release shall not apply to the negligence or willful misconduct of Landlord or its agents, employees, contractors, licensees or invitees, or Landlord's violation of this Lease. Should Landlord be named as a defendant in any suit

brought against Tenant in connection with or arising out of Tenant's occupancy of the Premises, Tenant shall pay to Landlord its costs and expenses incurred in such suit, including without limitation, its actual professional fees such as reasonable appraisers', accountants' and attorneys' fees. Notwithstanding anything to the contrary in this Lease, Landlord shall not be released or indemnified from, and shall indemnify, defend, protect and hold harmless Tenant from, all losses, damages, liabilities, claims, attorneys' fees, costs and expenses arising from the gross negligence or willful misconduct of Landlord or its agents, contractors, licensees or invitees, or a violation of Landlord's obligations or representations under this Lease. The provisions of this Section 10.1 shall survive the expiration or sooner termination of this Lease with respect to any claims or liability arising in connection with any event occurring prior to such expiration or termination.

10.2 **Tenant's Compliance With Landlord's Property Insurance**. Landlord shall insure the Building, Tenant Improvements and any Alterations during the Lease Term against loss or damage under an "all risk" property insurance policy. Such coverage shall be in such amounts, from such companies, and on such other terms and conditions, as Landlord may from time to time reasonably determine. Additionally, at the option of Landlord, such insurance coverage may include the risks of earthquakes and/or flood damage and additional hazards, a rental loss endorsement and one or more loss payee endorsements in favor of the holders of any mortgages or deeds of trust encumbering the interest of Landlord in the Building or the ground or underlying lessors of the Building, or any portion thereof. The costs of such insurance shall be included in Operating Expenses, subject to the terms of Section 4.2.4. Tenant shall, at Tenant's expense, comply with all insurance company requirements pertaining to the use of the Premises. If Tenant's conduct or use of the Premises causes any increase in the premium for such insurance policies then Tenant shall reimburse Landlord for any such increase. Tenant, at Tenant's expense, shall comply with all rules, orders, regulations or requirements of the American Insurance Association (formerly the National Board of Fire Underwriters) and with any similar body. Notwithstanding anything to the contrary in this Lease, Tenant shall not be required to comply with or cause the Premises to comply with any laws, rules, regulations or insurance requirements requiring the construction of alterations unless such compliance is necessitated solely due to Tenant's particular use of the Premises.

10.3 **Tenant's Insurance**. Tenant shall maintain the following coverages in the following amounts.

10.3.1 Commercial General Liability Insurance on an occurrence form covering the insured against claims of bodily injury and property damage (including loss of use thereof) arising out of Tenant's operations, and contractual liabilities including a contractual coverage for limits of liability (which limits may be met together with umbrella liability insurance) of not less than:

Bodily Injury and	$4,000,000 each occurrence
Property Damage Liability	$4,000,000 annual aggregate
Personal Injury Liability	$4,000,000 annual aggregate

10.3.2 Property Insurance covering all office furniture, business and trade fixtures, office and lab equipment, free-standing cabinet work, movable partitions, merchandise and all other items of Tenant's property on the Premises installed by, for, or at the expense of Tenant. Such insurance shall be written on an "**all risks**" of physical loss or damage basis, for the full replacement cost value (subject to reasonable deductible amounts) new without deduction for depreciation of the covered items and in amounts that meet any co-insurance clauses of the policies of insurance and shall include coverage for damage or other loss caused by fire or other peril including, but not limited to, vandalism and malicious mischief, theft, water damage (excluding flood), including sprinkler leakage, bursting or stoppage of pipes, and explosion, and providing business interruption coverage for a period of ninety (90) days.

10.3.3 Business Income Interruption for ninety (90) days plus Extra Expense insurance in such amounts as will reimburse Tenant for actual direct or indirect loss of earnings attributable to the risks outlined in Section 10.3.2 above.

10.3.4 Worker's Compensation and Employer's Liability or other similar insurance pursuant to all applicable state and local statutes and regulations. The policy shall include a waiver of subrogation in favor of Landlord, its employees, Lenders and any property manager or partners.

10.4 **Form of Policies**. The minimum limits of policies of insurance required of Tenant under this Lease shall in no event limit the liability of Tenant under this Lease. Such insurance shall (i) name Landlord, its subsidiaries and affiliates, its property manager (if any) and any other party the Landlord so specifies, as an additional insured on the liability insurance, including Landlord's managing agent, if any; (ii) be issued by an insurance company having a rating of not less than A-:VII in Best's Insurance Guide or which is otherwise acceptable to Landlord and authorized to do business in the State of California; and (iv) be primary insurance as to all claims thereunder and provide that any insurance carried by Landlord is excess and is non-contributing with any insurance required of Tenant. Tenant shall not cause said insurance to be canceled or coverage changed unless thirty (30) days' prior written notice shall have been given to Landlord and any mortgagee of Landlord (unless such cancellation is the result of non-payment of premiums, in which case note less than five (5) days' notice shall be provided). Tenant shall deliver said policy or policies or certificates thereof to Landlord on or before the Lease Commencement Date and at least ten (10) days before the expiration dates thereof. In the event Tenant shall fail to procure such insurance, or to deliver such policies or certificate, Landlord may, at its option, procure such policies for the account of Tenant, and the cost thereof shall be paid to Landlord within five (5) days after delivery to Tenant of bills therefor.

10.5 **Subrogation**. Landlord and Tenant hereby agree to look solely to, and seek recovery only from, their respective insurance carriers in the event of a property or business interruption loss to the extent that such coverage is agreed to be provided hereunder, notwithstanding the negligence of either party. Notwithstanding anything to the contrary in this Lease, the parties each hereby waive all rights and claims against each other for such losses, and waive all rights of subrogation of their respective insurers. The parties agree that their respective insurance policies do now, or shall, contain the waiver of subrogation.

10.6 **Additional Insurance Obligations**. Tenant shall carry and maintain during the entire Lease Term, at Tenant's sole cost and expense, increased amounts of the insurance required to be carried by Tenant pursuant to this Article 10 and such other reasonable types of insurance coverage and in such reasonable amounts covering the Premises and Tenant's operations therein, as may be reasonably requested by Landlord or Landlord's lender, but in no event in excess of the amounts and types of insurance then being required by landlords of buildings comparable to and in the vicinity of the Building.

10.7 **Construction Period**: The term "Construction Period" shall mean the period from the date of this Lease to the date that Landlord completes construction of the Landlord's Work (including any "**Additional Base Building Items**", as defined in Section 3(f) of the Tenant Work Letter), and Common Areas, regardless of the occurrence of any Tenant Delay and without regard to the effect of any provision of this Lease pursuant to which the Premises are deemed to be Ready for Occupancy in advance of its actual occurrence. Notwithstanding any provision of this Lease to the contrary, during the Construction Period only, the following provisions shall be applicable:

10.7.1 with respect to any indemnity obligation of Tenant arising at any time during the Construction Period only, (A) the term "Landlord Parties" shall mean and shall be limited to HCP Oyster Point III LLC, a Delaware limited liability company (or any entity that that succeeds to HCP Oyster Point III LLC's interest as Landlord under the Lease) and shall not include any other person or entity; provided, however, that Landlord may include in any claim owed by Tenant to it any amount which Landlord shall pay or be obligated to indemnify any other person or entity, and (B) any indemnity obligation shall be limited to losses caused by, or arising as a result of any act or failure to act of, Tenant or Tenant's employees, agents or contractors; and

10.7.2 during the Construction Period only, Tenant's liability under this Lease for Tenant's actions or failures to act under the Lease during the Construction Period, including, without limitation, (A) Tenant's indemnity obligations, plus (B) Base Rent and Additional Rent (as a consequence of Tenant Delay), plus (C) any and all other costs payable to Landlord or otherwise payable by Tenant under this Lease, which amount shall calculated to include (i) the accreted value of any payments previously made by Tenant plus (ii) the present value of the maximum amount that Tenant could be required to pay as of that point in time (whether or not construction is completed) discounted at Tenant's incremental borrowing rate used to classify the Lease under ASC 840 (FAS 13), shall be limited to 89.9% of Landlord's Project Costs determined as of the date of Landlord's claim for such amount owed by Tenant. As used herein, "**Landlord's Project Costs**" shall mean the amount capitalized in the Project by Landlord in accordance with GAAP, plus other costs related to the Project (including related site improvements and

other Project costs) paid by Landlord to third parties other than lenders or owners of Landlord (excluding land acquisition costs, but including land carrying costs, such as interest or ground rent incurred during the Construction Period, and including all costs incurred by Landlord in connection with the development and construction of the Project); and

10.7.3 the provisions of Section 21.1(H) of the Lease shall not apply during the Construction Period.

10.8 For the avoidance of doubt, Landlord and Tenant agree that:

10.8.1 no claim by Landlord for Tenant's repudiation of this Lease at any time shall be limited under this section; and

10.8.2 for any claim other than under clause (x) above, if during the Construction Period Landlord makes any claim for any anticipatory breach by Tenant of any obligation under this Lease owed to Landlord for any period after the Construction Period and the amount payable by Tenant for such claim is limited by the provisions of Section 10.7.2 above, the entire amount (to the extent not theretofore paid) shall be payable promptly after the Construction Period; and

10.8.3 following the end of the Construction Period, the terms of this Section 10.7 shall be of no further force or effect.

11. DAMAGE AND DESTRUCTION.

11.1 **Repair of Damage to Premises by Landlord**. Tenant shall promptly notify Landlord of any damage to the Premises resulting from fire or any other casualty. If the Premises or any Common Areas serving or providing access to the Premises shall be damaged by fire or other casualty, Landlord shall promptly and diligently, subject to reasonable delays for insurance adjustment or other matters beyond Landlord's reasonable control, and subject to all other terms of this Article 11, restore the Premises and such Common Areas. Such restoration shall be to substantially the same condition of the Premises and the Common Areas prior to the casualty, except for modifications required by zoning and building codes and other laws or any other modifications to the Common Areas deemed desirable by Landlord, which are consistent with the character of the Project, provided that access to the Premises shall not be materially impaired. Landlord shall not be liable for any inconvenience or annoyance to Tenant or its visitors, or injury to Tenant's business resulting in any way from such damage or the repair thereof; provided however, that if such fire or other casualty shall have damaged the Premises or Common Areas necessary to Tenant's occupancy, and the damaged portions of the Premises are not occupied by Tenant as a result thereof, then during the time and to the extent the Premises are unfit for occupancy, the Rent shall be abated in proportion to the ratio that the amount of rentable square feet of the Premises which is unfit for occupancy for the purposes permitted under this Lease bears to the total rentable square feet of the Premises.

11.2 **Landlord's Option to Repair**. Notwithstanding the terms of Section 11.1 of this Lease, Landlord may elect not to rebuild and/or restore the Premises, Building and/or Project, and instead terminate this Lease, by notifying Tenant in writing of such termination within sixty (60) days after the date of discovery of the damage, such notice to include a termination date giving Tenant sixty (60) days to vacate the Premises, but Landlord may so elect only if the Building shall be damaged by fire or other casualty or cause, and one or more of the following conditions is present: (i) in Landlord's reasonable judgment, repairs cannot reasonably be completed within one (1) year after the date of discovery of the damage (when such repairs are made without the payment of overtime or other premiums); (ii) the damage is due to a risk that Landlord is not required to insure under this Lease, and the cost of restoration exceed five percent (5%) of the replacement cost of the Building (unless Tenant agrees to pay any uninsured amount in excess of such five percent (5%)); or (iii) the damage occurs during the last twelve (12) months of the Lease Term and will take more than sixty (60) days to restore; provided, however, that if Landlord does not elect to terminate this Lease pursuant to Landlord's termination right as provided above, and the repairs cannot, in the reasonable opinion of Landlord, be completed within eight (8) months days after the date of discovery of the damage (or are not in fact completed within nine (9) months after the date of discovery of the damage), Tenant may elect, no earlier than sixty (60) days after the date of the damage and not later than ninety (90) days after the date of such damage, or within thirty (30) days after such repairs are not timely completed, to terminate this Lease by written notice to Landlord effective as of the date specified in the notice, which date shall not be less than thirty (30) days nor more than sixty (60) days after the date such notice is given by Tenant.

11.3 **Waiver of Statutory Provisions**. The provisions of this Lease, including this Article 11, constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, the Building or the Project, and any statute or regulation of the State of California, including, without limitation, Sections 1932(2) and 1933(4) of the California Civil Code, with respect to any rights or obligations concerning damage or destruction in the absence of an express agreement between the parties, and any other statute or regulation, now or hereafter in effect, shall have no application to this Lease or any damage or destruction to all or any part of the Premises, the Building or the Project.

12. NONWAIVER. No provision of this Lease shall be deemed waived by either party hereto unless expressly waived in a writing signed thereby. The waiver by either party hereto of any breach of any term, covenant or condition herein contained shall not be deemed to be a waiver of any subsequent breach of same or any other term, covenant or condition herein contained. The subsequent acceptance of Rent hereunder by Landlord shall not be deemed to be a waiver of any preceding breach by Tenant of any term, covenant or condition of this Lease, other than the failure of Tenant to pay the particular Rent so accepted, regardless of Landlord's knowledge of such preceding breach at the time of acceptance of such Rent. No acceptance of a lesser amount than the Rent herein stipulated shall be deemed a waiver of Landlord's right to receive the full amount due, nor shall any endorsement or statement on any check or payment or any letter accompanying such check or payment be deemed an accord and satisfaction, and Landlord may accept such check or payment without prejudice to Landlord's right to recover the full amount due. No receipt of monies by Landlord from Tenant after the termination of this Lease shall in any way alter the length of the Lease Term or of Tenant's right of possession hereunder, or after the giving of any notice shall reinstate, continue or extend the Lease Term or affect any notice given Tenant prior to the receipt of such monies, it being agreed that after the service of notice or the commencement of a suit, or after final judgment for possession of the Premises, Landlord may receive and collect any Rent due, and the payment of said Rent shall not waive or affect said notice, suit or judgment.

13. CONDEMNATION. If the whole or any part of the Premises shall be taken by power of eminent domain or condemned by any competent authority for any public or quasi-public use or purpose, or if any adjacent property or street shall be so taken or condemned, or reconfigured or vacated by such authority in such manner as to require the use or reconstruction of any part of the Premises, or if Landlord shall grant a deed or other instrument in lieu of such taking by eminent domain or condemnation, Landlord shall have the option to terminate this Lease effective as of the date possession is required to be surrendered to the authority. Tenant shall not because of such taking assert any claim against Landlord or the authority for any compensation because of such taking and Landlord shall be entitled to the entire award or payment in connection therewith, except that Tenant shall have the right to file any separate claim available to Tenant for any taking of Tenant's personal property and fixtures belonging to Tenant and removable by Tenant upon expiration of the Lease Term pursuant to the terms of this Lease, for moving expenses, for the unamortized value of any improvements paid for by Tenant and for the Lease "bonus value", so long as such claims are payable separately to Tenant. All Rent shall be apportioned as of the date of such termination. If any part of the Premises shall be taken, and this Lease shall not be so terminated, the Rent shall be proportionately abated. Tenant hereby waives any and all rights it might otherwise have pursuant to Section 1265.130 of The California Code of Civil Procedure. Notwithstanding anything to the contrary contained in this Article 13, in the event of a temporary taking of all or any portion of the Premises for a period of one hundred and eighty (180) days or less, then this Lease shall not terminate but the Base Rent and the Additional Rent shall be abated for the period of such taking in proportion to the ratio that the amount of rentable square feet of the Premises taken bears to the total rentable square feet of the Premises. Landlord shall be entitled to receive the entire award made in connection with any such temporary taking.

14. ASSIGNMENT AND SUBLETTING.

14.1 **Transfers**. Tenant shall not, without the prior written consent of Landlord, assign, mortgage, pledge, hypothecate, encumber, or permit any lien to attach to, or otherwise transfer, this Lease or any interest hereunder, permit any assignment, or other transfer of this Lease or any interest hereunder by operation of law, sublet the Premises or any part thereof, or enter into any license or concession agreements or otherwise permit the occupancy or use of the Premises or any part thereof by any persons other than Tenant and its employees and

contractors (all of the foregoing are hereinafter sometimes referred to collectively as "**Transfers**" and any person to whom any Transfer is made or sought to be made is hereinafter sometimes referred to as a "**Transferee**"). If Tenant desires Landlord's consent to any Transfer, Tenant shall notify Landlord in writing, which notice (the "**Transfer Notice**") shall include (i) the proposed effective date of the Transfer, which shall not be less than thirty (30) days nor more than one hundred eighty (180) days after the date of delivery of the Transfer Notice, (ii) a description of the portion of the Premises to be transferred (the "**Subject Space**"), (iii) all of the terms of the proposed Transfer and the consideration therefor, including calculation of the "**Transfer Premium**", as that term is defined in Section 14.3 below, in connection with such Transfer, the name and address of the proposed Transferee, and a copy of all existing executed and/or proposed documentation pertaining to the proposed Transfer, and (iv) current financial statements of the proposed Transferee certified by an officer, partner or owner thereof, and any other information reasonably required by Landlord which will enable Landlord to determine the financial responsibility, character, and reputation of the proposed Transferee, nature of such Transferee's business and proposed use of the Subject Space. Any Transfer made without Landlord's prior written consent shall, at Landlord's option, be null, void and of no effect, and shall, at Landlord's option, constitute a default by Tenant under this Lease. Whether or not Landlord consents to any proposed Transfer, Tenant shall pay Landlord's reasonable review and processing fees, as well as any reasonable professional fees (including, without limitation, attorneys', accountants', architects', engineers' and consultants' fees) incurred by Landlord (not to exceed $3,500 in the aggregate for any particular Transfer), within thirty (30) days after written request by Landlord.

14.2 **Landlord's Consent**. Landlord shall not unreasonably withhold or delay its consent to any proposed Transfer of the Subject Space to the Transferee on the terms specified in the Transfer Notice. Without limitation as to other reasonable grounds for withholding consent, the parties hereby agree that it shall be reasonable under this Lease and under any applicable law for Landlord to withhold consent to any proposed Transfer where one or more of the following apply:

14.2.1 The Transferee is of a character or reputation or engaged in a business which is not consistent with the quality of the Building or the Project;

14.2.2 The Transferee is either a governmental agency or instrumentality thereof;

14.2.3 The Transferee is not a party of reasonable financial worth and/or financial stability in light of the responsibilities to be undertaken in connection with the Transfer on the date consent is requested; or

14.2.4 The proposed Transfer would cause a violation of another lease for space in the Project, or would give an occupant of the Project a right to cancel its lease.

If Landlord consents to any Transfer pursuant to the terms of this Section 14.2 (and does not exercise any recapture rights Landlord may have under Section 14.4 of this Lease), Tenant may within six (6) months after Landlord's consent, but not later than the expiration of said six-month period, enter into such Transfer of the Premises or portion thereof, upon substantially the same terms and conditions as are set forth in the Transfer Notice furnished by Tenant to Landlord pursuant to Section 14.1 of this Lease, provided that if there are any changes in the terms and conditions from those specified in the Transfer Notice such that Landlord would initially have been entitled to refuse its consent to such Transfer under this Section 14.2, Tenant shall again submit the Transfer to Landlord for its approval and other action under this Article 14 (including Landlord's right of recapture, if any, under Section 14.4 of this Lease). Notwithstanding anything to the contrary in this Lease, if Tenant or any proposed Transferee claims that Landlord has unreasonably withheld or delayed its consent under Section 14.2 or otherwise has breached or acted unreasonably under this Article 14, their sole remedies shall be a suit for contract damages (other than damages for injury to, or interference with, Tenant's business including, without limitation, loss of profits, however occurring) or declaratory judgment and an injunction for the relief sought, and Tenant hereby waives all other remedies, including, without limitation, any right at law or equity to terminate this Lease, on its own behalf and, to the extent permitted under all applicable laws, on behalf of the proposed Transferee.

