Table of Contents

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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2017

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____ to_____

Commission File Number: 001-38311

Denali Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**46-3872213**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

151 Oyster Point Blvd., 2nd Floor
South San Francisco, CA, 94080
(Address of principal executive offices and zip code)

(650) 866-8548
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common stock, par value $0.01 per share	**The NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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. (Check one):

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 13(a) of the Exchange Act. ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant, based on the closing price of a share of common stock on December 8, 2017 as reported by the NASDAQ Global Select Market on such date was approximately $628.4 million. The registrant has elected to use December 8, 2017, which was the initial trading date on the NASDAQ Global Select Market, as the calculation date because on June 30, 2017 (the last business day of the registrant's most recently completed second fiscal quarter), the registrant was a privately held company. Shares of the registrant's common stock held by each executive officer, director and holder of 5% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose.

The number of outstanding shares of the registrant's common stock as of March 12, 2018 was 94,429,245.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's Definitive Proxy Statement relating to the registrant's 2018 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such Definitive Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's 2017 fiscal year ended December 31, 2017.

Denali Therapeutics Inc.
Annual Report on Form 10-K
TABLE OF CONTENTS

PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this report, 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 report 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 blood-brain barrier (“BBB”) platform technology, core programs and biomarkers;
- the extent to which any dosing limitations that we have been subject to, and/or may be subject to in the future, may affect the success of our product candidates;
- the impact of preclinical findings on our ability to achieve exposures of our product candidates that allow us to explore a robust pharmacodynamic range of these candidates in humans;
- the expected potential benefits of strategic collaborations with third parties 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 and commercialized;
- 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; and
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act.

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 report and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this report. 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 undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report on Form 10-K to conform these statements to actual results or to changes in expectations.

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 report, 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.

This report 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 report 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.

ITEM 1. BUSINESS

Overview and Strategy

Our goal is to 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 ("ALS"), and other neurodegenerative diseases. The burden of these diseases to patients and society is massive.

We believe the time is right to make a strong and ambitious effort to defeat neurodegeneration. We believe that we can succeed in a field that has seen limited success in the past, because of our team of experienced and passionately dedicated scientists and drug developers, our focused scientific strategy, and our proprietary blood-brain barrier ("BBB"), platform delivery technology. We are developing a broad portfolio of targeted therapeutic candidates for neurodegenerative diseases and currently have two programs in Phase 1 clinical development.

Historical challenges in developing effective therapeutics for patients with neurodegenerative 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 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 likelihood of success of developing effective therapeutics for neurodegenerative diseases.

Our scientific strategy is guided by three overarching principles. We believe that the application of these principles will significantly increase our 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 genes that, when mutated, cause, or are major risk factors for, neurodegenerative diseases, which we refer to as degenogenes. 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.

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.

Our total portfolio currently consists of thirteen programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have seven core programs and six 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.

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 to the later stages of clinical development that show strong preclinical and early clinical data. 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 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 ("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 programs, including the programs partnered with Takeda where we share responsibility for development and share commercialization rights in the US and China.

The following table summarizes key information about our programs:

PROGRAM TARGET	DRUG CANDIDATE	THERAPEUTIC MODALITY	DISEASE INDICATION	DRUG DEVELOPMENT	VALIDATED BIOMARKER			PARTNERSHIP
				LEAD FINDING / LEAD OP / PRECLINICAL / PH 1	P	C	PS	
LYSOSOMAL FUNCTION PATHWAY								
LRRK2	DNL201	Small Molecule	Parkinson's Disease		✓	✓	✓	
	DNL151	Small Molecule	Parkinson's Disease		✓	✓	✓	
Alpha-Synuclein	ATV:aSyn	Antibody	Parkinson's Disease, DLB, MSA		✓			
Iduronate 2-sulfatase	ETV:IDS	Enzyme	MPS II (Hunter Syndrome)		✓	✓	✓	
LF1	LF1	Protein	Neurodegeneration		✓	✓	✓	Takeda
LF2	LF2	Small Molecule	Neurodegeneration		✓	✓	✓	
LF3	ETV:LF3	Enzyme	LSD		✓	✓	✓	
GLIAL BIOLOGY PATHWAY								
RIPK1	DNL747	Small Molecule	Alzheimer's Disease, ALS		✓	✓		
	DNL788	Small Molecule	Alzheimer's Disease, ALS		✓	✓		
TREM2	ATV:TREM2	Antibody	Alzheimer's Disease		✓			Takeda
CELLULAR HOMEOSTASIS								
BACE1/Tau	ATV:BACE1/Tau	Antibody	Alzheimer's Disease		✓	✓	✓	Takeda
CH1	CH1	Small Molecule	Neurodegeneration		✓			
CH2	CH2	Antibody	Neurodegeneration				✓	
CH3	CH3	Small Molecule	Neurodegeneration		✓			
OTHER								
OP1	OP1	Small Molecule	TBD		✓	✓		

CORE program (7)
SEED program (6)

VALIDATED BIOMARKER
P = Preclinical
C = Clinical
PS = Patient Selection

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 proprietary drug delivery platform technologies, Antibody Transport Vehicle ("ATV") and Enzyme Transport Vehicle ("ETV"), designed to deliver large molecules across the BBB. We have achieved proof of concept for the ATV platform in both a mouse model and in nonhuman primates. 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. Therapeutic candidates enabled by the ATV or ETV 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 a mouse model across three studies designed to demonstrate proof of concept of the ATV platform, an antibody engineered with our ATV technology has demonstrated an average 20-fold greater brain penetration than a control antibody not enabled by this technology. In addition, initial data from an ongoing study in nonhuman primates designed to show proof of concept for the ATV platform demonstrates a robust and sustained pharmacodynamic ("PD") effect in the brain after intravenous dosing of an ATV-enabled antibody, while a standard antibody had minimal PD effect. The 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 ("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 ("aSyn"); iduronate 2-sulfatase ("IDS"); triggering receptor expressed in myeloid cells 2 ("TREM2"); beta-secretase 1 ("BACE1"); and Tau. On January 3, 2018, we entered into an Option and Collaboration Agreement ("Collaboration Agreement") with Takeda Pharmaceutical Company Limited ("Takeda"), pursuant to which we granted Takeda an option to develop and commercialize, jointly with us, three of our programs (ATV:TREM2 and ATV:BACE1/Tau and a third identified, but yet undisclosed discovery stage program) that are enabled by our blood-brain barrier delivery technology and intended for the treatment of neurodegenerative diseases. If Takeda exercises its option for a particular target, we and Takeda will share equally the clinical development costs and the commercial profits for each collaboration program on a world-wide basis.