14.3 **Transfer Premium**. If Landlord consents to a Transfer, as a condition thereto which the parties hereby agree is reasonable, Tenant shall pay to Landlord fifty percent (50%) of any "**Transfer Premium**," as that term is defined in this Section 14.3, received by Tenant from such Transferee. "**Transfer Premium**" shall mean all rent, additional rent or other consideration payable by such Transferee in connection with the Transfer in excess of

the Rent and Additional Rent payable by Tenant under this Lease during the term of the Transfer on a per rentable square foot basis if less than all of the Premises is transferred, and after deduction of (i) any costs of improvements made to the Subject Space in connection with such Transfer, (ii) brokerage commissions paid in connection with such Transfer, and (iii) reasonable legal fees incurred in connection with such Transfer. "**Transfer Premium**" shall also include, but not be limited to, key money, bonus money or other cash consideration paid by Transferee to Tenant in connection with such Transfer, and any payment in excess of fair market value for services rendered by Tenant to Transferee or for assets, fixtures, inventory, equipment, or furniture transferred by Tenant to Transferee in connection with such Transfer. The determination of the amount of Landlord's applicable share of the Transfer Premium shall be made on a monthly basis as rent or other consideration is received by Tenant under the Transfer.

14.4 **Landlord's Option as to Subject Space**. Notwithstanding anything to the contrary contained in this Article 14, in the event Tenant contemplates a Transfer other than to a Permitted Transferee which, together with all prior Transfers then remaining in effect, would cause fifty percent (50%) or more of the Premises to be Transferred for more than fifty percent (50%) of the then remaining Lease Term (taking into account any extension of the Lease Term which has irrevocably exercised by Tenant), Tenant shall give Landlord notice (the "**Intention to Transfer Notice**") of such contemplated Transfer (whether or not the contemplated Transferee or the terms of such contemplated Transfer have been determined). The Intention to Transfer Notice shall specify the portion of and amount of rentable square feet of the Premises which Tenant intends to Transfer in the subject Transfer (the "**Contemplated Transfer Space**"), the contemplated date of commencement of the Contemplated Transfer (the "**Contemplated Effective Date**"), and the contemplated length of the term of such contemplated Transfer. Thereafter, Landlord shall have the option, by giving written notice to Tenant within thirty (30) days after receipt of any Intention to Transfer Notice, to recapture the Contemplated Transfer Space. Such recapture shall cancel and terminate this Lease with respect to such Contemplated Transfer Space as of the Contemplated Effective Date. In the event of a recapture by Landlord, if this Lease shall be canceled with respect to less than the entire Premises, the Rent reserved herein shall be prorated on the basis of the number of rentable square feet retained by Tenant in proportion to the number of rentable square feet contained in the Premises, and this Lease as so amended shall continue thereafter in full force and effect, and upon request of either party, the parties shall execute written confirmation of the same. If Landlord declines, or fails to elect in a timely manner, to recapture such Contemplated Transfer Space under this Section 14.4, then, subject to the other terms of this Article 14, for a period of nine (9) months (the "**Nine Month Period**") commencing on the last day of such thirty (30) day period, Landlord shall not have any right to recapture the Contemplated Transfer Space with respect to any Transfer made during the Nine Month Period, provided that any such Transfer is substantially on the terms set forth in the Intention to Transfer Notice, and provided further that any such Transfer shall be subject to the remaining terms of this Article 14. If such a Transfer is not so consummated within the Nine Month Period (or if a Transfer is so consummated, then upon the expiration of the term of any Transfer of such Contemplated Transfer Space consummated within such Nine Month Period), Tenant shall again be required to submit a new Intention to Transfer Notice to Landlord with respect any contemplated Transfer, as provided above in this Section 14.4. Tenant shall not be required to provide a separate Intention to Transfer Notice and Tenant's request for Landlord's consent to a Transfer shall satisfy Tenant's obligations in this Section 14.4.

14.5 **Effect of Transfer**. If Landlord consents to a Transfer, (i) the terms and conditions of this Lease shall in no way be deemed to have been waived or modified, (ii) such consent shall not be deemed consent to any further Transfer by either Tenant or a Transferee, (iii) Tenant shall deliver to Landlord, promptly after execution, an original executed copy of all documentation pertaining to the Transfer in form reasonably acceptable to Landlord, (iv) Tenant shall furnish upon Landlord's request a complete statement, certified by an independent certified public accountant, or Tenant's chief financial officer, setting forth in detail the computation of any Transfer Premium Tenant has derived and shall derive from such Transfer, and (v) no Transfer relating to this Lease or agreement entered into with respect thereto, whether with or without Landlord's consent, shall relieve Tenant or any guarantor of the Lease from any liability under this Lease, including, without limitation, in connection with the Subject Space. Landlord or its authorized representatives shall have the right at all reasonable times to audit the books, records and papers of Tenant relating to any Transfer, and shall have the right to make copies thereof. If the Transfer Premium respecting any Transfer shall be found understated, Tenant shall, within thirty (30) days after demand, pay the deficiency, and if understated by more than two percent (2%), Tenant shall pay Landlord's costs of such audit.

14.6 **Additional Transfers**. For purposes of this Lease, the term "**Transfer**" shall also include if Tenant is a partnership, the withdrawal or change, voluntary, involuntary or by operation of law, of fifty percent (50%) or more of the partners, or transfer of fifty percent (50%) or more of partnership interests, within a twelve (12)-month period, or the dissolution of the partnership without immediate reconstitution thereof.

14.7 **Occurrence of Default**. Any Transfer hereunder shall be subordinate and subject to the provisions of this Lease, and if this Lease shall be terminated during the term of any Transfer, Landlord shall have the right to: (i) treat such Transfer as cancelled and repossess the Subject Space by any lawful means, or (ii) require that such Transferee attorn to and recognize Landlord as its landlord under any such Transfer. If Tenant shall be in default under this Lease, Landlord is hereby irrevocably authorized, as Tenant's agent and attorney-in-fact, to direct any Transferee to make all payments under or in connection with the Transfer directly to Landlord (which Landlord shall apply towards Tenant's obligations under this Lease) until such default is cured. Such Transferee shall rely on any representation by Landlord that Tenant is in default hereunder, without any need for confirmation thereof by Tenant. Upon any assignment, the assignee shall assume in writing all obligations and covenants of Tenant thereafter to be performed or observed under this Lease. No collection or acceptance of rent by Landlord from any Transferee shall be deemed a waiver of any provision of this Article 14 or the approval of any Transferee or a release of Tenant from any obligation under this Lease, whether theretofore or thereafter accruing. In no event shall Landlord's enforcement of any provision of this Lease against any Transferee be deemed a waiver of Landlord's right to enforce any term of this Lease against Tenant or any other person. If Tenant's obligations hereunder have been guaranteed, Landlord's consent to any Transfer shall not be effective unless the guarantor also consents to such Transfer.

14.8 **Non-Transfers**. Notwithstanding anything to the contrary contained in this Article 14, (i) an assignment or subletting of all or a portion of the Premises to an affiliate of Tenant (an entity which is controlled by, controls, or is under common control with, Tenant), (ii) an assignment of the Premises to an entity which acquires all or substantially all of the assets or interests (partnership, stock or other) of Tenant, (iii) an assignment of the Premises to an entity which is the resulting entity of a merger or consolidation of Tenant with another entity, or (iv) a sale of corporate shares of capital stock in Tenant in connection with an initial public offering of Tenant's stock on a nationally-recognized stock exchange (collectively, a "**Permitted Transferee**"), shall not be deemed a Transfer under this Article 14, provided that (A) Tenant notifies Landlord of any such assignment or sublease and promptly supplies Landlord with any documents or information requested by Landlord regarding such assignment or sublease or such affiliate, (B) such assignment or sublease is not a subterfuge by Tenant to avoid its obligations under this Lease, (C) such Permitted Transferee shall be of a character and reputation consistent with the quality of the Building, and (D) such Permitted Transferee described in subpart (ii) or (iii) above shall have a tangible net worth (not including goodwill as an asset) computed in accordance with generally accepted accounting principles ("**Net Worth**") at least equal to the Net Worth of Tenant on the day immediately preceding the effective date of such assignment or sublease. An assignee of Tenant's entire interest that is also a Permitted Transferee may also be known as a "**Permitted Assignee**". "**Control**," as used in this Section 14.8, shall mean the ownership, directly or indirectly, of at least fifty-one percent (51%) of the voting securities of, or possession of the right to vote, in the ordinary direction of its affairs, of at least fifty-one percent (51%) of the voting interest in, any person or entity. No such permitted assignment or subletting shall serve to release Tenant from any of its obligations under this Lease.

15. SURRENDER OF PREMISES; OWNERSHIP AND REMOVAL OF TRADE FIXTURES.

15.1 **Surrender of Premises**. No act or thing done by Landlord or any agent or employee of Landlord during the Lease Term shall be deemed to constitute an acceptance by Landlord of a surrender of the Premises unless such intent is specifically acknowledged in writing by Landlord. The delivery of keys to the Premises to Landlord or any agent or employee of Landlord shall not constitute a surrender of the Premises or effect a termination of this Lease, whether or not the keys are thereafter retained by Landlord, and notwithstanding such delivery Tenant shall be entitled to the return of such keys at any reasonable time upon request until this Lease shall have been properly terminated. The voluntary or other surrender of this Lease by Tenant, whether accepted by Landlord or not, or a mutual termination hereof, shall not work a merger, and at the option of Landlord shall operate as an assignment to Landlord of all subleases or subtenancies affecting the Premises or terminate any or all such sublessees or subtenancies.

15.2 **Removal of Tenant Property by Tenant**. Upon the expiration of the Lease Term, or upon any earlier termination of this Lease, Tenant shall, subject to the provisions of this Article 15, quit and surrender possession of the Premises to Landlord in as good order and condition as when Tenant took possession and as

thereafter improved by Landlord and/or Tenant, reasonable wear and tear, damage caused by casualty, repairs required as a result of condemnation, and repairs which are specifically made the responsibility of Landlord hereunder excepted. Upon such expiration or termination, Tenant shall, without expense to Landlord, remove or cause to be removed from the Premises all debris and rubbish, and such items of furniture, equipment, free-standing cabinet work, movable partitions (but not demountable walls) and other articles of personal property owned by Tenant or installed or placed by Tenant at its expense in the Premises, and such similar articles of any other persons claiming under Tenant, as Landlord may, in its sole discretion, require to be removed, and Tenant shall repair at its own expense all damage to the Premises and Building resulting from such removal.

15.3 **Environmental Assessment**. In connection with its surrender of the Premises, Tenant shall submit to Landlord, at least fifteen (15) days prior to the expiration date of this Lease (or in the event of an earlier termination of this Lease, as soon as reasonably possible following such termination), an environmental Assessment of the Premises by a competent and experienced environmental engineer or engineering firm reasonably satisfactory to Landlord (pursuant to a contract approved by Landlord and providing that Landlord can rely on the Environmental Assessment). If such Environmental Assessment reveals that remediation or Clean-up is required under any Environmental Laws that Tenant is responsible for under this Lease, Tenant shall submit a remediation plan prepared by a recognized environmental consultant and shall be responsible for all costs of remediation and Clean-up, as more particularly provided in Section 5.3, above.

15.4 **Condition of the Building and Premises Upon Surrender**. In addition to the above requirements of this Article 15, upon the expiration of the Lease Term, or upon any earlier termination of this Lease, Tenant shall, surrender the Premises and Building with Tenant having complied with all of Tenant's obligations under this Lease, including those relating to improvement, repair, maintenance, compliance with law, testing and other related obligations of Tenant set forth in Article 7 of this Lease. In the event that the Building and Premises shall be surrendered in a condition which does not comply with the terms of this Section 15.4, because Tenant failed to comply with its obligations set forth in Lease, then following thirty (30) days' notice to Tenant, during which thirty (30) day period Tenant shall have the right to cure such noncompliance, Landlord shall be entitled to expend all reasonable costs in order to cause the same to comply with the required condition upon surrender and Tenant shall immediately reimburse Landlord for all such costs upon notice and, commencing on the later of the termination of this Lease and three (3) business days after Landlord's delivery of notice of such failure and that it elects to treat such failure as a holdover, Tenant shall be deemed during the period that Tenant or Landlord, as the case may be, perform obligations relating to the Surrender Improvements to be in holdover under Article 16 of this Lease.

16. HOLDING OVER. If Tenant holds over after the expiration of the Lease Term or earlier termination thereof, with the express or implied consent of Landlord, such tenancy shall be from month-to-month only, and shall not constitute a renewal hereof or an extension for any further term. If Tenant holds over after the expiration of the Lease Term of earlier termination thereof, without the express or implied consent of Landlord, such tenancy shall be deemed to be a tenancy by sufferance only, and shall not constitute a renewal hereof or an extension for any further term. In either case, Base Rent shall be payable at a monthly rate equal to one hundred fifty percent (150%) of the Base Rent applicable during the last rental period of the Lease Term under this Lease. Such month-to-month tenancy or tenancy by sufferance, as the case may be, shall be subject to every other applicable term, covenant and agreement contained herein. Nothing contained in this Article 16 shall be construed as consent by Landlord to any holding over by Tenant, and Landlord expressly reserves the right to require Tenant to surrender possession of the Premises to Landlord as provided in this Lease upon the expiration or other termination of this Lease. The provisions of this Article 16 shall not be deemed to limit or constitute a waiver of any other rights or remedies of Landlord provided herein or at law. If Tenant fails to surrender the Premises upon the termination or expiration of this Lease, in addition to any other liabilities to Landlord accruing therefrom, Tenant shall protect, defend, indemnify and hold Landlord harmless from all loss, costs (including reasonable attorneys' fees) and liability resulting from such failure, including, without limiting the generality of the foregoing, any claims made by any succeeding tenant founded upon such failure to surrender and any lost profits to Landlord resulting therefrom.

17. ESTOPPEL CERTIFICATES. Within ten (10) business days following a request in writing by Landlord, Tenant shall execute, acknowledge and deliver to Landlord an estoppel certificate, which, as submitted by Landlord, shall be substantially in the form of **Exhibit D**, attached hereto (or such other form as may be reasonably required by any prospective mortgagee or purchaser of the Project, or any portion thereof), indicating therein any exceptions thereto that may exist at that time, and shall also contain any other information reasonably requested by Landlord or

Landlord's mortgagee or prospective mortgagee. Any such certificate may be relied upon by any prospective mortgagee or purchaser of all or any portion of the Project. Tenant shall execute and deliver whatever other instruments may be reasonably required for such purposes. At any time during the Lease Term, in connection with a sale or financing of the Building by Landlord, Landlord may require Tenant to provide Landlord with its most recent annual financial statement and annual financial statements of the preceding two (2) years. Such statements shall be prepared in accordance with generally accepted accounting principles and, if such is the normal practice of Tenant, shall be audited by an independent certified public accountant. Landlord shall hold such statements confidential. Failure of Tenant to timely execute, acknowledge and deliver such estoppel certificate or other instruments shall constitute an acceptance of the Premises and an acknowledgment by Tenant that statements included in the estoppel certificate are true and correct, without exception.

18. SUBORDINATION. Landlord hereby represents and warrants to Tenant that the Project is not currently subject to any ground lease, or to the lien of any mortgage or deed of trust. This Lease shall be subject and subordinate to all future ground or underlying leases of the Building or Project and to the lien of any mortgage, trust deed or other encumbrances now or hereafter in force against the Building or Project or any part thereof, if any, and to all renewals, extensions, modifications, consolidations and replacements thereof, and to all advances made or hereafter to be made upon the security of such mortgages or trust deeds, unless the holders of such mortgages, trust deeds or other encumbrances, or the lessors under such ground lease or underlying leases, require in writing that this Lease be superior thereto. The subordination of this Lease to any such future ground or underlying leases of the Building or Project or to the lien of any mortgage, trust deed or other encumbrances, shall be subject to Tenant's receipt of a commercially reasonable subordination, non-disturbance, and attornment agreement in favor of Tenant. Tenant covenants and agrees in the event any proceedings are brought for the foreclosure of any such mortgage or deed in lieu thereof (or if any ground lease is terminated), to attorn, without any deductions or set-offs whatsoever, to the lienholder or purchaser or any successors thereto upon any such foreclosure sale or deed in lieu thereof (or to the ground lessor), if so requested to do so by such purchaser or lienholder or ground lessor, and to recognize such purchaser or lienholder or ground lessor as the lessor under this Lease, provided such lienholder or purchaser or ground lessor shall agree to accept this Lease and not disturb Tenant's occupancy, so long as Tenant timely pays the rent and observes and performs the terms, covenants and conditions of this Lease to be observed and performed by Tenant. Landlord's interest herein may be assigned as security at any time to any lienholder. Tenant shall, within ten (10) days of request by Landlord, execute such further instruments or assurances as Landlord may reasonably deem necessary to evidence or confirm the subordination or superiority of this Lease to any such mortgages, trust deeds, ground leases or underlying leases. Tenant waives the provisions of any current or future statute, rule or law which may give or purport to give Tenant any right or election to terminate or otherwise adversely affect this Lease and the obligations of the Tenant hereunder in the event of any foreclosure proceeding or sale.

19. DEFAULTS; REMEDIES.

19.1 **Events of Default**. The occurrence of any of the following shall constitute a default of this Lease by Tenant:

19.1.1 Any failure by Tenant to pay any Rent or any other charge required to be paid under this Lease, or any part thereof, when due unless such failure is cured within five (5) business days after notice; or

19.1.2 Except where a specific time period is otherwise set forth for Tenant's performance in this Lease, in which event the failure to perform by Tenant within such time period shall be a default by Tenant under this Section 19.1.2, any failure by Tenant to observe or perform any other provision, covenant or condition of this Lease to be observed or performed by Tenant where such failure continues for thirty (30) days after written notice thereof from Landlord to Tenant; provided that if the nature of such default is such that the same cannot reasonably be cured within a thirty (30) day period, Tenant shall not be deemed to be in default if it diligently commences such cure within such period and thereafter diligently proceeds to rectify and cure such default; or

19.1.3 Abandonment or vacation of all or a substantial portion of the Premises by Tenant while Tenant is in default under the Lease; or

19.1.4 The failure by Tenant to observe or perform according to the provisions of Articles 5, 14, 17 or 18 of this Lease where such failure continues for more than five (5) business days after notice from Landlord.

19.2 **Remedies Upon Default**. Upon the occurrence of any event of default by Tenant, Landlord shall have, in addition to any other remedies available to Landlord at law or in equity (all of which remedies shall be distinct, separate and cumulative), the option to pursue any one or more of the following remedies, each and all of which shall be cumulative and nonexclusive, without any notice or demand whatsoever.

19.2.1 Terminate this Lease, in which event Tenant shall immediately surrender the Premises to Landlord, and if Tenant fails to do so, Landlord may, without prejudice to any other remedy which it may have for possession or arrearages in rent, enter upon and take possession of the Premises and expel or remove Tenant and any other person who may be occupying the Premises or any part thereof, without being liable for prosecution or any claim or damages therefor; and Landlord may recover from Tenant the following:

(i) The worth at the time of award of the unpaid rent which has been earned at the time of such termination; plus

(ii) The worth at the time of award of the amount by which the unpaid rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(iii) The worth at the time of award of the amount by which the unpaid rent for the balance of the Lease Term after the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(iv) Any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of things would be likely to result therefrom, specifically including but not limited to, in each case to the extent allocable to the remaining Lease Term, brokerage commissions and advertising expenses incurred to obtain a new tenant, expenses of remodeling the Premises or any portion thereof for a new tenant, whether for the same or a different use, and any special concessions made to obtain a new tenant; and

(v) At Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted from time to time by applicable law.

The term "**rent**" as used in this Section 19.2 shall be deemed to be and to mean all sums of every nature required to be paid by Tenant pursuant to the terms of this Lease, whether to Landlord or to others. As used in Sections 19.2.1(i) and (ii), above, the "worth at the time of award" shall be computed by allowing interest at the rate set forth in Article 25 of this Lease, but in no case greater than the maximum amount of such interest permitted by law. As used in Section 19.2.1(iii) above, the "**worth at the time of award**" shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of award plus one percent (1%).

19.2.2 Landlord shall have the remedy described in California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover rent as it becomes due, if lessee has the right to sublet or assign, subject only to reasonable limitations). Accordingly, if Landlord does not elect to terminate this Lease on account of any default by Tenant, Landlord may, from time to time, without terminating this Lease, enforce all of its rights and remedies under this Lease, including the right to recover all rent as it becomes due.

19.2.3 Landlord shall at all times have the rights and remedies (which shall be cumulative with each other and cumulative and in addition to those rights and remedies available under Sections 19.2.1 and 19.2.2, above, or any law or other provision of this Lease), without prior demand or notice except as required by applicable law, to seek any declaratory, injunctive or other equitable relief, and specifically enforce this Lease, or restrain or enjoin a violation or breach of any provision hereof.

19.3 **Subleases of Tenant**. If Landlord elects to terminate this Lease on account of any default by Tenant, as set forth in this Article 19, Landlord shall have the right to terminate any and all subleases, licenses, concessions or other consensual arrangements for possession entered into by Tenant and affecting the Premises or may, in Landlord's sole discretion, succeed to Tenant's interest in such subleases, licenses, concessions or arrangements. In the event of Landlord's election to succeed to Tenant's interest in any such subleases, licenses, concessions or arrangements, Tenant shall, as of the date of notice by Landlord of such election, have no further right to or interest in the rent or other consideration receivable thereunder.

19.4 **Efforts to Relet**. No re-entry, repairs, maintenance, changes, alterations and additions, appointment of a receiver to protect Landlord's interests hereunder, or any other action or omission by Landlord shall be construed as an election by Landlord to terminate this Lease or Tenant's right to possession, or to accept a surrender of the Premises, nor shall same operate to release Tenant in whole or in part from any of Tenant's obligations hereunder, unless express written notice of such intention is sent by Landlord to Tenant.

20. COVENANT OF QUIET ENJOYMENT. Landlord covenants that Tenant, on paying the Rent, charges for services and other payments herein reserved and on keeping, observing and performing all the other terms, covenants, conditions, provisions and agreements herein contained on the part of Tenant to be kept, observed and performed, shall, during the Lease Term, peaceably and quietly have, hold and enjoy the Premises subject to the terms, covenants, conditions, provisions and agreements hereof without interference by any persons lawfully claiming by or through Landlord. The foregoing covenant is in lieu of any other covenant express or implied.

21. LETTER OF CREDIT.

21.1 **Delivery of Letter of Credit**. Tenant shall deliver to Landlord, concurrently with Tenant's execution of this Lease, an unconditional, clean, irrevocable letter of credit (the "**L-C**") in the amount set forth in Section 8 of the Lease Summary (the "**L-C Amount**"), which L-C shall be issued by a money-center, solvent and nationally recognized bank (a bank which accepts deposits, maintains accounts, has a local San Francisco Bay Area office which will negotiate a letter of credit, and whose deposits are insured by the FDIC) reasonably acceptable to Landlord (such approved, issuing bank being referred to herein as the "**Bank**"), which Bank must have a rating from Standard and Poors Corporation of A- or better (or any equivalent rating thereto from any successor or substitute rating service selected by Lessor) and a letter of credit issuer rating from Moody's Investor Service of A3 or better (or any equivalent rating thereto from any successor rating agency thereto)) (collectively, the "**Bank's Credit Rating Threshold**"), and which L-C shall be in the form of **Exhibit H**, attached hereto. Notwithstanding the foregoing, Landlord hereby approves Silicon Valley Bank as the Bank. Tenant shall pay all expenses, points and/or fees incurred by Tenant in obtaining the L-C. The L-C shall (i) be "callable" at sight, irrevocable and unconditional, (ii) be maintained in effect, whether through renewal or extension, for the period commencing on the date of this Lease and continuing until the date (the "**L-C Expiration Date**") that is no less than sixty (60) days after the expiration of the Lease Term as the same may be extended, and Tenant shall deliver a new L-C or certificate of renewal or extension to Landlord at least thirty (30) days prior to the expiration of the L-C then held by Landlord, without any action whatsoever on the part of Landlord, (iii) be fully assignable by Landlord, its successors and assigns, (iv) permit partial draws and multiple presentations and drawings, and (v) be otherwise subject to the Uniform Customs and Practices for Documentary Credits (1993-Rev), International Chamber of Commerce Publication #500, or the International Standby Practices-ISP 98, International Chamber of Commerce Publication #590. Landlord, or its then managing agent, shall have the right to draw down an amount up to the face amount of the L-C if any of the following shall have occurred or be applicable: (A) such amount is due to Landlord under the terms and conditions of this Lease, and has not been paid within applicable notice and cure periods (or, if Landlord is prevented by law from providing notice, within the period for payment set forth in the Lease), or (B) Tenant has filed a voluntary petition under the U. S. Bankruptcy Code or any state bankruptcy code (collectively, "**Bankruptcy Code**"), or (C) an involuntary petition has been filed against Tenant under the Bankruptcy Code that is not dismissed within thirty (30) days, or (D) the Lease has been rejected, or is deemed rejected, under Section 365 of the U.S. Bankruptcy Code, following the filing of a voluntary petition by Tenant under the Bankruptcy Code, or the filing of an involuntary petition against Tenant under the Bankruptcy Code, or (E) the Bank has notified Landlord that the L-C will not be renewed or extended through the L-C Expiration Date, and Tenant has not provided a replacement L-C that satisfies the requirements of this Lease at least thirty (30) days prior to such expiration, or (F) Tenant is placed into receivership or conservatorship, or becomes subject to similar proceedings under Federal or State law, or (G) Tenant executes an assignment for the benefit of creditors, or (H) if (1) any of the Bank's (other

than Silicon Valley Bank) Fitch Ratings (or other comparable ratings to the extent the Fitch Ratings are no longer available) have been reduced below the Bank's Credit Rating Threshold, or (2) there is otherwise a material adverse change in the financial condition of the Bank, and Tenant has failed to provide Landlord with a replacement letter of credit, conforming in all respects to the requirements of this Article 21 (including, but not limited to, the requirements placed on the issuing Bank more particularly set forth in this Section 21.1 above), in the amount of the applicable L-C Amount, within ten (10) days following Landlord's written demand therefor (with no other notice or cure or grace period being applicable thereto, notwithstanding anything in this Lease to the contrary) (each of the foregoing being an "**L-C Draw Event**"). The L-C shall be honored by the Bank regardless of whether Tenant disputes Landlord's right to draw upon the L-C. In addition, in the event the Bank is placed into receivership or conservatorship by the Federal Deposit Insurance Corporation or any successor or similar entity, then, effective as of the date such receivership or conservatorship occurs, said L-C shall be deemed to fail to meet the requirements of this Article 21, and, within ten (10) days following Landlord's notice to Tenant of such receivership or conservatorship (the "**L-C FDIC Replacement Notice**"), Tenant shall replace such L-C with a substitute letter of credit from a different issuer (which issuer shall meet or exceed the Bank's Credit Rating Threshold and shall otherwise be acceptable to Landlord in its reasonable discretion) and that complies in all respects with the requirements of this Article 21. If Tenant fails to replace such L-C with such conforming, substitute letter of credit pursuant to the terms and conditions of this Section 21.1, then, notwithstanding anything in this Lease to the contrary, Landlord shall have the right to declare Tenant in default of this Lease for which there shall be no notice or grace or cure periods being applicable thereto (other than the aforesaid ten (10) day period). Tenant shall be responsible for the payment of any and all Tenant's and Bank's costs incurred with the review of any replacement L-C, which replacement is required pursuant to this Section or is otherwise requested by Tenant. In the event of an assignment by Tenant of its interest in the Lease (and irrespective of whether Landlord's consent is required for such assignment), the acceptance of any replacement or substitute letter of credit by Landlord from the assignee shall be subject to Landlord's prior written approval, in Landlord's reasonable discretion, and the actual and reasonable attorney's fees incurred by Landlord in connection with such determination shall be payable by Tenant to Landlord within ten (10) days of billing.

21.2 **Application of L-C**. Tenant hereby acknowledges and agrees that Landlord is entering into this Lease in material reliance upon the ability of Landlord to draw upon the L-C upon the occurrence of any L-C Draw Event. In the event of any L-C Draw Event, Landlord may, but without obligation to do so, and without notice to Tenant (except in connection with an L-C Draw Event under Section 21.1(H) above), draw upon the L-C, in part or in whole, in the amount necessary to cure any such L-C Draw Event and/or to compensate Landlord for any and all damages of any kind or nature sustained or which Landlord reasonably estimates that it will sustain resulting from Tenant's breach or default of the Lease or other L-C Draw Event and/or to compensate Landlord for any and all damages arising out of, or incurred in connection with, the termination of this Lease, including, without limitation, those specifically identified in Section 1951.2 of the California Civil Code. The use, application or retention of the L-C, or any portion thereof, by Landlord shall not prevent Landlord from exercising any other right or remedy provided by this Lease or by any applicable law, it being intended that Landlord shall not first be required to proceed against the L-C, and such L-C shall not operate as a limitation on any recovery to which Landlord may otherwise be entitled. Tenant agrees and acknowledges that (i) the L-C constitutes a separate and independent contract between Landlord and the Bank, (ii) Tenant is not a third party beneficiary of such contract, (iii) Tenant has no property interest whatsoever in the L-C or the proceeds thereof, and (iv) in the event Tenant becomes a debtor under any chapter of the Bankruptcy Code, Tenant is placed into receivership or conservatorship, and/or there is an event of a receivership, conservatorship or a bankruptcy filing by, or on behalf of, Tenant, neither Tenant, any trustee, nor Tenant's bankruptcy estate shall have any right to restrict or limit Landlord's claim and/or rights to the L-C and/or the proceeds thereof by application of Section 502(b)(6) of the U. S. Bankruptcy Code or otherwise.

21.3 **Maintenance of L-C by Tenant**. If, as a result of any drawing by Landlord of all or any portion of the L-C, the amount of the L-C shall be less than the L-C Amount, Tenant shall, within five (5) days thereafter, provide Landlord with additional letter(s) of credit in an amount equal to the deficiency, and any such additional letter(s) of credit shall comply with all of the provisions of this Article 21. Tenant further covenants and warrants that it will neither assign nor encumber the L-C or any part thereof and that neither Landlord nor its successors or assigns will be bound by any such assignment, encumbrance, attempted assignment or attempted encumbrance. Without limiting the generality of the foregoing, if the L-C expires earlier than the L-C Expiration Date, Landlord will accept a renewal thereof (such renewal letter of credit to be in effect and delivered to Landlord, as applicable, not later than thirty (30) days prior to the expiration of the L-C), which shall be irrevocable and automatically

renewable as above provided through the L-C Expiration Date upon the same terms as the expiring L-C or such other terms as may be acceptable to Landlord in its sole discretion. If Tenant exercises its option to extend the Lease Term pursuant to Section 2.2 of this Lease then, not later than thirty (30) days prior to the commencement of the Option Term, Tenant shall deliver to Landlord a new L C or certificate of renewal or extension evidencing the L-C Expiration Date as thirty (30) days after the expiration of the Option Term. However, if the L-C is not timely renewed, or if Tenant fails to maintain the L-C in the amount and in accordance with the terms set forth in this Article 21, Landlord shall have the right to present the L-C to the Bank in accordance with the terms of this Article 21, and the proceeds of the L-C may be applied by Landlord against any Rent payable by Tenant under this Lease that is not paid when due and/or to pay for all losses and damages that Landlord has suffered or that Landlord reasonably estimates that it will suffer as a result of any breach or default by Tenant under this Lease. In the event Landlord elects to exercise its rights as provided above, (I) any unused proceeds shall constitute the property of Landlord (and not Tenant's property or, in the event of a receivership, conservatorship, or a bankruptcy filing by, or on behalf of, Tenant, property of such receivership, conservatorship or Tenant's bankruptcy estate) and need not be segregated from Landlord's other assets, and (II) Landlord agrees to pay to Tenant within thirty (30) days after the L-C Expiration Date the amount of any proceeds of the L-C received by Landlord and not applied against any Rent payable by Tenant under this Lease that was not paid when due or used to pay for any losses and/or damages suffered by Landlord (or reasonably estimated by Landlord that it will suffer) as a result of any breach or default by Tenant under this Lease; provided, however, that if prior to the L-C Expiration Date a voluntary petition is filed by Tenant, or an involuntary petition is filed against Tenant by any of Tenant's creditors, under the Bankruptcy Code, then Landlord shall not be obligated to make such payment in the amount of the unused L-C proceeds until either all preference issues relating to payments under this Lease have been resolved in such bankruptcy or reorganization case or such bankruptcy or reorganization case has been dismissed. If Landlord draws on the L-C due to Tenant's failure to timely renew or provide a replacement L-C, such failure shall not be considered a default under this Lease and Landlord shall return such cash proceeds upon Tenant's presentation of a replacement L-C that satisfies the requirements of this Lease, subject to reasonable satisfaction of any preference risk to Landlord.

21.4 **Transfer and Encumbrance**. The L-C shall also provide that Landlord may, at any time and without notice to Tenant and without first obtaining Tenant's consent thereto, transfer (one or more times) all or any portion of its interest in and to the L-C to another party, person or entity, regardless of whether or not such transfer is from or as a part of the assignment by Landlord of its rights and interests in and to this Lease. In the event of a transfer of Landlord's interest in under this Lease, Landlord shall transfer the L-C, in whole or in part, to the transferee and thereupon Landlord shall, without any further agreement between the parties, be released by Tenant from all liability therefor, and it is agreed that the provisions hereof shall apply to every transfer or assignment of the whole of said LC to a new landlord. In connection with any such transfer of the L-C by Landlord, Tenant shall, at Tenant's sole cost and expense, execute and submit to the Bank such applications, documents and instruments as may be necessary to effectuate such transfer and, Tenant shall be responsible for paying the Bank's transfer and processing fees in connection therewith; provided that, Landlord shall have the right (in its sole discretion), but not the obligation, to pay such fees on behalf of Tenant, in which case Tenant shall reimburse Landlord within ten (10) days after Tenant's receipt of an invoice from Landlord therefor.

21.5 **L-C Not a Security Deposit**. Landlord and Tenant (1) acknowledge and agree that in no event or circumstance shall the L-C or any renewal thereof or substitute therefor or any proceeds thereof be deemed to be or treated as a "security deposit" under any law applicable to security deposits in the commercial context, including, but not limited to, Section 1950.7 of the California Civil Code, as such Section now exists or as it may be hereafter amended or succeeded (the "**Security Deposit Laws**"), (2) acknowledge and agree that the L-C (including any renewal thereof or substitute therefor or any proceeds thereof) is not intended to serve as a security deposit, and the Security Deposit Laws shall have no applicability or relevancy thereto, and (3) waive any and all rights, duties and obligations that any such party may now, or in the future will, have relating to or arising from the Security Deposit Laws. Tenant hereby irrevocably waives and relinquishes the provisions of Section 1950.7 of the California Civil Code and any successor statute, and all other provisions of law, now or hereafter in effect, which (x) establish the time frame by which a landlord must refund a security deposit under a lease, and/or (y) provide that a landlord may claim from a security deposit only those sums reasonably necessary to remedy defaults in the payment of rent, to repair damage caused by a tenant or to clean the premises, it being agreed that Landlord may, in addition, claim those sums specified in this Article 21 and/or those sums reasonably necessary to (a) compensate Landlord for any loss or damage caused by Tenant's breach of this Lease, including any damages Landlord suffers following termination of this Lease, and/or (b) compensate Landlord for any and all damages arising out of, or incurred in

connection with, the termination of this Lease, including, without limitation, those specifically identified in Section 1951.2 of the California Civil Code. Tenant agrees not to interfere in any way with any payment to Landlord of the proceeds of the L-C, either prior to or following a "draw" by Landlord of all or any portion of the L-C, regardless of whether any dispute exists between Tenant and Landlord as to Landlord's right to draw down all or any portion of the L-C. No condition or term of this Lease shall be deemed to render the L-C conditional and thereby afford the Bank a justification for failing to honor a drawing upon such L-C in a timely manner. Tenant shall not request or instruct the Bank of any L-C to refrain from paying sight draft(s) drawn under such L-C.

21.6 **Remedy for Improper Drafts**. Tenant's sole remedy in connection with the improper presentment or payment of sight drafts drawn under any L-C shall be the right to obtain from Landlord a refund of the amount of any sight draft(s) that were improperly presented or the proceeds of which were misapplied, and reasonable actual out-of-pocket attorneys' fees, provided that at the time of such refund, Tenant increases the amount of such L-C to the amount (if any) then required under the applicable provisions of this Lease. Tenant acknowledges that the presentment of sight drafts drawn under any L-C, or the Bank's payment of sight drafts drawn under such L-C, could not under any circumstances cause Tenant injury that could not be remedied by an award of money damages, and that the recovery of money damages would be an adequate remedy therefor. In the event Tenant shall be entitled to a refund as aforesaid and Landlord shall fail to make such payment within ten (10) business days after demand, Tenant shall have the right to deduct the amount thereof from the next installment(s) of Base Rent.

22. COMMUNICATIONS AND COMPUTER LINE. Tenant may install, maintain, replace, remove or use any communications or computer wires and cables serving the Premises (collectively, the "**Lines**"), provided that Tenant shall obtain Landlord's prior written consent, use an experienced and qualified contractor approved in writing by Landlord, and comply with all of the other provisions of Articles 7 and 8 of this Lease. Tenant shall pay all costs in connection therewith. Landlord reserves the right, upon notice to Tenant prior to the expiration or earlier termination of this Lease, to require that Tenant, at Tenant's sole cost and expense, remove any Lines located in or serving the Premises prior to the expiration or earlier termination of this Lease.