For small molecules, we follow a rigorous approach to designing these molecules to cross the BBB. DNL201 and DNL151, our small molecule inhibitors of leucine-rich repeat kinase 2 ("LRRK2"), and DNL747, our small molecule inhibitor of receptor interacting serine/threonine protein kinase 1 ("RIPK1"), 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. Our two LRRK2 product candidates, DNL201 and DNL151, are currently in Phase 1 clinical trials.

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 has been shown to have beneficial effects in preclinical models of Alzheimer's disease, ALS and other diseases. We submitted a CTA for DNL747 to the Netherlands Health Authority in February 2018 and initiated a Phase 1 clinical trial in healthy volunteers in March 2018.

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, F-star and Takeda, 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, foundations such as the Michael J. Fox Foundation, and patient-focused data companies such as 23andMe and Patients Like Me, to gain access to new product candidates, deepen our scientific understanding of certain areas of biology and enable and accelerate the development of our programs. We believe that accessing external innovation is important to our success and we plan to remain active in 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 the aging of the population and the lack of effective therapeutic options causing a rapid increase in the number of patients. 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, 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 of caring for individuals with Alzheimer's disease and other dementias in the United States were an estimated $259 billion in 2017, and are 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 deoxyribonucleic acid ("DNA") sequencing has contributed to the discovery of numerous genetic mutations that have been linked to neurodegeneration (Figure 1).

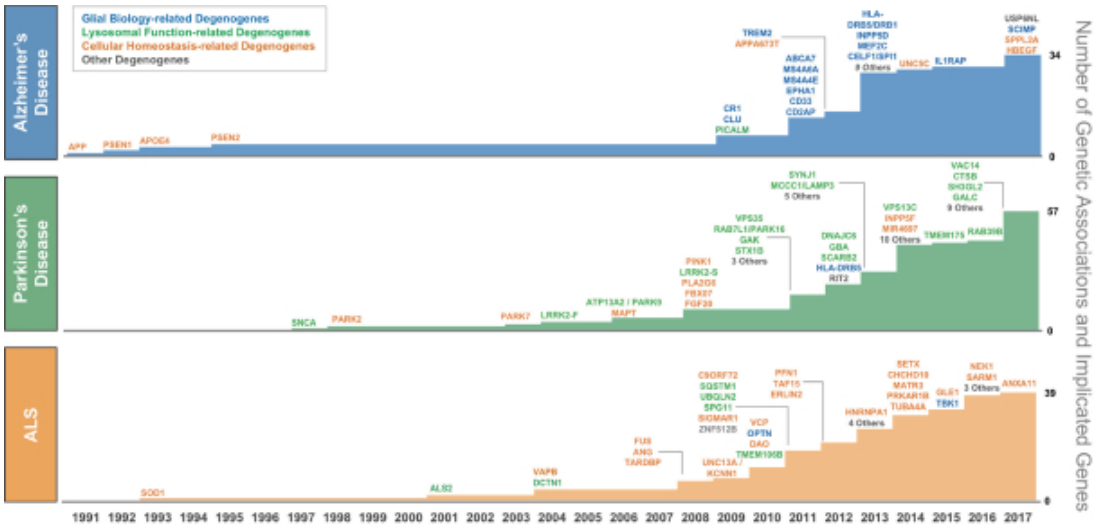
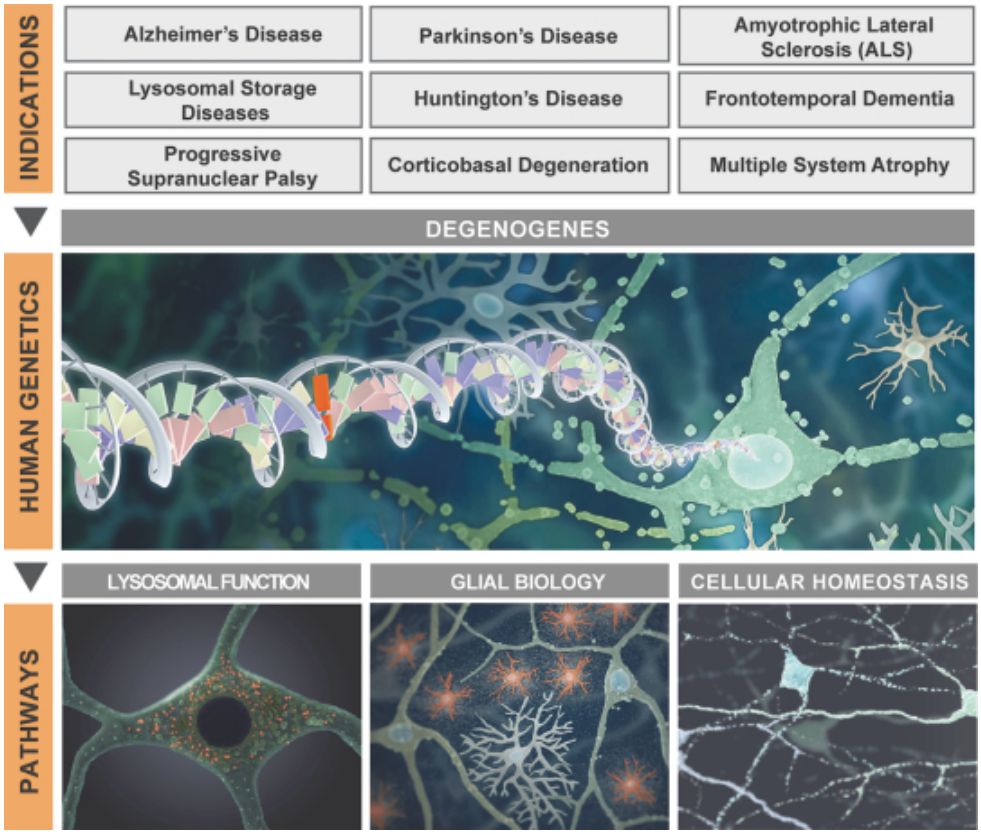