23. SIGNS.

23.1 **Exterior Signage**. Subject to Landlord's prior written approval, which shall not be unreasonably withheld, conditioned or delayed, and provided all signs are in keeping with the quality, design and style of the Building and Project, Tenant, at its sole cost and expense, may install (i) identification signage on the monument sign outside the front entrance to the Building (which Landlord shall install at its sole cost prior to the Lease Commencement Date), (ii) internal directional and lobby identification signage, and (iii) signage in the elevator lobby on the floor containing the Premises (collectively, "**Tenant Signage**"); provided, however, in no event shall Tenant's Signage include an "Objectionable Name," as that term is defined in Section 23.3, of this Lease. All such signage shall be subject to Tenant's obtaining all required governmental approvals. All permitted signs shall be maintained by Tenant at its expense in a first-class and safe condition and appearance. Upon the expiration or earlier termination of this Lease, Tenant shall remove all of its signs at Tenant's sole cost and expense. The graphics, materials, color, design, lettering, lighting, size, illumination, specifications and exact location of Tenant's Signage (collectively, the "**Sign Specifications**") shall be subject to the prior written approval of Landlord, which approval shall not be unreasonably withheld, conditioned or delayed, and shall be consistent and compatible with the quality and nature of the Project. Tenant hereby acknowledges that, notwithstanding Landlord's approval of Tenant's Signage, Landlord has made no representation or warranty to Tenant with respect to the probability of obtaining all necessary governmental approvals and permits for Tenant's Signage. In the event Tenant does not receive the necessary governmental approvals and permits for Tenant's Signage, Tenant's and Landlord's rights and obligations under the remaining terms of this Lease shall be unaffected. Except as required by applicable law, Landlord shall not install any other signage on the Building. If Landlord elects to install a multi-tenant identification sign at the entrance to the Project, Tenant shall be entitled to install its name on such sign (subject to availability on a pro-rata basis based on the relative square footages leased by the tenants of the Project), at Tenant's sole cost and expense.

23.2 **Objectionable Name**. Tenant's Signage shall not include a name or logo which relates to an entity which is of a character or reputation, or is associated with a political faction or orientation, which is inconsistent with the quality of the Project, or which would otherwise reasonably offend a landlord of the Comparable Buildings (an "**Objectionable Name**"). Landlord agrees that "Denali Therapeutics Inc." or "Denali" is not an Objectionable Name.

23.3 **Prohibited Signage and Other Items**. Any signs, notices, logos, pictures, names or advertisements which are installed and that have not been separately approved by Landlord may be removed without notice by Landlord at the sole expense of Tenant. Any signs, window coverings, or blinds (even if the same are located behind the Landlord-approved window coverings for the Building), or other items visible from the exterior of the Premises or Building, shall be subject to the prior approval of Landlord, in its sole discretion.

24. COMPLIANCE WITH LAW. Tenant shall not do anything or suffer anything to be done in or about the Premises or the Project which will in any way conflict with any law, statute, ordinance or other governmental rule, regulation or requirement now in force or which may hereafter be enacted or promulgated. At its sole cost and expense, Tenant shall promptly comply with all such governmental measures. Should any standard or regulation now or hereafter be imposed on Landlord or Tenant by a state, federal or local governmental body charged with the establishment, regulation and enforcement of occupational, health or safety standards for employers, employees, landlords or tenants, then Tenant agrees, at its sole cost and expense, to comply promptly with such standards or regulations. Tenant shall be responsible, at its sole cost and expense, to make all alterations to the Building and Premises as are required to comply with the governmental rules, regulations, requirements or standards described in this Article 24. The judgment of any court of competent jurisdiction or the admission of Tenant in any judicial action, regardless of whether Landlord is a party thereto, that Tenant has violated any of said governmental measures, shall be conclusive of that fact as between Landlord and Tenant. Tenant's obligations under this Article 24 are subject to the limitation in Section 10.2, above.

25. LATE CHARGES. If any installment of Rent or any other sum due from Tenant shall not be received by Landlord or Landlord's designee within five (5) business days after Tenant's receipt of written notice from Landlord that said amount is delinquent, then Tenant shall pay to Landlord a late charge equal to five percent (5%) of the overdue amount plus any reasonable attorneys' fees incurred by Landlord by reason of Tenant's failure to pay Rent and/or other charges when due hereunder. The late charge shall be deemed Additional Rent and the right to require it shall be in addition to all of Landlord's other rights and remedies hereunder or at law and shall not be construed as liquidated damages or as limiting Landlord's remedies in any manner. In addition to the late charge described above, any Rent or other amounts owing hereunder which are not paid within ten (10) days after Tenant's receipt of written notice that said amount is delinquent shall bear interest from the date when due until paid at a rate per annum equal to the lesser of (i) the annual "Bank Prime Loan" rate cited in the Federal Reserve Statistical Release Publication G.13(415), published on the first Tuesday of each calendar month (or such other comparable index as Landlord and Tenant shall reasonably agree upon if such rate ceases to be published) plus four (4) percentage points, and (ii) the highest rate permitted by applicable law.

26. LANDLORD'S RIGHT TO CURE DEFAULT; PAYMENTS BY TENANT.

26.1 **Landlord's Cure**. All covenants and agreements to be kept or performed by Tenant under this Lease shall be performed by Tenant at Tenant's sole cost and expense and without any reduction of Rent, except to the extent, if any, otherwise expressly provided herein. If Tenant shall fail to perform any obligation under this Lease, and such failure shall continue in excess of the time allowed under Section 19.1.2, above, unless a specific time period is otherwise stated in this Lease, Landlord may, but shall not be obligated to, make any such payment or perform any such act on Tenant's part without waiving its rights based upon any default of Tenant and without releasing Tenant from any obligations hereunder.

26.2 **Tenant's Reimbursement**. Except as may be specifically provided to the contrary in this Lease, Tenant shall pay to Landlord, upon delivery by Landlord to Tenant of statements therefor: (i) sums equal to expenditures reasonably made and obligations incurred by Landlord in connection with the remedying by Landlord of Tenant's defaults pursuant to the provisions of Section 26.1; (ii) sums equal to all losses, costs, liabilities, damages and expenses referred to in Article 10 of this Lease; and (iii) subject to Section 29.21, sums equal to all expenditures made and obligations incurred by Landlord in collecting or attempting to collect the Rent or in enforcing or attempting to enforce any rights of Landlord under this Lease or pursuant to law, including, without limitation, all reasonable legal fees and other amounts so expended. Tenant's obligations under this Section 26.2 shall survive the expiration or sooner termination of the Lease Term.

27. ENTRY BY LANDLORD. Landlord reserves the right at all reasonable times and upon reasonable notice to Tenant (except in the case of an Emergency) to enter the Premises to (i) inspect them; (ii) show the Premises to prospective purchasers, or to current or prospective mortgagees, ground or underlying lessors or insurers or, during the last nine (9) months of the Lease Term, to prospective tenants; (iii) post notices of nonresponsibility (to the extent applicable pursuant to then applicable law); or (iv) repair the Premises or the Building, or for structural repairs to the Building or the Building's systems and equipment as provided under the Lease. Landlord may make any such entries without the abatement of Rent, except as otherwise provided in this Lease, and may take such reasonable steps as required to accomplish the stated purposes. In an Emergency, Landlord shall have the right to use any means that Landlord may deem proper to open the doors in and to the Premises. Any entry into the Premises by Landlord in the manner hereinbefore described shall not be deemed to be a forcible or unlawful entry into, or a detainer of, the Premises, or an actual or constructive eviction of Tenant from any portion of the Premises. Landlord shall use commercially reasonable efforts to minimize any interference with Tenant's use of or access to the Premises in connection with any such entry, and shall comply with Tenant's reasonable security measures. Landlord shall hold confidential any information regarding Tenant's business that it may learn as a result of such entry.

28. TENANT PARKING. Tenant shall have the right, without the payment of any parking charge or fee (other than as a reimbursement of operating expenses to the extent allowed pursuant to the terms or Article 4 of this Lease, above), commencing on the Lease Commencement Date, to use the amount of parking set forth in Section 9 of the Summary, in the on-site parking lot and garage which serves the Building. Tenant shall abide by all reasonable rules and regulations which are prescribed from time to time for the orderly operation and use of the parking facility where the parking passes are located (including any sticker or other identification system established by Landlord and the prohibition of vehicle repair and maintenance activities in the parking facilities), and shall cooperate in seeing that Tenant's employees and visitors also comply with such rules and regulations. Tenant's use of the Project parking facility shall be at Tenant's sole risk and Tenant acknowledges and agrees that Landlord shall have no liability whatsoever for damage to the vehicles of Tenant, its employees and/or visitors, or for other personal injury or property damage or theft relating to or connected with the parking rights granted herein or any of Tenant's, its employees' and/or visitors' use of the parking facilities.

29. MISCELLANEOUS PROVISIONS.

29.1 **Terms; Captions**. The words "**Landlord**" and "**Tenant**" as used herein shall include the plural as well as the singular. The necessary grammatical changes required to make the provisions hereof apply either to corporations or partnerships or individuals, men or women, as the case may require, shall in all cases be assumed as though in each case fully expressed. The captions of Articles and Sections are for convenience only and shall not be deemed to limit, construe, affect or alter the meaning of such Articles and Sections.

29.2 **Binding Effect**. Subject to all other provisions of this Lease, each of the covenants, conditions and provisions of this Lease shall extend to and shall, as the case may require, bind or inure to the benefit not only of Landlord and of Tenant, but also of their respective heirs, personal representatives, successors or assigns, provided this clause shall not permit any assignment by Tenant contrary to the provisions of Article 14 of this Lease.

29.3 **No Air Rights**. No rights to any view or to light or air over any property, whether belonging to Landlord or any other person, are granted to Tenant by this Lease. If at any time any windows of the Premises are temporarily darkened or the light or view therefrom is obstructed by reason of any repairs, improvements, maintenance or cleaning in or about the Project, the same shall be without liability to Landlord and without any reduction or diminution of Tenant's obligations under this Lease.

29.4 **Modification of Lease**. Should any current or prospective mortgagee or ground lessor for the Building or Project require a modification of this Lease, which modification will not cause an increased cost or expense to Tenant or in any other way materially and adversely change the rights and obligations of Tenant hereunder or interfere with Tenant's use of the Premises, then and in such event, Tenant agrees that this Lease may be so modified and agrees to execute whatever documents are reasonably required therefor and to deliver the same to Landlord within ten (10) business days following a request therefor. At the request of Landlord or any mortgagee or ground lessor, Tenant agrees to execute a short form of Lease and deliver the same to Landlord within ten (10) business days following the request therefor.

29.5 **Transfer of Landlord's Interest**. Tenant acknowledges that Landlord has the right to transfer all or any portion of its interest in the Project or Building and in this Lease, and Tenant agrees that in the event of any such transfer, Landlord shall automatically be released from all liability under this Lease and Tenant agrees to look solely to such transferee for the performance of Landlord's obligations hereunder accruing after the date of transfer provided such transferee shall have fully assumed and agreed in writing to be liable for all obligations of this Lease to be performed by Landlord, including the return of any security deposit or L-C, and Tenant shall attorn to such transferee.

29.6 **Prohibition Against Recording**. Except as provided in Section 29.4 of this Lease, neither this Lease, nor any memorandum, affidavit or other writing with respect thereto, shall be recorded by Tenant or by anyone acting through, under or on behalf of Tenant.

29.7 **Landlord's Title**. Landlord's title is and always shall be paramount to the title of Tenant. Nothing herein contained shall empower Tenant to do any act which can, shall or may encumber the title of Landlord.

29.8 **Relationship of Parties**. Nothing contained in this Lease shall be deemed or construed by the parties hereto or by any third party to create the relationship of principal and agent, partnership, joint venturer or any association between Landlord and Tenant.

29.9 **Payment under Protest**. If Tenant in good faith disputes any amounts billed by Landlord, other than (i) Base Rent, (ii) Tenant's Share of Direct Expenses (as to which Tenant may exercise its rights under Section 4.6, above), Tenant may make payment of such amounts under protest, and reserve all of its rights with respect to such amounts (the "**Disputed Amounts**"). Landlord and Tenant shall meet and confer to discuss the Disputed Amounts and attempt, in good faith, to resolve the particular dispute. If, despite such good faith efforts, Landlord and Tenant are unable to reach agreement regarding the Disputed Amounts, either party may submit the matter to binding arbitration under the JAMS Streamlined Arbitration Rules & Procedures. The non-prevailing party, as determined by JAMS, will be responsible to pay all fees and costs incurred in connection with the JAMS procedure, as well as all other costs and expenses, including reasonable attorneys' fees, incurred by the prevailing party. This Section 29.9 shall not apply to claims relating to Landlord's exercise of any unlawful detainer rights pursuant to California law or rights or remedies used by Landlord to gain possession of the Premises or terminate Lessee's right of possession to the Premises.

29.10 **Time of Essence**. Time is of the essence with respect to the performance of every provision of this Lease in which time of performance is a factor.

29.11 **Partial Invalidity**. If any term, provision or condition contained in this Lease shall, to any extent, be invalid or unenforceable, the remainder of this Lease, or the application of such term, provision or condition to persons or circumstances other than those with respect to which it is invalid or unenforceable, shall not be affected thereby, and each and every other term, provision and condition of this Lease shall be valid and enforceable to the fullest extent possible permitted by law.

29.12 **No Warranty**. In executing and delivering this Lease, Tenant has not relied on any representations, including, but not limited to, any representation as to the amount of any item comprising Additional Rent or the amount of the Additional Rent in the aggregate or that Landlord is furnishing the same services to other tenants, at all, on the same level or on the same basis, or any warranty or any statement of Landlord which is not set forth herein or in one or more of the exhibits attached hereto.

29.13 **Landlord Exculpation**. The liability of Landlord or the Landlord Parties to Tenant for any default by Landlord under this Lease or arising in connection herewith or with Landlord's operation, management, leasing, repair, renovation, alteration or any other matter relating to the Project or the Premises shall be limited solely and exclusively to an amount which is equal to the lesser of (a) the interest of Landlord in the Project or (b) the equity interest Landlord would have in the Project if the Project were encumbered by third-party debt in an amount equal to eighty percent (80%) of the value of the Project (as such value is determined by Landlord), including any rental, condemnation, sales and insurance proceeds received by Landlord or the Landlord Parties in connection with the Project, Building or Premises. No Landlord Parties (other than Landlord) shall have any

personal liability therefor, and Tenant hereby expressly waives and releases such liability on behalf of itself and all persons claiming by, through or under Tenant. The limitations of liability contained in this Section 29.13 shall inure to the benefit of Landlord's and the Landlord Parties' present and future partners, beneficiaries, officers, directors, trustees, shareholders, agents and employees, and their respective partners, heirs, successors and assigns. Under no circumstances shall any present or future partner of Landlord (if Landlord is a partnership), or trustee or beneficiary (if Landlord or any partner of Landlord is a trust), have any liability for the performance of Landlord's obligations under this Lease. Notwithstanding any contrary provision herein, neither Landlord nor the Landlord Parties shall be liable under any circumstances for injury or damage to, or interference with, Tenant's business, including but not limited to, loss of profits, loss of rents or other revenues, loss of business opportunity, loss of goodwill or loss of use, in each case, however occurring, or loss to inventory, scientific research, scientific experiments, laboratory animals, products, specimens, samples, and/or scientific, business, accounting and other records of every kind and description kept at the premises and any and all income derived or derivable therefrom.

29.14 **Entire Agreement**. It is understood and acknowledged that there are no oral agreements between the parties hereto affecting this Lease and this Lease constitutes the parties' entire agreement with respect to the leasing of the Premises and supersedes and cancels any and all previous negotiations, arrangements, brochures, agreements and understandings, if any, between the parties hereto or displayed by Landlord to Tenant with respect to the subject matter thereof, and none thereof shall be used to interpret or construe this Lease. None of the terms, covenants, conditions or provisions of this Lease can be modified, deleted or added to except in writing signed by the parties hereto.

29.15 **Right to Lease**. Landlord reserves the absolute right to effect such other tenancies in the Project as Landlord in the exercise of its sole business judgment shall determine to best promote the interests of the Building or Project. Tenant does not rely on the fact, nor does Landlord represent, that any specific tenant or type or number of tenants shall, during the Lease Term, occupy any space in the Building or Project.

29.16 **Force Majeure**. Any prevention, delay or stoppage due to strikes, lockouts, labor disputes, acts of God, acts of war, terrorist acts, inability to obtain services, labor, or materials or reasonable substitutes therefor, governmental actions, civil commotions, fire or other casualty, and other causes beyond the reasonable control of the party obligated to perform, except with respect to the obligations imposed with regard to Rent and other charges to be paid by Tenant pursuant to this Lease (collectively, a "**Force Majeure**"), notwithstanding anything to the contrary contained in this Lease, shall excuse the performance of such party for a period equal to any such prevention, delay or stoppage and, therefore, if this Lease specifies a time period for performance of an obligation of either party, that time period shall be extended by the period of any delay in such party's performance caused by a Force Majeure, provided, however, the foregoing delays shall not apply to Tenant's termination rights hereunder.

29.17 **Intentionally Omitted**.

29.18 **Notices**. All notices, demands, statements, designations, approvals or other communications (collectively, "**Notices**") given or required to be given by either party to the other hereunder or by law shall be in writing, shall be (A) sent by United States certified or registered mail, postage prepaid, return receipt requested ("**Mail**"), (B) delivered by a nationally recognized overnight courier, or (C) delivered personally. Any Notice shall be sent, transmitted, or delivered, as the case may be, to Tenant at the appropriate address set forth in Section 10 of the Summary, or to such other place as Tenant may from time to time designate in a Notice to Landlord, or to Landlord at the addresses set forth below, or to such other places as Landlord may from time to time designate in a Notice to Tenant. Any Notice will be deemed given (i) three (3) business days after the date it is posted if sent by Mail, (ii) the date the overnight courier delivery is made, or (iii) the date personal delivery is made. As of the date of this Lease, any Notices to Landlord must be sent, transmitted, or delivered, as the case may be, to the following addresses:

HCP, Inc.
1920 Main Street, Suite 1200
Irvine, CA 92614
Attention: Legal Department

with a copy to:

HCP Life Science Estates
950 Tower Lane, Suite 1650
Foster City, CA 94404
Attention: Jonathan M. Bergschneider

and

Allen Matkins Leck Gamble Mallory & Natsis LLP
1901 Avenue of the Stars, Suite 1800
Los Angeles, California 90067
Attention: Anton N. Natsis, Esq.

29.19 **Joint and Several**. If there is more than one tenant, the obligations imposed upon Tenant under this Lease shall be joint and several.

29.20 **Authority**. If Tenant is a corporation, trust or partnership, Tenant hereby represents and warrants that Tenant is a duly formed and existing entity qualified to do business in the State of California and that Tenant has full right and authority to execute and deliver this Lease and that each person signing on behalf of Tenant is authorized to do so.

29.21 **Attorneys' Fees**. In the event that either Landlord or Tenant should bring suit for the possession of the Premises, for the recovery of any sum due under this Lease, or because of the breach of any provision of this Lease or for any other relief against the other, then all costs and expenses, including reasonable attorneys' fees, incurred by the prevailing party therein shall be paid by the other party, which obligation on the part of the other party shall be deemed to have accrued on the date of the commencement of such action and shall be enforceable whether or not the action is prosecuted to judgment.

29.22 **Governing Law; WAIVER OF TRIAL BY JURY**. This Lease shall be construed and enforced in accordance with the laws of the State of California. IN ANY ACTION OR PROCEEDING ARISING HEREFROM, LANDLORD AND TENANT HEREBY CONSENT TO (I) THE JURISDICTION OF ANY COMPETENT COURT WITHIN THE STATE OF CALIFORNIA, (II) SERVICE OF PROCESS BY ANY MEANS AUTHORIZED BY CALIFORNIA LAW, AND (III) IN THE INTEREST OF SAVING TIME AND EXPENSE, TRIAL WITHOUT A JURY IN ANY ACTION, PROCEEDING OR COUNTERCLAIM BROUGHT BY EITHER OF THE PARTIES HERETO AGAINST THE OTHER OR THEIR SUCCESSORS IN RESPECT OF ANY MATTER ARISING OUT OF OR IN CONNECTION WITH THIS LEASE, THE RELATIONSHIP OF LANDLORD AND TENANT, TENANT'S USE OR OCCUPANCY OF THE PREMISES, AND/OR ANY CLAIM FOR INJURY OR DAMAGE, OR ANY EMERGENCY OR STATUTORY REMEDY. IN THE EVENT LANDLORD COMMENCES ANY SUMMARY PROCEEDINGS OR ACTION FOR NONPAYMENT OF BASE RENT OR ADDITIONAL RENT, TENANT SHALL NOT INTERPOSE ANY COUNTERCLAIM OF ANY NATURE OR DESCRIPTION (UNLESS SUCH COUNTERCLAIM SHALL BE MANDATORY) IN ANY SUCH PROCEEDING OR ACTION, BUT SHALL BE RELEGATED TO AN INDEPENDENT ACTION AT LAW.

29.23 **Submission of Lease**. Submission of this instrument for examination or signature by Tenant does not constitute a reservation of, option for or option to lease, and it is not effective as a lease or otherwise until execution and delivery by both Landlord and Tenant.

29.24 **Brokers**. Landlord and Tenant hereby warrant to each other that they have had no dealings with any real estate broker or agent in connection with the negotiation of this Lease, excepting only the real estate brokers or agents specified in Section 12 of the Summary (the "**Brokers**"), and that they know of no other real estate broker or agent who is entitled to a commission in connection with this Lease. Each party agrees to indemnify and defend the other party against and hold the other party harmless from any and all claims, demands, losses, liabilities, lawsuits, judgments, costs and expenses (including without limitation reasonable attorneys' fees) with respect to any leasing commission or equivalent compensation alleged to be owing on account of any dealings with any real estate broker or agent, other than the Brokers, occurring by, through, or under the indemnifying party. The terms of this Section 29.24 shall survive the expiration or earlier termination of the Lease Term.

29.25 **Independent Covenants**. This Lease shall be construed as though the covenants herein between Landlord and Tenant are independent and not dependent and Tenant hereby expressly waives the benefit of any statute to the contrary and agrees that if Landlord fails to perform its obligations set forth herein, Tenant shall not be entitled to make any repairs or perform any acts hereunder at Landlord's expense or to any setoff of the Rent or other amounts owing hereunder against Landlord.

29.26 **Project or Building Name, Address and Signage**. Landlord shall have the right at any time to change the name and/or address of the Project or Building (and Landlord shall reimburse Tenant its actual, reasonable costs incurred as a result of such change, if any) and, subject to Section 23.1, to install, affix and maintain any and all signs on the exterior and on the interior of the Project or Building as Landlord may, in Landlord's sole discretion, desire. Tenant shall not use the name of the Project or Building or use pictures or illustrations of the Project or Building in advertising or other publicity or for any purpose other than as the address of the business to be conducted by Tenant in the Premises, without the prior written consent of Landlord.

29.27 **Counterparts**. This Lease may be executed in counterparts with the same effect as if both parties hereto had executed the same document. Both counterparts shall be construed together and shall constitute a single lease.

29.28 **Good Faith**. Except (i) for matters for which there is a standard of consent or discretion specifically set forth in this Lease; (ii) matters which could have an adverse effect on the Building Structure or the Building Systems, or which could affect the exterior appearance of the Building, or (iii) matters covered by Article 4 (Additional Rent), or Article 19 (Defaults; Remedies) of this Lease (collectively, the "**Excepted Matters**"), any time the consent of Landlord or Tenant is required, such consent shall not be unreasonably withheld or delayed, and, except with regard to the Excepted Matters, whenever this Lease grants Landlord or Tenant the right to take action, exercise discretion, establish rules and regulations or make an allocation or other determination, Landlord and Tenant shall act reasonably and in good faith.

29.29 **Development of the Project**.

29.29.1 **Subdivision**. Landlord reserves the right to subdivide all or a portion of the buildings and Common Areas, so long as the same does not interfere with Tenant's use of or access to the Premises or Tenant's parking rights. Tenant agrees to execute and deliver, upon demand by Landlord and in the form requested by Landlord, any additional documents needed to conform this Lease to the circumstances resulting from a subdivision and any all maps in connection therewith, so long as the same does not increase Tenant's obligations or decrease Tenant's rights under this Lease. Notwithstanding anything to the contrary set forth in this Lease, the separate ownership of any buildings and/or Common Areas by an entity other than Landlord shall not affect the calculation of Direct Expenses or Tenant's payment of Tenant's Share of Direct Expenses.

29.29.2 **Construction of Property and Other Improvements**. Tenant acknowledges that portions of the Project may be under construction following Tenant's occupancy of the Premises, and that such construction may result in levels of noise, dust, obstruction of access, etc. which are in excess of that present in a fully constructed project. Tenant hereby waives any and all rent offsets or claims of constructive eviction which may arise in connection with such construction, so long as the same does not interfere with Tenant's use of or access to the Premises or Tenant's parking rights.

29.30 **No Violation**. Tenant hereby warrants and represents that neither its execution of nor performance under this Lease shall cause Tenant to be in violation of any agreement, instrument, contract, law, rule or regulation by which Tenant is bound, and Tenant shall protect, defend, indemnify and hold Landlord harmless against any claims, demands, losses, damages, liabilities, costs and expenses, including, without limitation, reasonable attorneys' fees and costs, arising from Tenant's breach of this warranty and representation.

29.31 **Transportation Management**. Tenant shall fully comply with all present or future programs intended to manage parking, transportation or traffic in and around the Project and/or the Building, and in connection therewith, Tenant shall take responsible action for the transportation planning and management of all employees located at the Premises by working directly with Landlord, any governmental transportation management organization or any other transportation-related committees or entities. Such programs may include, without limitation: (i) restrictions on the number of peak-hour vehicle trips generated by Tenant; (ii) increased vehicle occupancy; (iii) implementation of an in-house ridesharing program and an employee transportation coordinator; (iv) working with employees and any Project, Building or area-wide ridesharing program manager; (v) instituting employer-sponsored incentives (financial or in-kind) to encourage employees to rideshare; and (vi) utilizing flexible work shifts for employees.

IN WITNESS WHEREOF, Landlord and Tenant have caused this Lease to be executed the day and date first above written.

LANDLORD:

HCP OYSTER POINT III LLC,
a Delaware limited liability company

By: /s/Jonathan M. Bergschneider
Jonathan M. Bergschneider
Executive Vice President

TENANT

DENALI THERAPEUTICS INC.,
a Delaware corporation

By: /s/Ryan Watts
Name: Ryan Watts
Its: CEO

By: _____
Name: _____
Its: _____

EXHIBIT A

OUTLINE OF PREMISES; PROJECT SITE PLAN

EXHIBIT B

TENANT WORK LETTER

1. Defined Terms. As used in this Tenant Work Letter, the following capitalized terms have the following meanings:

(a) **Approved TI Plans**: Plans and specifications prepared by the applicable Architect for the Tenant Improvements and approved by Landlord and Tenant in accordance with Paragraph 2 of this Tenant Work Letter, subject to further modification from time to time to the extent provided in and in accordance with such Paragraph 2.

(b) **Architect**: DGA, or any other architect selected and engaged by Landlord and approved by Tenant in their reasonable discretion, with respect to any Tenant Improvements which Landlord is to cause to be constructed pursuant to this Tenant Work Letter.

(c) **Tenant Change Request**: See definition in Paragraph 2(c)(ii) hereof.

(d) **Final TI Working Drawings**: See definition in Paragraph 2(a) hereof.

(e) **General Contractor**: Hathaway Dinwiddie, Landmark Builders or another general contractor reasonably selected by Landlord and in any case approved by Tenant as a result of competitive bidding of the cost of the Tenant Improvements with respect to Landlord's TI Work. Tenant shall have no right to direct or control such General Contractor.

(f) **Landlord's TI Work**: Any Tenant Improvements which Landlord is to construct or install pursuant to this Tenant Work Letter or by mutual agreement of Landlord and Tenant from time to time.

(g) **Project Manager**. Project Management Advisors, Inc., or any other project manager designated by Landlord in its reasonable discretion from time to time to act in a supervisory, oversight, project management or other similar capacity on behalf of Landlord in connection with the design and/or construction of the Tenant Improvements.

(h) **Punch List Work**: Minor corrections of construction or decoration details, and minor mechanical adjustments, that are required in order to cause any applicable portion of the Tenant Improvements as constructed to conform to the Approved TI Plans in all material respects and that do not materially interfere with Tenant's use or occupancy of the Building and the Premises.

(i) **Substantial Completion Certificate**: See definition in Paragraph 3(a) hereof.

(j) **Tenant Delay**: Any of the following types of delay in the completion of construction of Landlord's TI Work (but in each instance, only to the extent that any of the following has actually and proximately caused substantial completion of Landlord's TI Work to be delayed):

(i) Any delay resulting from Tenant's failure to furnish, in a timely manner, information reasonably requested by Landlord or by Landlord's Project Manager in connection with the design or construction of Landlord's TI Work, or from Tenant's failure to approve in a timely manner any matters requiring approval by Tenant;

(ii) Any delay resulting from Tenant Change Requests initiated by Tenant, including any delay resulting from the need to revise any drawings or obtain further governmental approvals as a result of any such Tenant Change Request;

(iii) Any delay caused by Tenant (or Tenant's contractors, agents or employees) materially interfering with the performance of Landlord's TI Work, provided that Landlord shall have given Tenant prompt notice of such material interference and, before the first time a Tenant Delay is deemed to have occurred as a result of such delay, such interference has continued for more than twenty-four (24) hours after Tenant's receipt of such notice.

(k) **Tenant Improvements**: The improvements to or within the Building shown on the Approved TI Plans from time to time and to be constructed by Landlord pursuant to the Lease and this Tenant Work Letter. The term "Tenant Improvements" does not include the improvements existing in the Building and Premises at the date of execution of the Lease.

(l) **Unavoidable Delays**: Delays due to acts of God, acts of public agencies, labor disputes, strikes, fires, freight embargoes, inability (despite the exercise of due diligence) to obtain supplies, materials, fuels or permits, or other causes or contingencies (excluding financial inability) beyond the reasonable control of Landlord or Tenant, as applicable. Landlord shall use commercially reasonable efforts to provide Tenant with prompt notice of any Unavoidable Delays.

(m) Capitalized terms not otherwise defined in this Tenant Work Letter shall have the definitions set forth in the Lease.

2. **Plans and Construction**. Landlord and Tenant shall comply with the procedures set forth in this Paragraph 2 in preparing, delivering and approving matters relating to the Tenant Improvements.

(a) Approved Plans and Working Drawings for Tenant Improvements. Tenant shall promptly and diligently work with the Architect to cause to be prepared and delivered to Landlord for approval (which approval shall not be unreasonably withheld, conditioned or delayed by Landlord) proposed schematic plans and outline specifications for the Tenant Improvements. Following mutual approval of such proposed schematic plans and outline specifications by Landlord and by Tenant (as so approved, the "**Approved Schematic Plans**"), Tenant shall then work with the Architect to cause to be prepared, promptly and diligently (assuming timely delivery by Landlord of any information and decisions required to be furnished or made by Landlord in order to permit preparation of final working drawings, all of which information and decisions Landlord will deliver promptly and with reasonable diligence), and delivered to Landlord for approval (which approval shall not be unreasonably withheld, conditioned or delayed by Landlord) final detailed working drawings and specifications for the Tenant Improvements, including (without limitation) any applicable life safety, mechanical, electrical and plumbing working drawings and final architectural drawings (collectively, "**Final TI Working Drawings**"), which Final TI Working Drawings shall substantially conform to the Approved Schematic Plans. Upon receipt from Tenant of proposed schematic plans and outline specifications, proposed Final TI Working Drawings, any other plans and specifications, or any revisions or resubmittals of any of the foregoing, as applicable, Landlord shall promptly and diligently (and in all events within 10 business days after receipt in the case of an initial submittal of schematic plans and outline specifications or proposed Final TI Working Drawings, and within 7 business days after receipt in the case of any other plans and specifications or any revisions or resubmittals of any of the foregoing) either approve such proposed schematic plans and outline specifications or proposed Final TI Working Drawings, as applicable, or set forth in writing with particularity any changes necessary to bring the aspects of such proposed schematic plans and outline specifications or proposed Final TI Working Drawings into a form which will be reasonably acceptable to Landlord. Upon approval of the Final TI Working Drawings by Landlord and Tenant, the Final TI Working Drawings shall constitute the **"Approved TI Plans,"** superseding (to the extent of any inconsistencies) any inconsistent features of the previously existing Approved Schematic Plans. Tenant shall respond to any request for information or approval of plans or drawings from Landlord or Architect within five (5) business days. Tenant acknowledges that the Tenant Improvements will include the items set forth on Schedule 2 to this Exhibit B, in order to allow the Premises to achieve a LEED "Silver" certification level.

(b) Cost of Improvements. "**Cost of Improvement**" shall mean, with respect to any item or component for which a cost must be determined in order to allocate such cost, or an increase in such cost, to Tenant pursuant to this Tenant Work Letter, the sum of the following (unless otherwise agreed in writing by Landlord and Tenant with respect to any specific item or component or any category of items or components): (i) all sums paid to contractors or subcontractors for labor and materials furnished in connection with construction of such item or

component; (ii) all costs, expenses, payments, fees and charges (other than penalties) paid to or at the direction of any city, county or other governmental or quasi-governmental authority or agency which are required to be paid in order to obtain all necessary governmental permits, licenses, inspections and approvals relating to construction of such item or component; (iii) engineering and architectural fees for services rendered in connection with the design and construction of such item or component (including, but not limited to, the Architect for such item or component and an electrical engineer, mechanical engineer, structural engineer and civil engineer, if applicable); (iv) sales and use taxes; (v) testing and inspection costs; (vi) the cost of power, water and other utility facilities and the cost of collection and removal of debris required in connection with construction of such item or component; (vii) costs for builder's risk insurance; and (viii) all other "hard" and "soft" costs incurred in the construction of such item or component in accordance with the Approved TI Plans (if applicable) and this Tenant Work Letter; provided that the Cost of Improvements shall not include any internal or third-party costs incurred by Landlord except as provided in Section 2(e).

(c) **Construction of Landlord's TI Work**. Following completion of the Approved TI Plans, Landlord shall apply for and use reasonable efforts to obtain the necessary permits and approvals to allow construction of all Tenant Improvements. Upon receipt of such permits and approvals, Landlord shall, at Tenant's expense (subject to Landlord's payment of the Tenant Improvement Allowance), construct and complete the Tenant Improvements substantially in accordance with the Approved TI Plans, subject to Unavoidable Delays and Tenant Delays (if any). Such construction of the Tenant Improvements and Landlord's Work shall be performed in a neat, good and workmanlike manner, free of defects, using new materials and equipment of good quality, and shall materially conform to all applicable laws, rules, regulations, codes, ordinances, requirements, covenants, conditions and restrictions applicable thereto in force at the time such work is completed. Landlord shall cause Hathaway Dinwiddie, Landmark Builders and any other potential general contractors to bid for construction of the Tenant Improvements. All bids will be opened together with Landlord selecting the general contractor to construct the Tenant Improvements, subject to the reasonable approval of Tenant. Tenant shall also have the right to approve all subcontractors engaged by the General Contractor.

(d) **Changes**.

(i) If Landlord determines at any time that changes in the Final TI Working Drawings or in any other aspect of the Approved TI Plans relating to any item of Landlord's TI Work are required as a result of applicable law or governmental requirements, or are required at the insistence of any other third party whose approval may be required with respect to the Tenant Improvements, or are required as a result of unanticipated conditions encountered in the course of construction, then Landlord shall promptly (A) advise Tenant of such circumstances and (B) at Tenant's sole cost and expense, subject to Landlord's payment of the Tenant Improvement Allowance, cause revised Final TI Working Drawings to be prepared by the Architect and submitted to Tenant, for Tenant's approval, which shall not be unreasonably withheld. Failure of Tenant to deliver to Landlord written notice of disapproval and specification of such required changes on or before any deadline reasonably specified by Landlord (which shall not be less than three (3) business days after delivery thereof to Tenant) shall constitute and be deemed to be a Tenant Delay to the extent Landlord is delayed in completing Landlord's TI Work.

(ii) If Tenant at any time desires any changes, alterations or additions to the Final TI Working Drawings, Tenant shall submit a detailed written request to Landlord specifying such changes, alterations or additions (a "**Tenant Change Request**"). Upon receipt of any such request, Landlord shall promptly notify Tenant of (A) whether the matters proposed in the Tenant Change Request are approved by Landlord (which approval shall not be unreasonably withheld, conditioned or delayed by Landlord), (B) Landlord's estimate of the number of days of delay, if any, which shall be caused in the construction of the Tenant Improvements by such Tenant Change Request if implemented (including, without limitation, delays due to the need to obtain any revised plans or drawings and any governmental approvals), and (C) Landlord's estimate of the increase, if any, which shall occur in the cost of design, permitting, project management and construction of the Tenant Improvements affected by such Tenant Change Request if such Tenant Change Request is implemented (including, but not limited to, any costs of compliance with laws or governmental regulations that become applicable because of the implementation of the Tenant Change Request). If Landlord approves the Tenant Change Request and Tenant notifies Landlord in writing, within three (3) business days after receipt of such notice from Landlord, of Tenant's approval of the Tenant Change Request

(including the estimated delays and cost increases, if any, described in Landlord's notice), then Landlord shall cause such Tenant Change Request to be implemented and Tenant shall be responsible for all actual costs or cost increases resulting from or attributable to the implementation of the Tenant Change Request, and any delays resulting therefrom shall be deemed to be a Tenant Delay (subject to Landlord's payment of the Tenant Improvement Allowance). If Tenant fails to notify Landlord in writing of Tenant's approval of such Tenant Change Request within said three (3) business day period, then such Tenant Change Request shall be deemed to be withdrawn and shall be of no further effect.

(e) **Project Management**. Unless and until revoked by Landlord by written notice delivered to Tenant, Landlord hereby (i) delegates to Project Manager the authority to exercise all approval rights, supervisory rights and other rights or powers of Landlord under this Tenant Work Letter with respect to the design and construction of the Tenant Improvements, and (ii) requests that Tenant work with Project Manager with respect to any logistical or other coordination matters arising in the course of construction of the Tenant Improvements, including monitoring Tenant's compliance with its obligations under this Tenant Work Letter and under the Lease with respect to the design and construction of the Tenant Improvements. Tenant acknowledges the foregoing delegation and request, and agrees to cooperate reasonably with Project Manager as Landlord's representative pursuant to such delegation and request. Fees and charges of Project Manager for such services shall be at Tenant's sole expense, subject to Landlord's payment of the Tenant Improvement Allowance. Such fees shall be equal to $3.71 per RSF of the Premises (provided that in the event Tenant elects to utilize all or any portion of the Additional TI Allowance pursuant to the terms of Section 4(b) below, such fees to the Project Manager shall increase by an amount equal to the product of (A) 2.56% and (B) the amount of the Additional TI Allowance which Tenant elects to utilize).