Figure 1: The number of associated genetic mutations linked to Alzheimer's disease, Parkinson's disease and ALS from 1991 to 2017. For genome-wide association studies, disease genes were selected based on genome-wide significance (p<5×10-8). Rare disease-causing and/or high penetrance mutations were 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. These 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 ("LSDs"). Degenogenes linked to lysosomal function include LRRK2, aSyn, and lysosomal enzymes dysfunctional in LSDs, including IDS, and glucocerebrosidase ("GBA"). 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 non-neuronal cells that are important for protecting and supporting neuronal function, generating myelin for nerve conduction, providing nutrition to neurons, and generally maintaining healthy brain function. A specific glial cell type, microglial cells, which are the macrophages of the brain and spinal cord, act as the resident immune system in the brain. Recently discovered degenogenes implicate immune dysfunction in microglial cells in 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, which is an enzyme that catalyzes the addition of a phosphate group to substrates, usually proteins, 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 homeostasis of protein or ribonucleic acid ("RNA") lead to the death of neurons and dysfunction of the nervous system. This spreading of protein aggregates resulting in a proteinopathy, a characteristic finding in Alzheimer's and Parkinson's diseases that results from disorders of protein synthesis, trafficking, folding, processing or degradation in cells. This also includes 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, which are accumulations of complex amyloid proteins deposited in tissues and neurofibrillary tangles, which are aggregates of hyperphosphorylated Tau protein that are a marker of Alzheimer's disease and other diseases known as tauopathies. With our ATV:BACE1/Tau program, 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, respectively. We believe this combination therapeutic approach has the potential for synergistic activity, restoring protein homeostasis of the two most common protein pathologies in Alzheimer's disease. We believe 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 approximately 400 miles of blood vessels. These blood vessels are lined by closely linked endothelial cells to form the BBB, which protects the brain from toxins by regulating the transfer of proteins, nutrients and waste products. Delivery of therapeutics to the brain has been challenging as most small molecule drugs are actively excluded by efflux pumps, and brain uptake of therapeutic antibodies and recombinant enzymes is severely limited by their size. (Figure 2).

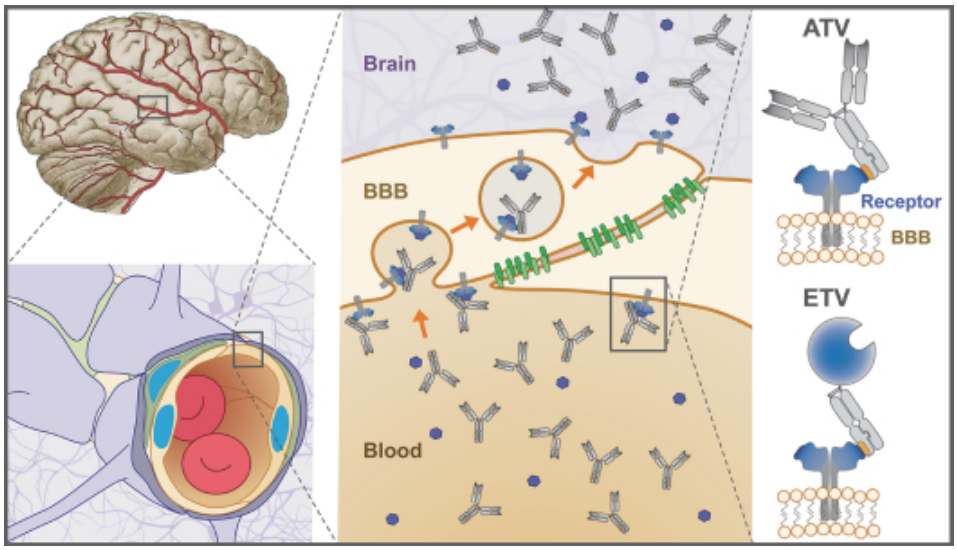


Figure 2. Schematic of the BBB. The specialized vessels of the brain represent a significant barrier for both small and large molecule therapeutics. Tight junctions between endothelial cells prevent the diffusion of large molecules while most small molecules are kept out of the brain by efflux pumps.

The protective nature of the BBB limits the passive uptake of small molecule and large molecule therapeutics in the brain. For example, the concentration of most therapeutic antibodies in the brain is only 0.1% of the concentration in the blood. 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 therefore 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 (“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 (“TV”), platform technology engineers BBB receptor binding into an Fc domain (Figure 3). We have selected transferrin

receptor (“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.

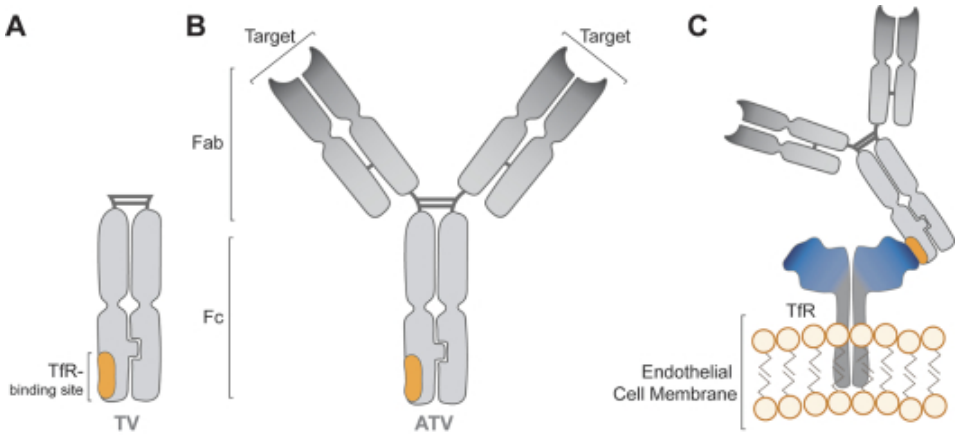


Figure 3. Schematic of the BBB large molecule Transport Vehicle (TV) technology. The TV platform technology contains BBB receptor (TfR) binding in the Fc domain (A). The TV can be fused to Fab arms constituting the Antibody Transport Vehicle (ATV) technology (B). ATVs bind to TfR, enabling TfR-mediated transcytosis and brain uptake (C).

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).