3. **Completion**.

(a) When Landlord receives written certification from Architect that construction of the Tenant Improvements and Landlord's Work has been completed in accordance with the Approved TI Plans and Section 3(e) below (except for Punch List Work), Landlord shall prepare and deliver to Tenant a certificate signed by Landlord, Architect and General Contractor (the "**Substantial Completion Certificate**") (i) certifying that the construction of the Tenant Improvements and Landlord's Work has been substantially completed in a good and workmanlike manner in accordance with the Approved TI Plans and Section 3(e) below in all material respects, subject only to completion of Punch List Work, and specifying the date of that completion, and (ii) certifying that the Tenant Improvements and Landlord's Work comply in all material respects with all laws, rules, regulations, codes, ordinances, requirements, covenants, conditions and restrictions applicable thereto at the time of such delivery. Upon receipt by Tenant of the Substantial Completion Certificate and tender of possession of the Premises by Landlord to Tenant, and receipt of any certificate of occupancy or its legal equivalent, or other required sign-offs from any applicable governmental authority, allowing the legal occupancy of the Premises, the Tenant Improvements will be deemed delivered to Tenant and "Ready for Occupancy" for all purposes of the Lease (subject to Landlord's continuing obligations with respect to any Punch List Work, and to any other express obligations of Landlord under the Lease or this Tenant Work Letter with respect to such Tenant Improvements).

(b) Immediately prior to delivery of the Substantial Completion Certificate for the Tenant Improvements and Landlord's Work, Project Manager or other representatives of Landlord shall conduct one or more "walkthroughs" of the Building with Tenant and Tenant's representatives, to identify any items of Punch List Work that may require correction and to prepare a joint punch list reflecting any such items, following which Landlord shall diligently complete the Punch List Work reflected in such joint punch list. The Punch List Work shall be attached to the Substantial Completion Certificate, and shall not include damage caused by Tenant or any of Tenant's agents in connection with any work performed by Tenant in the Premises, or required as a result of Tenant's move-in to the Premises. At any time within thirty (30) days after delivery of such Substantial Completion Certificate, Tenant shall be entitled to submit one or more lists to Landlord supplementing such joint punch list by specifying any additional items of Punch List Work to be performed on the applicable Tenant Improvements and Landlord's Work, and upon receipt of such list(s), Landlord shall diligently complete such additional Punch List Work. Promptly after Landlord provides Tenant with the Substantial Completion Certificate and completes all applicable Punch List Work for the Building, Landlord shall cause the recordation of a Notice of Completion (as defined in the California Civil Code) with respect to the Tenant Improvements.

(c) All construction, product and equipment warranties and guaranties obtained by Landlord with respect to the Tenant Improvements and Landlord's Work in the Premises shall, to the extent reasonably obtainable, include a provision that such warranties and guaranties shall also run to the benefit of Tenant, and Landlord shall cooperate with Tenant in a commercially reasonable manner to assist in enforcing all such warranties and guaranties for the benefit of Tenant.

(d) Notwithstanding any other provisions of this Tenant Work Letter or of the Lease, if Landlord is delayed in substantially completing any of the Tenant Improvements as a result of any Tenant Delay, and if the Lease Commencement Date is being determined under clause (i) of Section 3.2 of the Lease Summary, then notwithstanding any other provision of the Lease to the contrary, the Premises shall be deemed to have been Ready for Occupancy on the date the Premises would have been Ready for Occupancy absent such Tenant Delay.

(e) Notwithstanding any other provisions of this Tenant Work Letter or of the Lease, Landlord shall be responsible, at Landlord's sole cost and expense, and without deduction from the Tenant Improvement Allowance, to construct and deliver the Base Building and "Warm Shell" components of the Premises ("**Landlord's Work**"), which shall consist of the items set forth on Schedule 1 to this Exhibit B (the "**Warm Shell Schedule**").

(f) **Construction of Additional Base Building Items**. To the extent that the Final TI Working Drawings contain any structural items, or items which would not reasonably categorized as "normal tenant improvements" under applicable GAAP standards (the "**Additional Base Building Items**"), then such Additional Base Building Items shall not be constructed as a part of the Landlord's TI Work or the Tenant Improvements, but instead will be constructed by Landlord as a part of the Landlord's Work. The cost of construction of the Additional Base Building Items (the "**Additional Base Building Costs**") shall be borne by Landlord, provided that the amount of the Tenant Improvement Allowance shall be reduced by the amount of the Additional Base Building Costs. Landlord shall have the right to disapprove any aspect of the Final TI Working Drawing that would result in Additional Base Building Costs in excess of the then remaining Tenant Improvement Allowance, so that, while the Tenant Improvement Allowance may be reduced, under no circumstances would Tenant be required to pay for any Additional Base Building Items with its own funds.

4. **Payment of Costs**.

(a) **Tenant Improvement Allowance**. Subject to any restrictions, conditions or limitations expressly set forth in this Tenant Work Letter or in the Lease or as otherwise expressly provided by mutual written agreement of Landlord and Tenant, the cost of construction of the Tenant Improvements shall be paid or reimbursed by Landlord up to a maximum amount equal to $145 per RSF of the Premises (i.e. $5,525,805.00 (the "**Tenant Improvement Allowance**"), which amount is being made available by Landlord to be applied towards the Cost of Improvements for the construction of the Tenant Improvements in the Premises. Tenant shall be responsible, at its sole cost and expense, for payment of the entire Cost of Improvements of the Tenant Improvements in excess of the Tenant Improvement Allowance, including (but not limited to) any costs or cost increases incurred as a result of delays (unless caused by Landlord), governmental requirements or unanticipated conditions (unless caused by Landlord), and for payment of any and all costs and expenses relating to any alterations, additions, improvements, furniture, furnishings, equipment, fixtures and personal property items which are not eligible for application of Tenant Improvement Allowance funds under the restrictions expressly set forth below in this paragraph, but Tenant shall be entitled to use or apply the entire Tenant Improvement Allowance toward the Cost of Improvements of the Tenant Improvements (subject to any applicable restrictions, conditions, limitations, reductions or charges set forth in the Lease or in this Tenant Work Letter) prior to being required to expend any of Tenant's own funds for the Tenant Improvements. The funding of the Tenant Improvement Allowance shall be made on a monthly basis or at other convenient intervals mutually approved by Landlord and Tenant and in all other respects shall be based on such commercially reasonable disbursement conditions and procedures as Landlord, Project Manager and Landlord's lender (if any) may reasonably prescribe. Notwithstanding the foregoing provisions, under no circumstances shall the Tenant Improvement Allowance or any portion thereof be used or useable by Tenant for any moving or relocation expenses of Tenant, or for any Cost of Improvement (or any other cost or expense) associated with any

moveable furniture or trade fixtures, personal property or any other item or element which, under the applicable provisions of the Lease, will not become Landlord's property and remain with the Building upon expiration or termination of the Lease. Notwithstanding anything to the contrary herein, the Tenant Improvements shall not include (and Landlord shall be solely responsible for and the Tenant Improvement Allowance shall not be used for) the following: (a) costs incurred due to the presence of any Hazardous Materials in the Premises, if any, but with respect to removal and remediation of any such Hazardous Materials, only to the extent such removal or remediation is required by Applicable Laws enforced as of the date of this Lease for improvements in the Premises generally (as opposed to the specific Tenant Improvements) and to the extent the same required in order to allow Tenant to obtain a certificate of occupancy or its legal equivalent, for the Premises for the Permitted Use assuming a normal and customary office occupancy density; (b) costs to bring the Project into compliance with Applicable Laws to the extent required in order to allow Tenant to obtain a certificate of occupancy or its legal equivalent, for the Premises for the Permitted Use assuming a normal and customary office occupancy density; (c) construction costs in excess of the final contract amount in the contract with the General Contractor, as approved by Tenant (not to be unreasonably withheld), except for increases set forth in approved change orders; and (d) wages, labor and overhead for overtime and premium time unless approved by Tenant (which approval shall not be unreasonably withheld, conditioned or delayed);.

(b) **Additional TI Allowance**. In addition to the Tenant Improvement Allowance, Tenant shall have the right, by written notice to Landlord given on or before December 31, 2017, to use up to $50.00 per RSF of the Premises (i.e., up to $1,905,450.00) (the "**Additional TI Allowance**") towards the payment of the costs of the Tenant Improvement Allowance Items. In the event Tenant exercises its right to use all or any portion of the Additional TI Allowance, Tenant shall be required to pay Landlord, commencing on the date the Tenant Improvements are completed (the "**Additional Payment Commencement Date**"), the "Additional TI Allowance Payment," as that term is defined below, in consideration of Landlord provision of the Additional TI Allowance. The "**Additional TI Allowance Payment**" shall be determined as the missing component of an annuity, which annuity shall have (i) the amount of the Additional TI Allowance utilized by Tenant as the present value amount, (ii) a number equal to the number of full calendar months then remaining in the Lease Term as the number of payments, (iii) a monthly interest factor equal to (A) with respect to the first $25.00 per RSF of the Additional TI Allowance used by Tenant, seventy-five one-hundredths percent (0.75%), which is equal to nine percent (9%) divided by twelve (12) months per year, and (B) with respect to any amount the Additional TI Allowance used by Tenant in excess of $25.00 per RSF of the Premises (i.e., in excess of $952,725.00), 0.9167%, which is equal to eleven percent (11%) divided by twelve (12) months per year, and (iv) the Additional TI Allowance Payment as the missing component of the annuity. Following the calculation of the Additional TI Allowance Payment, Landlord and Tenant will enter into a lease amendment in the form of **Exhibit G** attached hereto, to confirm the amount thereof.

5. **No Agency**. Nothing contained in this Tenant Work Letter shall make or constitute Tenant as the agent of Landlord.

6. **Tenant Access**. Provided that Tenant and its agents do not interfere with Contactor's work in the Building and the Premises (including by the use of non-union vendors without prior coordination with Landlord), Contractor shall allow Tenant access to the Premises at least thirty (30) days prior to the Substantial Completion of the Landlord's TI Work without payment of Rent for the purpose of Tenant installing equipment or fixtures (including Tenant's data and telephone equipment) in the Premises and preparing the Premises for occupancy. Prior to Tenant's entry into the Premises as permitted by the terms of this Section 6, Tenant shall submit a schedule to Landlord and Contractor, for their approval, which schedule shall detail the timing and purpose of Tenant's entry. Tenant shall hold Landlord harmless from and indemnify, protect and defend Landlord against any loss or damage to the Building or Premises and against injury to any persons caused by Tenant's actions pursuant to this Section 6.

7. **Miscellaneous**. All references in this Tenant Work Letter to a number of days shall be construed to refer to calendar days, unless otherwise specified herein. In all instances where Landlord's or Tenant's approval is required, if no written notice of disapproval is given within the applicable time period, at the end of that period Landlord or Tenant shall be deemed to have given approval (unless the provision requiring Landlord's or Tenant's approval expressly states that non-response is deemed to be a disapproval or withdrawal of the pending action or request, in which event such express statement shall be controlling over the general statement set forth in this sentence) and the next succeeding time period shall commence. If any item requiring approval is disapproved by Landlord or Tenant (as applicable) in a timely manner, the procedure for preparation of that item and approval shall be repeated. Landlord hereby acknowledges that Tenant shall not be required to restore the initial Tenant Improvements constructed in the Premises pursuant to the terms of this Tenant Work Letter upon the termination of the Lease.

8. **Time Deadlines**. Tenant shall use commercially reasonable, good faith, efforts and all due diligence to cooperate with the Architect, General Contractor and Landlord to complete all phases of the construction drawings set forth in this Tenant Work Letter and the permitting process and to receive the permits as soon as possible after the execution of the. The applicable dates for approval of items, plans and drawings as described in this Tenant Work Letter are set forth and further elaborated upon in Schedule 3 to this Exhibit B attached hereto (the "**Time Deadlines**"), attached hereto. Tenant agrees to utilize commercially reasonable efforts to comply with the Time Deadlines.

9. **Rooftop Space**. Tenant hereby acknowledges that to the extent either (i) any portion of the Tenant Improvements, or (ii) any of Tenant's equipment installed in the Premises, requires a portion of the roof to be utilized by Tenant, that Tenant shall only be permitted to utilize that certain portion of the roof designated as "Zone 1" on Schedule 4 to this Exhibit B (the "**Rooftop Space**").

SCHEDULE 1 TO EXHIBIT B

BASE BUILDING "WARM SHELL" DELIVERY CONDITION

The Cove at Oyster Point
Building 3
151 Oyster Point Boulevard
South San Francisco, CA 94080
Warm-Shell Landlord Delivery Condition

	DESCRIPTION	Landlord	Landlord at Tenant's Expense
SITEWORK			
1.	Exterior hardscape and landscape, including site lighting, perimeter sidewalks, street curbs, miscellaneous site furnishings, and bio-retention basins	X	
2.	Surface parking lot	X	
3.	Electric vehicle charging stations, for allocation amongst Tenants	X	
4.	Exterior amenities space including all hardscape and landscape, lighting, and recreational infrastructure (volleyball/basketball sport court, bocce ball, trellis)	X	
5.	Exterior bike racks	X	
6.	Bus stop wind screens for local commuter shuttle service	X	
7.	Service yard foundation, structure, covered enclosure, and waterproofing for trash containers and dedicated bulk nitrogen storage area for allocation amongst tenants	X	
8.	Foundation and enclosure for Landlord provided diesel powered emergency generator	X	
9.	Loading dock with at-grade shipping/receiving area with (2) hydraulic scissor lifts	X	
STRUCTURE			
1.	Pile supported structural slab-on-grade foundation system consisting of steel-reinforced concrete auger- cast piles, pile caps, and horizontal grade beams	X	
2.	Steel superstructure consisting of steel columns, girders, beams, and concrete slab on composite metal deck, with live load capacity of 125 psf (reducible)	X	
3.	Type II A construction, code required primary structural fireproofing	X	
4.	Slab edge fire safing	X	

DESCRIPTION		Landlord	Landlord at Tenant's Expense
5.	Lateral seismic system utilizing buckling-restrained braced frames. Importance factor is 1.0	X	
6.	Roof deck framing with live load capacity of 20 psf	X	
7.	Mechanical platform and roof penthouse with live load capacity of 75 psf	X	
8.	Roof screen and associated secondary steel	X	
9.	Floor to floor height of 17', all floors	X	
10.	Framed openings for Base Building utility risers	X	
11.	Stairs and stair enclosures per code requirements, including enclosure doors, handrails, and guardrails. Roof penthouse access for (1) set of stairs	X	
12.	Window washing davit bases and arms	X	
13.	Miscellaneous metals items and/or concrete pads for Base Building equipment	X	
ROOFING			
1.	60 MIL single-ply thermoplastic polyolefin (TPO) white roof membrane	X	
2.	Rigid insulation, flashing, and sealants	X	
3.	Roofing penetrations for Base Building equipment/systems	X	
4.	Walkway pads along roof perimeter, outside of screened area	X	
5.	Penthouse roof penetrations – not allowed	N/A	N/A
EXTERIOR			
1.	Non load-bearing glazed aluminum curtain wall and glass fiber reinforced concrete (GFRC) panel building enclosure system	X	
2.	Building entrances and openings	X	
3.	Service Yard overhead door, serving Base Building Electrical Room	X	
4.	Service Yard rolling green screen gate	X	
COMMON AREAS			
1.	Accessible Main Lobby	X	
2.	Main Lobby Computer Room	X	
3.	Interior Service Area corridor	X	
4.	Stair enclosures painted at all building levels	X	
5.	2 hour rated Chemical Storage Area, with depressed slab, for allocation amongst tenants	X	
6.	Electrical Room	X	
7.	Emergency Electrical Room	X	
8.	Domestic Pump Room	X	
9.	Fire Booster Pump Room	X	

DESCRIPTION		Landlord	Landlord at Tenant's Expense
10.	Storage Room for allocation amongst Tenants	X	
11.	Elevator Control Room	X	
12.	Amenities Space including food service, fitness center, and recreational area	X	
13.	Telecommunications Main Point of Entry (MPOE) Room	X	
14.	Service Yard/Loading Dock Area, including space for trash enclosure, nitrogen storage, and generator enclosure	X	
ELEVATORS			
1.	Two (2) passenger elevators; 3,500 lbs., 350 fpm	X	
2.	One (1) freight elevator; 5,000 lbs., 200 fpm	X	
3.	Recessed elevator pits for three (3) elevators	X	
4.	No elevator access to roof	N/A	N/A
TENANT AREAS			
1.	Restroom Cores: one (1) set per floor including Men's and Women's Restrooms with (1) ADA shower each with bench and lockers, ceramic tile floors and wet walls, solid surface countertops, floor mounted metal partitions, hard lid ceiling, down lights and ADA low-flow plumbing fixtures	X	
2.	Janitor Closet – one (1) per floor	X	
3.	Freight elevator lobby consisting of double-door, concrete floor, unfinished drywall and taped walls, no ceiling	X	
4.	Electrical Room – one (1) per floor consisting of concrete floor, unfinished drywall and taped walls, no ceiling.	X	
5.	Intermediate Distribution Frame (IDF) Room – one (1) per floor consisting of concrete floor, unfinished drywall and taped walls, no ceiling	X	
6.	Finishes at common corridors on floors with multiple Tenants	X	
7.	Shaft enclosures for Base Building system risers	X	
FIRE PROTECTION			
1.	Fire booster pump room including fire department connection, alarm valve, and fire sprinkler booster pump	X	
2.	Wet fire protection system (risers, Core area risers, distribution piping, and sprinkler heads)	X	
3.	Stair risers, distribution piping, and sprinkler heads	X	

DESCRIPTION		Landlord	Landlord at Tenant's Expense
4.	Primary distribution and sprinkler heads adequate for "Ordinary Hazard, Group 2"	X	
5.	Fire extinguisher cabinets at core areas	X	
6.	Fire safing at Base Building vertical penetrations, including penetrations for mechanical, electrical, and plumbing systems	X	
PLUMBING			
1.	Building storm and overflow drainage system, including site underground storm sewer system and connection to storm sewer mains	X	
2.	Domestic water service with backflow prevention and Base Building risers to Tenant spaces	X	
3.	Domestic water booster pump	X	
4.	Lab waste risers and stubs in Tenant space	X	
5.	Lab waste sewer connection to sanitary sewer, lab waste sampling port at connection	X	
6.	Building sanitary sewer service with piping distribution to restroom cores and risers stubbed in Tenant space	X	
7.	Domestic sanitary sewer connection to street	X	
8.	Main water meter and irrigation meter	X	
9.	One (1) roof mounted electric water heater serving all Restrooms	X	
10.	Core restroom plumbing fixtures compliant with accessibility requirements	X	
NATURAL GAS			
1.	Natural gas service to Building	X	
2.	Natural gas riser to the roof and service to Base Building boilers	X	
3.	Natural gas riser to the roof capped for future use	X	
HEATING, VENTILATION, AIR CONDITIONING			
1.	(2) 90,000 cfm 100% outside air roof mounted packaged air handlers serving lab areas, for allocation amongst Tenant floors	X	
2.	(2) 50,000 cfm supply/return roof mounted air handlers serving Tenant office areas, for allocation amongst Tenant floors	X	
3.	(3) 4,000 MBH input gas fired hot water boilers	X	
4.	(2) 550 ton centrifugal chillers	X	
5.	(2) 550 ton cooling towers	X	