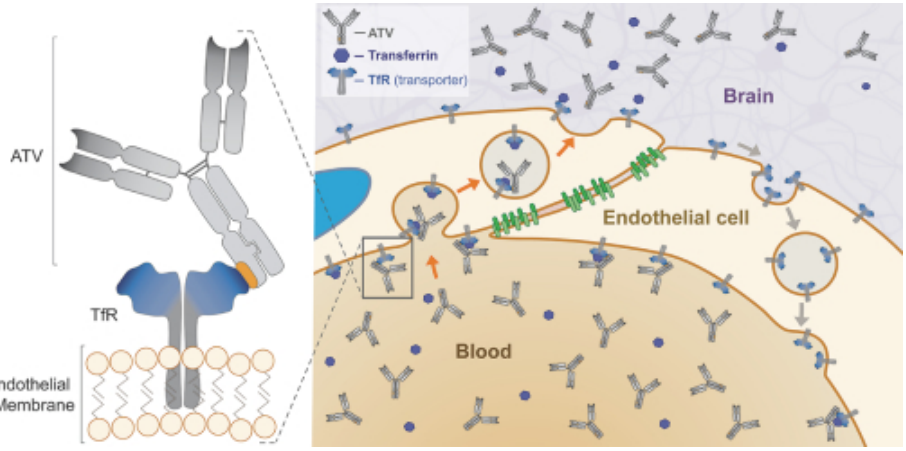


Figure 4. Schematic of receptor-mediated transport of ATV at the BBB. ATV molecules engage TfR on the blood vessel wall in the brain. Once bound, ATV is brought into vesicles that are transcytosed across the endothelial cell and released into the brain, thus substantially increasing antibody concentrations 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 express a portion of the human TfR gene at a specific location, or human TfR knock-in mice, and we have achieved *in viv*o proof of concept data in a study in nonhuman primates.

In the human TfR knock-in-mouse model, we have completed three preclinical studies designed to demonstrate proof of concept for the ATV platform. Such studies have demonstrated an average 20-fold increased antibody uptake in the brain, compared to a control antibody (Figure 5).

As a result of a dramatic improvement in brain antibody uptake with the ATV, we observed a robust brain PD response, which is the biochemical and physiological effect of a drug, as measured by reduction in levels of amyloid beta in brain. This represents a highly disease relevant proximal readout as amyloid beta levels are a primary driver of the amyloid plaque pathology 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).

ATV-enabled antibodies also showed broad distribution in the brain, effectively crossing the BBB and associating with brain cells. Using brain imaging techniques, human IgG1 distribution was compared between a control anti-BACE1 antibody and ATV1:BACE1 (Figure 5). Images show robust localization of ATV1:BACE1 with cells in the brain after systemic delivery. These proof of concept data in a human TfR knock-in-mouse model demonstrate the ability of ATV to achieve therapeutic concentrations and broad distribution in brain.

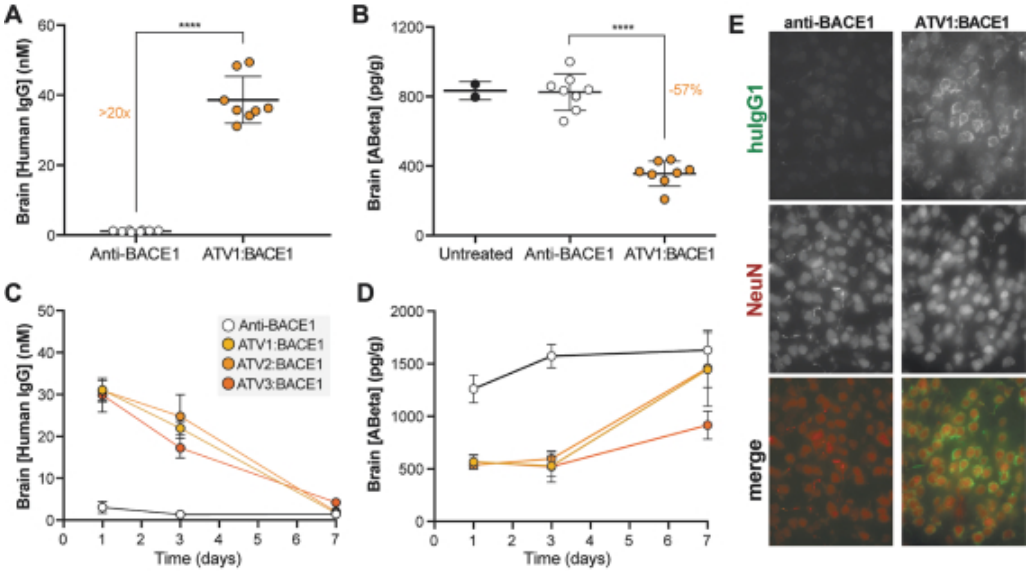


Figure 5: ATV therapeutics achieve robust brain uptake and pharmacodynamic activity in human TfR knock-in mice. Mice were injected with 50 mg/kg of anti-BACE1 or ATV1:BACE1. After 24 hours of circulation, brain antibody concentrations were compared between anti-BACE1 (1.2nM) and ATV1:BACE1 (38.6nM) (A). A significant reduction in brain Abeta levels (57%) was observed for mice injected with ATV:BACE1 compared to anti-BACE1, where no reduction was observed as compared to untreated mice (B). Mice were injected with 50 mg/kg of anti-BACE1, ATV1:BACE1, ATV2:BACE1 or ATV3:BACE1. All ATV:BACE1 variants show a significant increase in brain uptake at 1 and 3 days post-dose as compared to anti-BACE1 (C). Significant brain Abeta reduction was observed for all ATV:BACE1 variants at 1 and 3 days post-dose, and for ATV3:BACE1 at 7 days post-dose, as compared to anti-BACE1 (D). Immunohistochemistry staining of brain sections from mice injected with either anti-BACE1 or ATV1:BACE1 24 hours post-dose. Robust and broad neuronal distribution of systemically administered ATV1: BACE1, but not anti-BACE1 is observed (E). HulgG1 labels antibody; NeuN labels neurons; ** indicates p<0.0001.**

To further validate the ATV platform, we completed an *in vivo* study in nonhuman primates with an ATV designed to bind to cynomolgus monkey TfR (ATV4:BACE1). Data from this 28-day study demonstrated a robust and sustained brain PD response as measured from fluid taken from brains of

living monkeys (Figure 6). When measuring drug activity in blood (plasma) versus brain (CSF), both anti-BACE1 and ATV4:BACE1 show robust activity in the blood, however only the ATV-enabled antibody (ATV4:BACE1) demonstrated robust and sustained PD activity in the nonhuman primate brain. We believe these *in vivo* proof of concept data in nonhuman primates provide support for the translatability of the ATV platform for human studies.