DESCRIPTION		Landlord	Landlord at Tenant's Expense
6.	Secondary mechanical equipment, including pumps, roof ducting, piping, valves, manifolds, etc. to support Base Building mechanical systems	X	
7.	Hot water pipe risers, stubbed in Tenant space	X	
8.	Reheat coils within core areas	X	
9.	Vertical supply air duct risers	X	
10.	Vertical return air duct risers	X	
11.	Supply air duct distribution, VAV terminals, equipment connections, insulation, air terminals, dampers, hangers, etc. within core areas	X	
12.	Two (2) roof mounted dilution lab exhaust fan systems for allocation amongst Tenant floors	X	
13.	Exhaust air duct distribution, exhaust air valves, equipment connections, insulation, air terminals, dampers, hangers, etc. within core areas	X	
14.	Restroom exhaust for Base Building restrooms	X	
15.	Ventilation system for Base Building Electrical Room	X	
16.	Exhaust fan, side wall grille supply, and fire smoke dampers for ventilation of Base Building Electrical Rooms on each floor	X	
17.	Building Management System (BMS) for core area and Landlord infrastructure	X	
ELECTRICAL			
1.	Site campus medium voltage distribution system with connection to PG&E grid	X	
2.	5000 amp 480/277V Base Building substation with underground primary feeder to campus main switchgear	X	
3.	Standard power bus duct risers providing 400 amps per floor	X	
1.	(1) 1500 kW diesel standby power generator, for allocation amongst Tenants and Base Building systems	X	
2.	Standby power bus duct risers providing 250 amps per floor	X	
3.	Automatic transfer switch for Tenant load	X	
4.	Lighting and power distribution for core areas	X	
5.	Base Building common area life safety emergency lighting/signage	X	
6.	2” conduit riser for future Distributed Antenna System (DAS)	X	
7.	Distributed Antenna System (DAS), if required	X	

DESCRIPTION		Landlord	Landlord at Tenant's Expense
FIRE ALARM			
1.	Base Building fire alarm system with devices in core areas	X	
2.	Fire Alarm Termination Cabinet (FATC) within each Electrical Room	X	
TELEPHONE/DATA			
1.	Underground telephone carrier service to Main Point of Entry (MPOE) Room	X	
2.	Underground local fiber optic provider service to MPOE Room	X	
3.	(2) 4" conduit risers from MPOE to Intermediate Distribution Frame (IDF) Room on each floor	X	
4.	(1) 2" conduit riser from the roof to IDF Room on each floor	X	
5.	Campus telecommunications loop consisting of (2) 4" conduits, linking existing and future buildings on campus	X	
6.	(2) 4" conduits connecting Building 3 MPOE Room with Building 4 MPOE Room	X	
SECURITY			
1.	Card access at Building entries	X	
2.	Manned security station in lobby	X	

SCHEDULE 2 TO EXHIBIT B

LEED REQUIREMENTS

The following is a list of LEED prerequisites and credits that all tenants are required to meet compliance for their associated tenant-occupied spaces beyond the current Core & Shell project scope. By signing this lease, tenants are agreeing to comply with all of the outlined requirements.

- Water Efficiency Prerequisite 1 and Credit 3, Water Use Reduction
  - All toilets in the core or those that are tenant-installed shall be dual-flush toilets or "high-efficiency," using 1.28 gallons per flush (gpf) or less.
  - All urinals shall be waterless or ultra low-flow e.g., 0.125gpf or less.
  - Bathroom faucets are required to have flow restrictors limiting flow to .5 gallons per minute (gpm). Kitchen and breakroom faucets to allow 2.0 gpm.
- Energy and Atmosphere Prerequisite 2, Minimum Energy Performance, and Credit 1, Optimize Energy Performance
  - Envelope must meet the following requirements:
    - Walls: U = 0.082
    - Roof: U = 0.039
    - Curtain Glazing: U = 0.27, SHGC = 0.29 (Viracon)
  - Mechanical (Based on B3) systems must comply with the following:
    - Chiller Efficiency: 0.549 kw/ton
    - Boiler Efficiency: 93%
  - Plumbing (Based on B3) must comply with the following:
    - Water heater efficiency: 96%
  - Lighting requirements are as follows:
    - Office Spaces > 250 ft^2: 0.75 w/sf
    - Office Spaces <= 250 ft^2: 1.0 w/sf
    - Lab Spaces: 1.4 w/sf
- Energy and Atmosphere Credit 4, Enhanced Refrigerant Management
  - Tenants should specify HVAC systems that minimize refrigerant impact by avoiding refrigerants entirely or using systems that reduce their harmful impacts.
  - Tenants should not install or retain fire suppression systems with CFCs, HCFCs, or halons.
- Energy and Atmosphere Credit 5, Measurement & Verification
  - Tenants will be required to submeter
- Indoor Environmental Quality Prerequisite 1, Minimum Indoor Air Quality (IAQ) Performance
  - Tenant-installed mechanical ventilation systems must meet the requirements of ASHRAE 62.1-2007 sections 4-7.
- Indoor Environmental Quality Credit 1, Outdoor Air Delivery Monitoring
  - For mechanical ventilation systems that predominantly serve densely occupied spaces (those with a design occupant density greater than or equal to 25 people per 1000 sq. ft), tenants shall install a CO_2 sensor within each densely occupied space.
  - For all other mechanical ventilation systems, provide an outdoor airflow measurement device capable of measuring the minimum outdoor airflow rate at all expected system operating conditions within 15 percent of the design minimum outdoor air rate.
- Indoor Environmental Quality Credit 5, Indoor Chemical and Pollutant Source Control
  - Walk off mats are installed at all building main entrances as part of the core and shell scope.
  - All rooms that contain chemicals or pollutants (such as copy rooms, photo labs, laundry, and janitorial rooms) must be built with deck-to-deck full-height walls and self-closing doors, separate ventilation systems with minimum .50 cfm/sqft exhaust fans, and containment drains for appropriate disposal of hazardous liquids

- Tenants must also install MERV – 13 filters for all return and outside air intakes in regularly occupied mechanically ventilated spaces

- Indoor Environmental Quality Credit 6, Controllability of Systems - Thermal Comfort
  - Tenants shall provide thermal and ventilation controls for:
    - At least 50 percent of the occupants that enable adjustment to suit individual needs and preferences & all shared multi-occupant spaces where transient groups must share controls.

- Indoor Environmental Quality Credit 7, Thermal Comfort - Design
  - HVAC design must meet requirements of ASHRAE 55-2004, specifically in reference to air temperature, radiant temperature, humidity, and air speed

SCHEDULE 3 TO EXHIBIT B

TIME DEADLINES

THE COVE AT OYSTER POINT
South San Francisco, CA

151 Oyster Point, Second Floor — Denali TI
9/24/2015

Tenant Improvement Milestone Schedule

10/1/2015	TI Design Commencement (12 weeks)
10/16/2015	Tenant Submission of 100% Schematic Design
10/16/2015	Landlord Publication of TI Project Budget Estimate
10/23/2015	Landlord Approval of "Approved Schematic Plans"
11/13/2015	100% Design Development
12/4/2105	General Contractor Publication of 100% DD Estimate
12/11/2015	Tenant Approval of 100% DD Estimate and Scope
1/4/2016	Tenant Submission of 100% Construction Documents
1/4/2016	Landlord Submit for TI Permit (9.5 weeks)
1/11/2016	Landlord Approval of "Final TI Working Drawings"
1/15/2016	Release of long lead items (i.e. casework) — Tenant and Landlord Approval
1/29/2016	General Contractor Publish GMP
2/1/2016	Start TI Construction (26 weeks)
2/5/2016	Tenant Approval of GMP
3/10/2016	Obtain Permit (Anticipated — Dependent on Jurisdiction) — First Inspection
8/1/2016	Substantial Completion — Temporary Certificate of Occupancy (TCO)
8/1/2016	Rent Commencement
9/1/2016	Complete Punchlist/Final Completion

SCHEDULE 4 TO EXHIBIT B

ROOFTOP SPACE

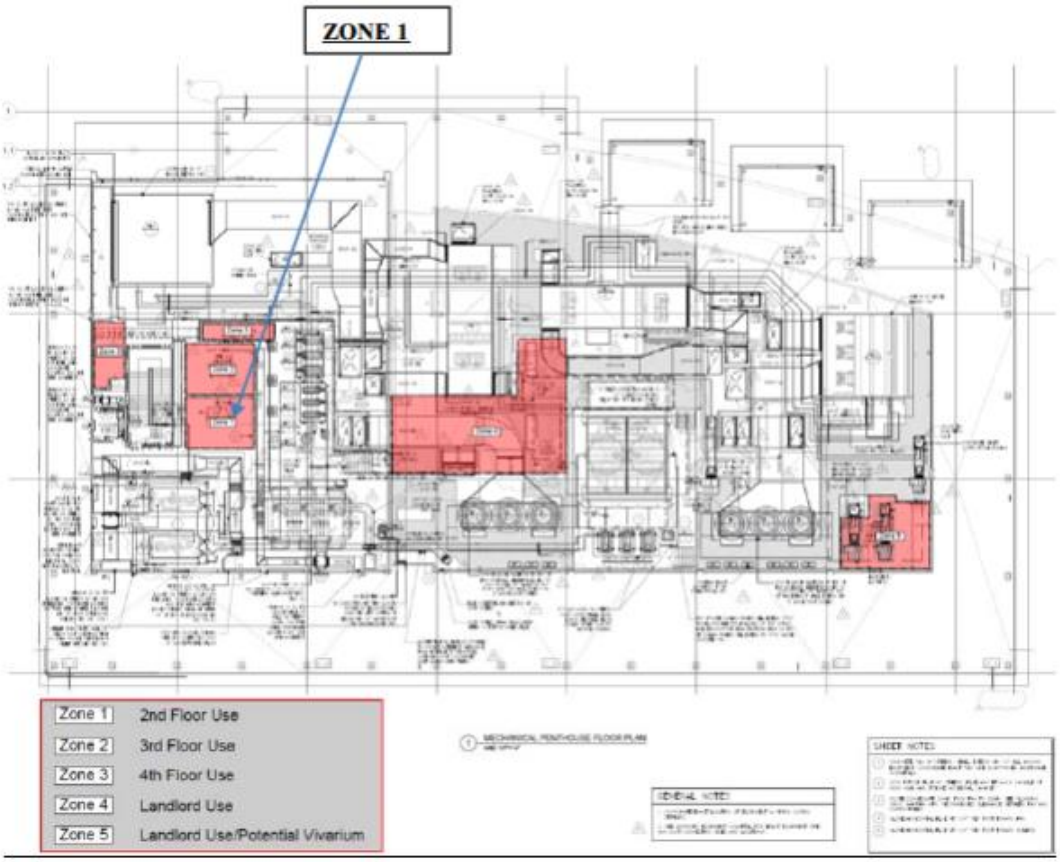

EXHIBIT C

NOTICE OF LEASE TERM DATES

To: _____
_____
_____
_____

Re: Lease dated , 20__ between , a ("**Landlord**"), and , a ("**Tenant**") concerning Suite on floor(s) of the building located at , California.

Gentlemen:

In accordance with the Lease (the "**Lease**"), we wish to advise you and/or confirm as follows:

1. The Lease Term shall commence on or has commenced on for a term of ending on .
2. Rent commenced to accrue on , in the amount of .
3. If the Lease Commencement Date is other than the first day of the month, the first billing will contain a pro rata adjustment. Each billing thereafter, with the exception of the final billing, shall be for the full amount of the monthly installment as provided for in the Lease.
4. Your rent checks should be made payable to at .
5. The number of rentable/usable square feet within the Premises is approximately square feet.
6. Tenant's Share as adjusted based upon the exact number of usable square feet within the Premises is %, subject to Section 6 of the Summary of Basic Lease Information.

"Landlord":

_____

a_____

By: _____

Its: _____

Agreed to and Accepted as
of , 20 .

"Tenant":

_____

a_____

By: _____

Its: _____

EXHIBIT D

FORM OF TENANT'S ESTOPPEL CERTIFICATE

The undersigned as Tenant under that certain Lease (the "**Lease**") made and entered into as of , 20 by and between as Landlord, and the undersigned as Tenant, for Premises consisting of a portion of the building located at , California, certifies as follows:

1. Attached hereto as **Exhibit A** is a true and correct copy of the Lease and all amendments and modifications thereto. The documents contained in **Exhibit A** represent the entire agreement between the parties as to the Premises.

2. The undersigned currently occupies the Premises described in the Lease, the Lease Term commenced on , and the Lease Term expires on , and the undersigned has no option to terminate or cancel the Lease or to purchase all or any part of the Premises, the Building and/or the Project, except as expressly set forth in the Lease.

3. Base Rent became payable on .

4. The Lease is in full force and effect and has not been modified, supplemented or amended in any way except as provided in **Exhibit A**.

5. Tenant has not transferred, assigned, or sublet any portion of the Premises nor entered into any license or concession agreements with respect thereto except as follows:

6. Tenant shall not modify the documents contained in **Exhibit A** without the prior written consent of Landlord's mortgagee.

7. All monthly installments of Base Rent, all Additional Rent and all monthly installments of estimated Additional Rent have been paid when due through . The current monthly installment of Base Rent is $.

8. To Tenant's actual knowledge, without inquiry, all conditions of the Lease to be performed by Landlord necessary to the enforceability of the Lease have been satisfied and Landlord is not in default thereunder. In addition, the undersigned has not delivered any notice to Landlord regarding a default by Landlord thereunder. The Lease does not require Landlord to provide any rental concessions or to pay any leasing brokerage commissions except as expressly set forth therein.

9. No rental has been paid more than thirty (30) days in advance and no security has been deposited with Landlord except as provided in the Lease. Neither Landlord, nor its successors or assigns, shall in any event be liable or responsible for, or with respect to, the retention, application and/or return to Tenant of any security deposit paid to any prior landlord of the Premises, whether or not still held by any such prior landlord, unless and until the party from whom the security deposit is being sought, whether it be a lender, or any of its successors or assigns, has actually received for its own account, as landlord, the full amount of such security deposit.

10. To Tenant's actual knowledge, without inquiry, as of the date hereof, there are no existing defenses or offsets, or, to the undersigned's knowledge, claims or any basis for a claim, that the undersigned has against Landlord.

11. If Tenant is a corporation or partnership, Tenant hereby represents and warrants that Tenant is a duly formed and existing entity qualified to do business in California and that Tenant has full right and authority to execute and deliver this Estoppel Certificate and that each person signing on behalf of Tenant is authorized to do so.

12. There are no actions pending against the undersigned under the bankruptcy or similar laws of the United States or any state.

13. Tenant is in full compliance with all federal, state and local laws, ordinances, rules and regulations affecting its use of the Premises, including, but not limited to, those laws, ordinances, rules or regulations relating to hazardous or toxic materials. Tenant has never permitted its agents, employees or contractors to engage in the generation, manufacture, treatment, use, storage, disposal or discharge of any hazardous, toxic or dangerous waste, substance or material in, on, under or about the Project or the Premises or any adjacent premises or property in violation of any federal, state or local law, ordinance, rule or regulation.

14. To the undersigned's knowledge, all tenant improvement work to be performed by Landlord under the Lease has been completed in accordance with the Lease and has been accepted by the undersigned and all reimbursements and allowances due to the undersigned under the Lease in connection with any tenant improvement work have been paid in full. All work (if any) in the common areas required by the Lease to be completed by Landlord has been completed and all parking spaces required by the Lease have been furnished and/or all parking ratios required by the Lease have been met.

The undersigned acknowledges that this Estoppel Certificate may be delivered to Landlord or to a prospective mortgagee or prospective purchaser, and acknowledges that said prospective mortgagee or prospective purchaser will be relying upon the statements contained herein in making the loan or acquiring the property of which the Premises are a part and that receipt by it of this certificate is a condition of making such loan or acquiring such property.

Executed at on the day of , 20 .

"Tenant":

_____

a_____

By:_____

Its:_____

By:_____

Its:_____

EXHIBIT E

ENVIRONMENTAL QUESTIONNAIRE

ENVIRONMENTAL QUESTIONNAIRE
FOR COMMERCIAL AND INDUSTRIAL PROPERTIES

Property Name: _____

Property Address: _____

Instructions: The following questionnaire is to be completed by the Lessee representative with knowledge of the planned operations for the specified building/location. Please print clearly and attach additional sheets as necessary.

1.0 PROCESS INFORMATION

Describe planned use, and include brief description of manufacturing processes employed.

_____

_____

_____

2.0 HAZARDOUS MATERIALS

Are hazardous materials used or stored? If so, continue with the next question. If not, go to Section 3.0.

2.1 Are any of the following materials handled on the Property? Yes ☐ No ☐

(A material is handled if it is used, generated, processed, produced, packaged, treated, stored, emitted, discharged, or disposed.) If so, complete this section. If this question is not applicable, skip this section and go on to Section 5.0.

☐ Explosives	☐ Fuels	☐ Oils
☐ Solvents	☐ Oxidizers	☐ Organics/Inorganics
☐ Acids	☐ Bases	☐ Pesticides
☐ Gases	☐ PCBs	☐ Radioactive Materials
☐ Other (please specify)		

2-2. If any of the groups of materials checked in Section 2.1, please list the specific material(s), use(s), and quantity of each chemical used or stored on the site in the Table below. If convenient, you may substitute a chemical inventory and list the uses of each of the chemicals in each category separately.

Material	Physical State (Solid, Liquid, or Gas)	Usage	Container Size	Number of Containers	Total Quantity

2-3. Describe the planned storage area location(s) for these materials. Please include site maps and drawings as appropriate.

_____

_____

_____

3.0 HAZARDOUS WASTES

Are hazardous wastes generated? Yes ☐ No ☐

If yes, continue with the next question. If not, skip this section and go to section 4.0.

3.1 Are any of the following wastes generated, handled, or disposed of (where applicable) on the Property?

☐ Hazardous wastes
☐ Waste oils
☐ Air emissions
☐ Regulated Wastes
☐ Industrial Wastewater
☐ PCBs
☐ Sludges
☐ Other (please specify)

3-2. List and quantify the materials identified in Question 3-1 of this section.

WASTE GENERATED	RCRA listed Waste?	SOURCE	APPROXIMATE MONTHLY QUANTITY	WASTE CHARACTERIZATION	DISPOSITION

3-3. Please include name, location, and permit number (e.g. EPA ID No.) for transporter and disposal facility, if applicable). Attach separate pages as necessary.

Transporter/Disposal Facility Name	Facility Location	Transporter (I) or Disposal (D) Facility	Permit Number

3-4. Are pollution controls or monitoring employed in the process to prevent or minimize the release of wastes into the environment? Yes ☐ No ☐

3-5. If so, please describe.

4.0 USTS/ASTS

4.1 Are underground storage tanks (USTs), aboveground storage tanks (ASTs), or associated pipelines used for the storage of petroleum products, chemicals, or liquid wastes present on site (lease renewals) or required for planned operations (new tenants)? Yes ☐ No ☐

If not, continue with section 5.0. If yes, please describe capacity, contents, age, type of the USTs or ASTs, as well any associated leak detection/spill prevention measures. Please attach additional pages if necessary.