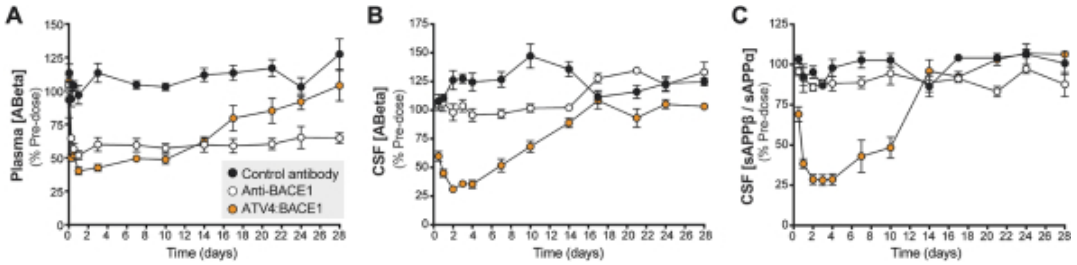


Figure 6. ATV therapeutics achieve CNS PD activity in nonhuman primates. Cynomolgus monkeys were systemically injected with 30 mg/kg of control antibody, anti-BACE1, or ATV4:BACE1. In plasma, anti-BACE1 and ATV4:BACE1 equally reduce Abeta levels (A). In CSF, a robust and sustained reduction in CSF Abeta (B) and soluble APPbeta/APPalpha ratio (C) was observed in monkeys with ATV4:BACE1 compared to control antibody. In contrast, anti-BACE1 has minimal impact on CSF Abeta and APPbeta/APPalpha levels (C).

Enzyme Transport Vehicle

Our ETV platform utilizes the same RMT 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 7). 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.

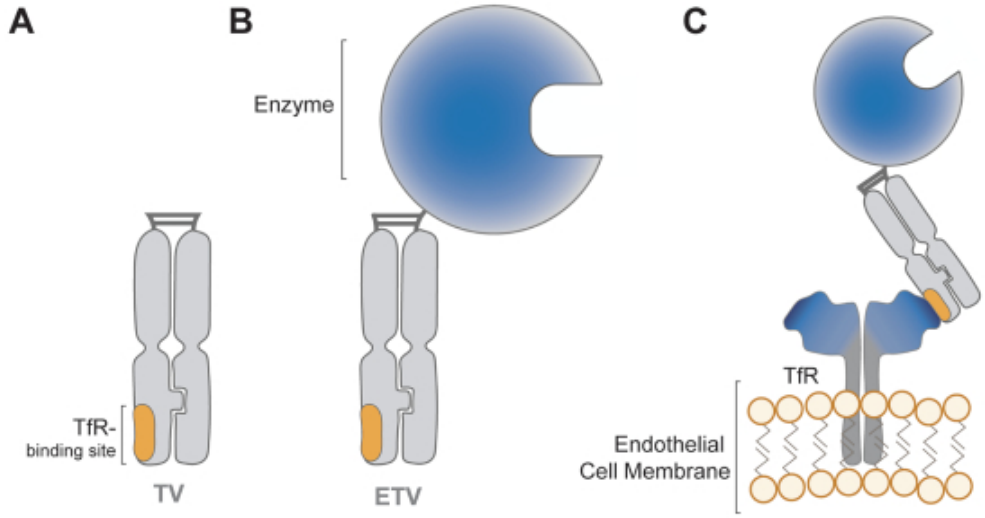


Figure 7: Engineering brain delivery using the ETV platform. The ETV platform technology contains BBB receptor (TfR) binding in the Fc domain (A) fused to an enzyme (B) to enable transport of enzymes into the brain through TfR-mediated transcytosis (C).

Platform Technology Development and Applications

We are advancing our ATV and ETV platforms through further preclinical studies in mice and nonhuman primates. We are currently undertaking and plan to commence further IND-enabling studies with multiple preclinical product candidates in 2018 and initiate our first platform-enabled clinical trials in 2019. We are also combining our proprietary human TfR knock-in-mice model with disease-specific animal models in order to more precisely assess the potential of our platform-enabled therapeutic candidates in relevant disease models. We expect that this will give us the ability to perform pharmacokinetic/pharmacodynamic ("PK/PD"), and efficacy studies and to quantitatively demonstrate the advantages of antibodies and proteins delivered using our platform technologies. To enable the development of our platform technologies, we have entered into a strategic licensing and collaboration agreement with F-star. For more information regarding our collaborations, see "Business - Licenses and Collaborations."

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. Efficacious orally administered small-molecule medicines for brain diseases must be readily absorbed from the gut into the blood and penetrate the BBB while avoiding transporter-mediated efflux (Figure 8). It has been estimated that approximately 98% of small molecule drugs do not cross the BBB.

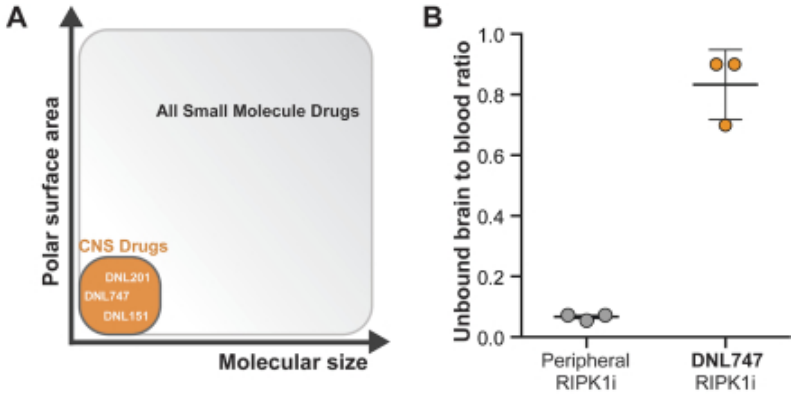


Figure 8: Generation of brain penetrant small molecules. The molecular properties compatible with CNS drugs are significantly more restricted than those generally used to design small molecule drugs, including tight restrictions on molecular weight and total polar surface area (A). This figure is not 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

We define 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.

In addition, we strive to develop a patient selection strategy guided by a genetic rationale and understanding of target biology for each of our programs. With this approach, we seek to increase the probability of success and 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 trials.

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 seven core programs and six seed programs. In addition, we continually evaluate additional targets for inclusion as seed programs from our discovery efforts, 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 six of our core programs in further detail below.

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 and DNL151 are both currently in Phase 1 clinical trials.

We have developed validated assays that measure pS935 LRRK2 and pRab10 phosphorylation as markers of LRRK2 kinase activity to demonstrate target engagement in humans. To provide greater insight into the effects of LRRK2 inhibitors on Parkinson's disease biology, in addition to pRab10 phosphorylation, we are also developing novel biomarkers linked to the lysosomal dysfunction associated with Parkinson's disease. Determining if LRRK2 inhibitors can alter these biomarkers in Parkinson's disease patients may help predict clinical efficacy. We are initiating efforts to recruit a targeted patient population with disease causing LRRK2 mutations, including G2019S, R1441C, R1441G, I2020T and Y1699C, to enroll in future clinical studies.

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 neurodegeneration and the formation of Lewy bodies, which are intracellular aggregates containing aSyn proteins (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 specific 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.

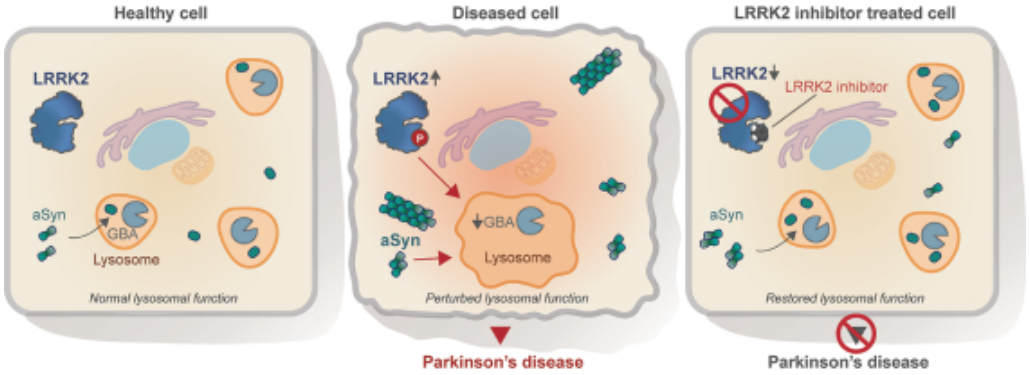


Figure 9: LRRK2 acts in healthy cells to maintain normal lysosomal function. Excessive LRRK2 activation or expression reduces lysosomal function and contributes to the progression of Parkinson's disease. Lysosomal dysfunction in Parkinson's disease can also be caused by high levels of aSyn and by loss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

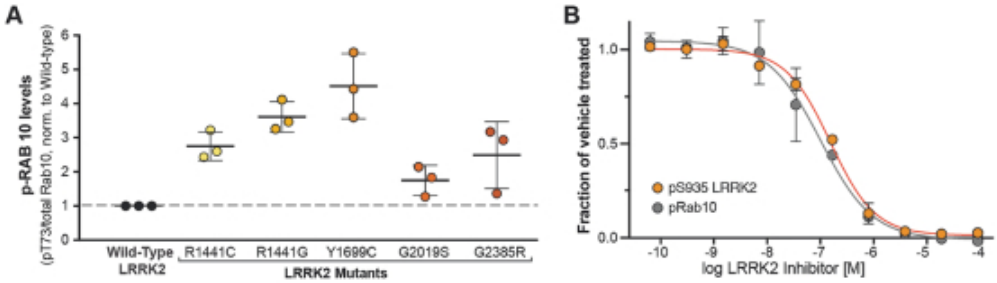


Figure 10. Phosphorylated Rabs are a novel marker of LRRK2 activity. Multiple distinct LRRK2 mutations result in elevated phosphorylation of the downstream marker Rab10 (A), while inhibition of LRRK2 results in a dose-dependent inhibition of Rab10 phosphorylation that is comparable to the inhibition of LRRK2 phosphorylation on Serine 935 (B).

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. 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.

Pharmacological Properties and Brain Exposure

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

Both DNL201 and DNL151 displayed comparable potency of LRRK2 inhibition in blood cells taken from LRRK2 mutation carriers and non-carriers, with a trend to increased potency in G2019S mutation carriers (Figure 11).

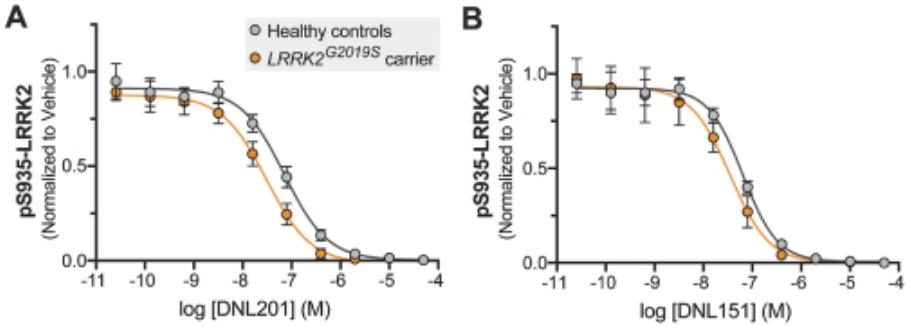


Figure 11. Treatment of peripheral blood mononuclear cells (PBMCs) derived from LRRK2 mutation carriers and healthy control non-carriers with our LRRK2 inhibitors. Both DNL201 (A) and DNL151 (B) demonstrated a small increase in potency in G2019S mutation carriers.

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.

Based on the DNL201 preclinical safety profile, the U.S. Food and Drug Administration ("FDA"), approved the Phase 1 clinical trial for DNL201 in May 2017 but placed DNL201 on a partial clinical hold in order to impose an exposure limit. In December 2017, the FDA removed the partial clinical hold based on our complete response submission including the safety and tolerability data generated by the DNL201 Phase 1 study in healthy volunteers and the results from additional preclinical studies. The DNL201 Phase 1 study is ongoing.

For DNL151, a CTA was submitted and accepted by the Netherlands Health Authority in December 2017. We believe the latest approved clinical protocol for DNL151 allows for exposures to achieve up to 85% LRRK2 inhibition on average over the dosing period and up to 80% at trough. The DNL151 Phase 1 study is ongoing.

Development Plan

We initiated a randomized, double-blind, placebo-controlled, single-center Phase 1 clinical trial in healthy young and healthy elderly subjects for DNL201 in June 2017 and for DNL151 in December 2017. These studies aim to investigate the safety and tolerability of single and multiple oral doses of DNL201 and DNL151 and characterize the PK and PD in plasma and CSF of each molecule respectively.

PK properties of DNL201 support twice a day dosing with a terminal half-life of approximately 14 to 22 hours. Steady state was achieved by approximately Study Day 8 after twice daily administration of DNL201 at 25 mg or 40 mg. PK profiles at Day 1 and steady state are shown in Figure 12.