Capacity	Contents	Year Installed	Type (Steel, Fiberglass, etc)	Associated Leak Detection / Spill Prevention Measures*

* Note: The following are examples of leak detection / spill prevention measures:

Integrity testing
Overfill spill protection
Inventory reconciliation
Secondary containment
Leak detection system
Cathodic protection

4-2. Please provide copies of written tank integrity test results and/or monitoring documentation, if available.

4-3. Is the UST/AST registered and permitted with the appropriate regulatory agencies? If so, please attach a copy of the required permits.
Yes ☐ No ☐

4-4. If this Questionnaire is being completed for a lease renewal, and if any of the USTs/ASTs have leaked, please state the substance released, the media(s) impacted (e.g., soil, water, asphalt, etc.), the actions taken, and all remedial responses to the incident.

4-5. If this Questionnaire is being completed for a lease renewal, have USTs/ASTs been removed from the Property? Yes ☐ No ☐

If yes, please provide any official closure letters or reports and supporting documentation (e.g., analytical test results, remediation report results, etc.).

4-6. For Lease renewals, are there any above or below ground pipelines on site used to transfer chemicals or wastes? Yes ☐ No ☐

For new tenants, are installations of this type required for the planned operations?

Yes ☐ No ☐

If yes to either question, please describe.

5.0 ASBESTOS CONTAINING BUILDING MATERIALS

Please be advised that an asbestos survey may have been performed at the Property. If provided, please review the information that identifies the locations of known asbestos containing material or presumed asbestos containing material. All personnel and appropriate subcontractors should be notified of the presence of these materials, and informed not to disturb these materials. Any activity that involves the disturbance or removal of these materials must be done by an appropriately trained individual/contractor.

6.0 REGULATORY

6-1. Does the operation have or require a National Pollutant Discharge Elimination System (NPDES) or equivalent permit? Yes ☐ No ☐

If so, please attach a copy of this permit.

6-2. Has a Hazardous Materials Business Plan been developed for the site? Yes ☐ No ☐

If so, please attach a copy.

CERTIFICATION

I am familiar with the real property described in this questionnaire. By signing below, I represent and warrant that the answers to the above questions are complete and accurate to the best of my knowledge. I also understand that
Lessor will rely on the completeness and accuracy of my answers in assessing any environmental liability risks associated with the property.

Signature: _____

Name: _____

Title: _____

Date: _____

Telephone: _____

EXHIBIT F

TENANT'S PROPERTY

The following items, to the extent not purchased with the Tenant Improvement Allowance or Additional Improvement Allowance, shall be deemed "Tenant's Property":

1. All moveable furniture and equipment that is not "built-in".
2. Moveable lab casework (other than "built-in" lab casework), including moveable lab benches.
3. Servers, server racks and back-up batteries.
4. Furniture.

EXHIBIT G

FORM OF AGREEMENT FOR ADDITIONAL MONTHLY BASE RENT

FIRST AMENDMENT TO LEASE

This FIRST AMENDMENT TO LEASE ("**Amendment**") is made and entered into as of , 2015, by and between HCP OYSTER POINT III LLC, a Delaware limited partner ("**Landlord**"), and DENALI THERAPEUTICS INC., a Delaware corporation ("**Tenant**").

R E C I T A L S :

A. Landlord and Tenant are parties to that certain Lease dated August , 2015, (the "**Lease**"), pursuant to which Tenant leases the second floor (the "**Premises**") containing approximately 37,945 rentable square feet of space in the building located at 151 Oyster Point Boulevard, South San Francisco, California (the "**Building**").

B. Landlord and Tenant desire to amend the Lease on the terms and conditions set forth in this Amendment.

A G R E E M E N T :

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. Terms. All capitalized terms when used herein shall have the same respective meanings as are given such terms in the Lease unless expressly provided otherwise in this Amendment.

2. Additional TI Allowance. Pursuant to the terms of Section 4 of the Tenant Work Letter attached to the Lease as **Exhibit** B, Tenant was entitled to an Additional TI Allowance of up to $1,897.250.00 (the "Additional TI Allowance"). Notwithstanding any provision to the contrary contained in the Lease, Landlord and Tenant hereby acknowledge and agree that Tenant has utilized and /100 Dollars ($.) of the Additional TI Allowance (the "Utilized Additional TI Allowance").

3. Additional Monthly Base Rent. As a result of Tenant's use of the Utilized Additional TI Allowance, Tenant is required to pay Additional Monthly Base Rent calculated as provided in Section 4 of the Tenant Work Letter, which Additional Monthly Base Rent shall be equal to $ per month, payable on or before the first (1st) day of each month commencing as of , and continuing through the expiration of the initial Lease Term.

4. No Further Modification. Except as specifically set forth in this Amendment, all of the terms and provisions of the Lease shall remain unmodified and in full force and effect.

IN WITNESS WHEREOF, this Amendment has been executed as of the day and year first above written.

LANDLORD:

HCP OYSTER POINT III LLC, a Delaware limited liability company

By: HCP-Pointe Granted, Incorporated
Its general partner

By: _____
Jonathan M. Bergschneider
Executive Vice President

TENANT:

DENALI THERAPEUTICS INC.,
a Delaware corporation

By _____

Name _____

Its _____

By: _____

Name: _____

Its: _____

EXHIBIT H

FORM OF LETTER OF CREDIT

(Letterhead of a money center bank acceptable to the Landlord)

FAX NO. [( ) -]
SWIFT: [Insert No., if any]

[Insert Bank Name And Address]

DATE OF ISSUE: _____

BENEFICIARY:
[Insert Beneficiary Name And Address]

APPLICANT:
[Insert Applicant Name And Address]

LETTER OF CREDIT NO. _____

EXPIRATION DATE:
_____ AT OUR COUNTERS

AMOUNT AVAILABLE:
USD[Insert Dollar Amount]
(U.S. DOLLARS [Insert Dollar Amount])

LADIES AND GENTLEMEN:

WE HEREBY ESTABLISH OUR IRREVOCABLE STANDBY LETTER OF CREDIT NO. IN YOUR FAVOR FOR THE ACCOUNT OF [Insert Tenant's Name], A [Insert Entity Type], UP TO THE AGGREGATE AMOUNT OF USD[Insert Dollar Amount] ([Insert Dollar Amount] U.S. DOLLARS) EFFECTIVE IMMEDIATELY AND EXPIRING ON (Expiration Date) AVAILABLE BY PAYMENT UPON PRESENTATION OF YOUR DRAFT AT SIGHT DRAWN ON [Insert Bank Name] WHEN ACCOMPANIED BY THE FOLLOWING DOCUMENT(S):

1. THE ORIGINAL OF THIS IRREVOCABLE STANDBY LETTER OF CREDIT AND AMENDMENT(S), IF ANY.

2. BENEFICIARY'S SIGNED STATEMENT PURPORTEDLY SIGNED BY AN AUTHORIZED REPRESENTATIVE OF [Insert Landlord's Name], A [Insert Entity Type] ("LANDLORD") STATING THE FOLLOWING:

"THE UNDERSIGNED HEREBY CERTIFIES THAT THE LANDLORD, EITHER (A) UNDER THE LEASE (DEFINED BELOW), OR (B) AS A RESULT OF THE TERMINATION OF SUCH LEASE, HAS THE RIGHT TO DRAW DOWN THE AMOUNT OF USD IN ACCORDANCE WITH THE TERMS OF THAT CERTAIN OFFICE LEASE DATED [Insert Lease Date], AS AMENDED (COLLECTIVELY, THE "LEASE"), OR SUCH AMOUNT CONSTITUTES DAMAGES OWING BY THE TENANT TO BENEFICIARY RESULTING FROM THE BREACH OF SUCH LEASE BY THE TENANT THEREUNDER, OR THE TERMINATION OF SUCH LEASE, AND SUCH AMOUNT REMAINS UNPAID AT THE TIME OF THIS DRAWING."

OR

"THE UNDERSIGNED HEREBY CERTIFIES THAT WE HAVE RECEIVED A WRITTEN NOTICE OF [Insert Bank Name]'S ELECTION NOT TO EXTEND ITS STANDBY LETTER OF CREDIT NO. AND HAVE NOT RECEIVED A REPLACEMENT LETTER OF CREDIT WITHIN AT LEAST THIRTY (30) DAYS PRIOR TO THE PRESENT EXPIRATION DATE."

OR

"THE UNDERSIGNED HEREBY CERTIFIES THAT BENEFICIARY IS ENTITLED TO DRAW DOWN THE FULL AMOUNT OF LETTER OF CREDIT NO. AS THE RESULT OF THE FILING OF A VOLUNTARY PETITION UNDER THE U.S. BANKRUPTCY CODE OR A STATE BANKRUPTCY CODE BY THE TENANT UNDER THAT CERTAIN OFFICE LEASE DATED [Insert Lease Date], AS AMENDED (COLLECTIVELY, THE "LEASE"), WHICH FILING HAS NOT BEEN DISMISSED AT THE TIME OF THIS DRAWING."

OR

"THE UNDERSIGNED HEREBY CERTIFIES THAT BENEFICIARY IS ENTITLED TO DRAW DOWN THE FULL AMOUNT OF LETTER OF CREDIT NO. AS THE RESULT OF AN INVOLUNTARY PETITION HAVING BEEN FILED UNDER THE U.S. BANKRUPTCY CODE OR A STATE BANKRUPTCY CODE AGAINST THE TENANT UNDER THAT CERTAIN OFFICE LEASE DATED [Insert Lease Date], AS AMENDED (COLLECTIVELY, THE "LEASE"), WHICH FILING HAS NOT BEEN DISMISSED AT THE TIME OF THIS DRAWING."

OR

"THE UNDERSIGNED HEREBY CERTIFIES THAT BENEFICIARY IS ENTITLED TO DRAW DOWN THE FULL AMOUNT OF LETTER OF CREDIT NO. AS THE RESULT OF THE REJECTION, OR DEEMED REJECTION, OF THAT CERTAIN OFFICE LEASE DATED [Insert Lease Date], AS AMENDED, UNDER SECTION 365 OF THE U.S. BANKRUPTCY CODE."

SPECIAL CONDITIONS:

PARTIAL DRAWINGS AND MULTIPLE PRESENTATIONS MAY BE MADE UNDER THIS STANDBY LETTER OF CREDIT, PROVIDED, HOWEVER, THAT EACH SUCH DEMAND THAT IS PAID BY US SHALL REDUCE THE AMOUNT AVAILABLE UNDER THIS STANDBY LETTER OF CREDIT.

ALL INFORMATION REQUIRED WHETHER INDICATED BY BLANKS, BRACKETS OR OTHERWISE, MUST BE COMPLETED AT THE TIME OF DRAWING. [Please Provide The Required Forms For Review, And Attach As Schedules To The Letter Of Credit.]

ALL SIGNATURES MUST BE MANUALLY EXECUTED IN ORIGINALS.

ALL BANKING CHARGES ARE FOR THE APPLICANT'S ACCOUNT.

IT IS A CONDITION OF THIS STANDBY LETTER OF CREDIT THAT IT SHALL BE DEEMED AUTOMATICALLY EXTENDED WITHOUT AMENDMENT FOR A PERIOD OF ONE YEAR FROM THE PRESENT OR ANY FUTURE EXPIRATION DATE, UNLESS AT LEAST SIXTY (60) DAYS PRIOR TO THE EXPIRATION DATE WE SEND YOU NOTICE BY NATIONALLY RECOGNIZED OVERNIGHT COURIER SERVICE THAT WE ELECT NOT TO EXTEND THIS LETTER OF CREDIT FOR ANY SUCH ADDITIONAL PERIOD. SAID NOTICE WILL BE SENT TO THE ADDRESS INDICATED ABOVE, UNLESS A CHANGE OF ADDRESS IS OTHERWISE NOTIFIED BY YOU TO US IN WRITING BY RECEIPTED MAIL OR COURIER. ANY NOTICE TO US WILL BE DEEMED EFFECTIVE ONLY UPON ACTUAL RECEIPT BY US AT OUR DESIGNATED OFFICE. IN NO EVENT, AND WITHOUT FURTHER NOTICE FROM OURSELVES, SHALL THE EXPIRATION DATE BE EXTENDED BEYOND A FINAL EXPIRATION DATE OF ___ (120 days from the Lease Expiration Date).

THIS LETTER OF CREDIT MAY BE TRANSFERRED SUCCESSIVELY IN WHOLE OR IN PART ONLY UP TO THE THEN AVAILABLE AMOUNT IN FAVOR OF A NOMINATED TRANSFEREE ("TRANSFEREE"), ASSUMING SUCH TRANSFER TO SUCH TRANSFEREE IS IN COMPLIANCE WITH ALL APPLICABLE U.S. LAWS AND REGULATIONS. AT THE TIME OF TRANSFER, THE ORIGINAL LETTER OF CREDIT

AND ORIGINAL AMENDMENT(S) IF ANY, MUST BE SURRENDERED TO US TOGETHER WITH OUR TRANSFER FORM (AVAILABLE UPON REQUEST) AND PAYMENT OF OUR CUSTOMARY TRANSFER FEES, WHICH FEES SHALL BE PAYABLE BY APPLICANT (PROVIDED THAT BENEFICIARY MAY, BUT SHALL NOT BE OBLIGATED TO, PAY SUCH FEES TO US ON BEHALF OF APPLICANT, AND SEEK REIMBURSEMENT THEREOF FROM APPLICANT). IN CASE OF ANY TRANSFER UNDER THIS LETTER OF CREDIT, THE DRAFT AND ANY REQUIRED STATEMENT MUST BE EXECUTED BY THE TRANSFEREE AND WHERE THE BENEFICIARY'S NAME APPEARS WITHIN THIS STANDBY LETTER OF CREDIT, THE TRANSFEREE'S NAME IS AUTOMATICALLY SUBSTITUTED THEREFOR.

ALL DRAFTS REQUIRED UNDER THIS STANDBY LETTER OF CREDIT MUST BE MARKED: "DRAWN UNDER [Insert Bank Name] STANDBY LETTER OF CREDIT NO. ."

WE HEREBY AGREE WITH YOU THAT IF DRAFTS ARE PRESENTED TO [Insert Bank Name] UNDER THIS LETTER OF CREDIT AT OR PRIOR TO [Insert Time – (*e.g.*, 11:00 AM)], ON A BUSINESS DAY, AND PROVIDED THAT SUCH DRAFTS PRESENTED CONFORM TO THE TERMS AND CONDITIONS OF THIS LETTER OF CREDIT, PAYMENT SHALL BE INITIATED BY US IN IMMEDIATELY AVAILABLE FUNDS BY OUR CLOSE OF BUSINESS ON THE SUCCEEDING BUSINESS DAY. IF DRAFTS ARE PRESENTED TO [Insert Bank Name] UNDER THIS LETTER OF CREDIT AFTER [Insert Time – (*e.g.*, 11:00 AM)], ON A BUSINESS DAY, AND PROVIDED THAT SUCH DRAFTS CONFORM WITH THE TERMS AND CONDITIONS OF THIS LETTER OF CREDIT, PAYMENT SHALL BE INITIATED BY US IN IMMEDIATELY AVAILABLE FUNDS BY OUR CLOSE OF BUSINESS ON THE SECOND SUCCEEDING BUSINESS DAY. AS USED IN THIS LETTER OF CREDIT, "BUSINESS DAY" SHALL MEAN ANY DAY OTHER THAN A SATURDAY, SUNDAY OR A DAY ON WHICH BANKING INSTITUTIONS IN THE STATE OF CALIFORNIA ARE AUTHORIZED OR REQUIRED BY LAW TO CLOSE. IF THE EXPIRATION DATE FOR THIS LETTER OF CREDIT SHALL EVER FALL ON A DAY WHICH IS NOT A BUSINESS DAY THEN SUCH EXPIRATION DATE SHALL AUTOMATICALLY BE EXTENDED TO THE DATE WHICH IS THE NEXT BUSINESS DAY.

PRESENTATION OF A DRAWING UNDER THIS LETTER OF CREDIT MAY BE MADE ON OR PRIOR TO THE THEN CURRENT EXPIRATION DATE HEREOF BY HAND DELIVERY, COURIER SERVICE, OVERNIGHT MAIL, OR FACSIMILE. PRESENTATION BY FACSIMILE TRANSMISSION SHALL BE BY TRANSMISSION OF THE ABOVE REQUIRED SIGHT DRAFT DRAWN ON US TOGETHER WITH THIS LETTER OF CREDIT TO OUR FACSIMILE NUMBER, [Insert Fax Number – ( ) -], ATTENTION: [Insert Appropriate Recipient], WITH TELEPHONIC CONFIRMATION OF OUR RECEIPT OF SUCH FACSIMILE TRANSMISSION AT OUR TELEPHONE NUMBER [Insert Telephone Number – ( ) -] OR TO SUCH OTHER FACSIMILE OR TELEPHONE NUMBERS, AS TO WHICH YOU HAVE RECEIVED WRITTEN NOTICE FROM US AS BEING THE APPLICABLE SUCH NUMBER. WE AGREE TO NOTIFY YOU IN WRITING, BY NATIONALLY RECOGNIZED OVERNIGHT COURIER SERVICE, OF ANY CHANGE IN SUCH DIRECTION. ANY FACSIMILE PRESENTATION PURSUANT TO THIS PARAGRAPH SHALL ALSO STATE THEREON THAT THE ORIGINAL OF SUCH SIGHT DRAFT AND LETTER OF CREDIT ARE BEING REMITTED, FOR DELIVERY ON THE NEXT BUSINESS DAY, TO [Insert Bank Name] AT THE APPLICABLE ADDRESS FOR PRESENTMENT PURSUANT TO THE PARAGRAPH FOLLOWING THIS ONE.

WE HEREBY ENGAGE WITH YOU THAT ALL DOCUMENT(S) DRAWN UNDER AND IN COMPLIANCE WITH THE TERMS OF THIS STANDBY LETTER OF CREDIT WILL BE DULY HONORED IF DRAWN AND PRESENTED FOR PAYMENT AT OUR OFFICE LOCATED AT [Insert Bank Name], [Insert Bank Address], ATTN: [Insert Appropriate Recipient], ON OR BEFORE THE EXPIRATION DATE OF THIS CREDIT, (Expiration Date)

IN THE EVENT THAT THE ORIGINAL OF THIS STANDBY LETTER OF CREDIT IS LOST, STOLEN, MUTILATED, OR OTHERWISE DESTROYED, WE HEREBY AGREE TO ISSUE A DUPLICATE ORIGINAL HEREOF UPON RECEIPT OF A WRITTEN REQUEST FROM YOU AND A CERTIFICATION BY YOU (PURPORTEDLY SIGNED BY YOUR AUTHORIZED REPRESENTATIVE) OF THE LOSS, THEFT, MUTILATION, OR OTHER DESTRUCTION OF THE ORIGINAL HEREOF.

EXCEPT SO FAR AS OTHERWISE EXPRESSLY STATED HEREIN, THIS STANDBY LETTER OF CREDIT IS SUBJECT TO THE "INTERNATIONAL STANDBY PRACTICES" (ISP 98) INTERNATIONAL CHAMBER OF COMMERCE (PUBLICATION NO. 590).

Very truly yours,

(Name of Issuing Bank)

By: _____