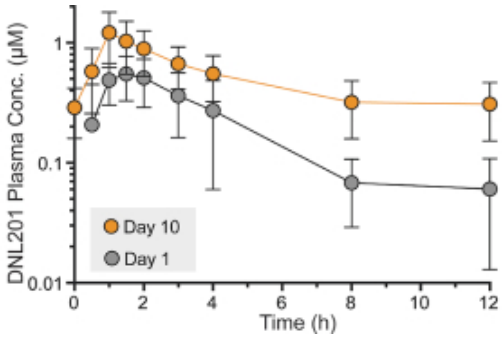


Figure 12: Mean DNL201 plasma concentration-time profiles on study days 1 and 10 in subjects administered 40 mg BID for 10 days.

DNL201 concentration was measured in CSF and plasma obtained from healthy subjects between 2 and 3.5 hours following a single 10 mg oral dose. DNL201 distributed extensively into CSF. The mean CSF/unbound plasma concentration ratio was 0.97. Comparable CSF distribution was observed after multiple dose administration of 25 mg BID, with a mean steady-state CSF/unbound plasma ratio of 1.17 (Figure 13).

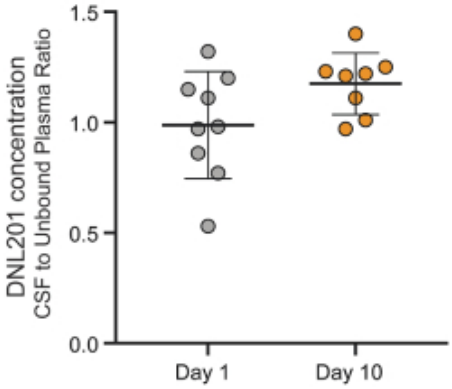


Figure 13: DNL201 concentrations in CSF and plasma from healthy subjects administered at 10mg on day 1 and 25mg BID on day 10.

We have two biomarkers in the Phase 1 studies for DNL201 and DNL151, pS935 and pRab10, that are secondary and exploratory endpoints to demonstrate target engagement, respectively. Phosphorylation of LRRK2 at serine 935 (pS935) is a well-established biomarker of LRRK2 kinase activity that has been demonstrated to respond to pharmacological inhibition. Rab10a is a member of the Rab GTPase family involved in endolysosomal function and is a direct substrate of LRRK2 kinase. Following single doses of DNL201, pS935 LRRK2 decreased by approximately 50% or greater in whole blood samples taken 1 to 3 hours postdose in subjects receiving 30 to 60 mg active drug. This response was both dose- and time-dependent.

In the multiple dose study, a peripheral PD effect of percent change in pS935 LRRK2 and change in pRab10 from baseline was assessed on Days 1 and 10 at multiple time points. Figure 14 shows the individual subject exposures for those treated with DNL201 40 mg BID on Days 1 and 10 of

dosing vs percent pS935 LRRK2 and pRab10 inhibition. These data provide evidence of concentration-dependent inhibition and target engagement, with means of greater than 50% and 90% inhibition of LRRK2 kinase activity observed at trough and peak drug levels, respectively (Figure 14), exceeding our LRRK2 clinical development goal of achieving at least 50% average target inhibition over the dosing interval. This target engagement goal is based on data indicating that LRRK2 activity in Parkinson's patients is estimated to be approximately twice that of healthy individuals.

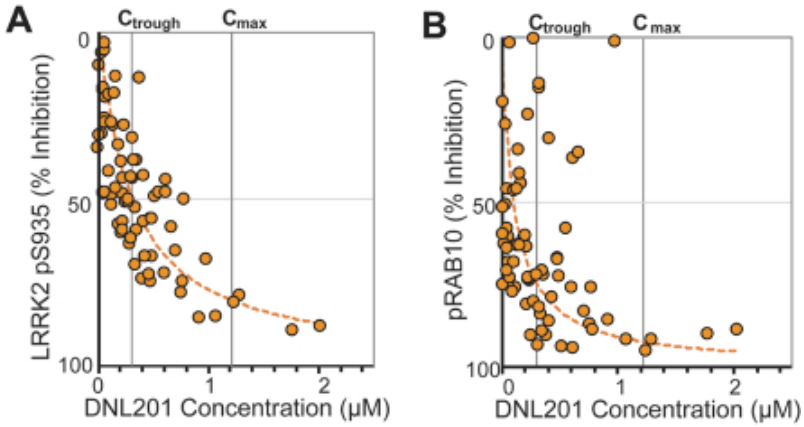


Figure 14: Percent change in whole blood pS935 (A) and PBMC pRAB10 (B) levels in healthy subjects treated with DNL201.

The same PK/PD analysis is being conducted with samples collected from the DNL151 Phase 1 clinical study.

After completion of the ongoing Phase 1 clinical trial in healthy volunteers for DNL201 and DNL151, we plan to progress either 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.

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. Our CTA for DNL747 was submitted and accepted by the Netherlands Health Authority in February 2018. We commenced and achieved first in human dosing in our Phase 1 clinical trial in healthy volunteers in March 2018.

During this Phase 1 trial, we are taking two biomarker approaches to determine the extent of target engagement achieved. First, a novel assay of autophosphorylation of RIPK1 at Serine 166 ("pS166"), will provide quantitative measurement of target engagement in the blood of subjects following single or multiple doses of our DNL747. Secondly, we are measuring exploratory biomarkers of inflammation in the CSF of subjects to confirm and measure target engagement in the central nervous system.

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. Genome wide association studies ("GWAS") identified that a large proportion of genetic risk factors for late-onset Alzheimer's disease are expressed almost exclusively by microglia, the resident immune cells of the brain, thus implicating microglia as an important effector of neurodegeneration. ALS-causing mutations in optineurin ("OPTN") result in increased RIPK1 activity in microglia, while two additional ALS-risk genes, Tank Binding Kinase ("TBK") and TNFAIP3-interacting protein 1 ("TNIP1"), regulate RIPK1 signaling in cell-based experiments.

Stimulation of RIPK1 signaling in cultured microglia produces cytokines and other pro-inflammatory factors, including Ccl2 ("MCP-1"), IL-1b, and IL-6, while treatment with RIPK1 inhibitors attenuates induction of these factors. Production of these pro-inflammatory cytokines by activated microglia can cause tissue damage and neuronal death. An increase in RIPK1 has been observed both in the brains of animal models of chronic neurodegeneration and patients with Alzheimer's disease that is correlated with the extent of pathology, suggesting RIPK1 activation is increased in disease.

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.

Pharmacological Properties and Brain Exposure

In vitro studies demonstrate that DNL747 is highly selective against kinase and receptor panels. 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. Target engagement has been characterized using a marker of RIPK1 activity, phosphorylation of RIPK1 at 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.

Comprehensive toxicity studies, including GLP 28-day repeat-dose studies in rat and monkey and safety pharmacology studies are complete. No concerns were identified in *in vitro* safety screening for genotoxicity, cardiovascular ion channel inhibition, and hepatotoxicity assessments. In the 28-day GLP study in rat, administration of DNL747 at dose levels up to the highest dose of 500 mg/kg BID were well tolerated; with findings limited to minimal, non-adverse changes associated with metabolic enzyme induction that are not considered relevant to humans. In the 28-day GLP study in cynomolgus monkey, administration of DNL747 was well tolerated to the mid dose of 100 mg/kg BID, with cutaneous/mucocutaneous lesions and immune-mediated histopathology findings noted at the high dose of 500 mg/kg BID.

Development Plan

Our Phase 1 clinical trial in healthy volunteers was initiated in March 2018. The Phase 1 study is a randomized, double-blind, placebo-controlled, single-center clinical trial in healthy 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 based on DNL747 exposures measured in CSF. 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 and 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 and ALS 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 and Phase 1b trials in healthy volunteers and patients, we plan to proceed to two Phase 2a studies evaluating biomarker endpoints in Alzheimer's disease and ALS. The primary objectives of these patient studies are 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 September 2016, we initiated a Phase 1 clinical trial in the Netherlands for an earlier RIPK1 inhibitor compound, 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 doses developed liver test abnormalities during the post dosing recovery period. 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 development of DNL104.

ETV:IDS Enzyme Replacement Therapy Program

We are developing ETV:IDS as a treatment for the lysosomal storage disorder MPS II. 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 ("GAGs"), heparan and dermatan sulfate, and its deficiency results in a toxic accumulation of these GAGs and perturbed lysosomal function. Approximately two-thirds of MPS II 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. MPS II is currently treated with intravenous infusions of recombinant IDS protein. These treatments 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.

We are developing therapeutic fusion proteins that effectively cross the BBB and diffuse to critical peripheral tissues. Lead ETV:IDS proteins are currently in preclinical development, and we plan to file an IND or CTA in early 2019.

ATV:aSyn Program

Our ATV:aSyn program targets aSyn, a protein that has been identified as genetically linked to 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.

We have developed high affinity antibodies binding to the multiple forms of aSyn and we 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. Following proof of concept in Parkinson's disease, patients with other synucleinopathies, such as dementia with Lewy bodies, or DLB, and multiple system atrophy ("MSA"), may also benefit and could be explored.

ATV:TREM2 Program

ATV: TREM2 is a therapeutic candidate designed to rescue microglial function in Alzheimer's disease through modulating the activity of TREM2, a genetically validated target. 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. 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.

We have developed high affinity antibodies for TREM2 and are currently characterizing antibodies 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.

As described in more detail in "Business - Licenses and Collaborations" below, Takeda has the right to opt in to our ATV:TREM2 program.

ATV:BACE1/Tau Program

ATV:BACE1/Tau is a bispecific program targeting the production of amyloid beta ("Abeta"), and the spreading of Tau, the two key pathological processes of Alzheimer's disease. 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 ("APP"), which is generated by cleavage of APP by BACE1 and gamma secretase. Mutations in APP processing components that increase Abeta levels are sufficient to cause early onset Alzheimer's disease. Tau is believed to regulate microtubule stability in neurons, but it can also aggregate to form neurofibrillary tangles present in many neurodegenerative diseases, including 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 believe our ATV:BACE1/Tau program may be the first therapeutic to target both of the hallmark pathologies of Alzheimer's disease in a single therapeutic agent and has the potential for synergistic activity, restoring protein homeostasis with regards to these pathologies. We plan to file an IND or CTA in 2020.

As described in more detail in "Business - Licenses and Collaborations" below, Takeda has the right to opt in to our ATV:BACE1/Tau program.

Licenses and Collaborations

Takeda Option and Collaboration Agreement

Overview

On January 3, 2018, we entered into the Collaboration Agreement with Takeda, pursuant to which we granted Takeda an option with respect to our ATV:BACE1/Tau program, our ATV: TREM2 program, and a third identified, but yet undisclosed discovery stage program. The Collaboration Agreement became effective on February 12, 2018 when the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976 were satisfied.

Research Phase and Takeda's Option

Under the Collaboration Agreement and unless we otherwise agree jointly with Takeda, we will be responsible, at our cost, for conducting activities relating to pre-IND development of biologic products directed to the three identified targets and enabled by our BBB delivery technology targeting transferrin receptor during the applicable option period. The option period continues for each target until the first biologic product candidate directed to the relevant target is IND-ready or about five years after selection of the target, whichever is earlier.

For a limited period of time, subject to further limitations and the mutual agreement of the parties, the ATV:TREM2 program and the undisclosed program can each be replaced one time. If the parties cannot agree on a proposed replacement target, the rejecting party will be restricted, subject to certain exceptions and only for a specified period of time, from conducting additional activities related to any antibody or other protein-based therapeutic product directed to the proposed replacement target outside the collaboration.

Takeda is obligated to pay us up to an aggregate of $25.0 million with respect to each program under the Collaboration Agreement directed to a target and based upon the achievement of certain preclinical milestone events, up to $75.0 million in total. $5.0 million of this amount became due when the Collaboration Agreement became effective.

Collaboration Activities Following Takeda's Option Exercise

If Takeda exercises its option with respect to a particular target and collaboration program (i.e., the biologic products directed to the target for which Takeda has exercised its option), then Takeda will have the right to develop and commercialize, jointly with us, a specified number of biologic products enabled by our blood-brain barrier delivery technology that were developed during the option period and which are directed to the relevant target, and we will grant to Takeda a co-exclusive license under the intellectual property we control related to those biologic products.

Takeda is obligated to pay us a $5.0 million option fee for each target for which Takeda exercises its option, up to $15.0 million in total.

In addition, Takeda will be obligated to pay us up to an aggregate of $707.5 million upon achievement of certain clinical and regulatory milestone events if Takeda exercises its option for all three collaboration programs. Further, Takeda will be obligated to pay us up to $75.0 million per biologic product upon achievement of a certain sales-based milestone, or an aggregate of $225.0 million if one biologic product from each program achieves the milestone.

After Takeda exercises its option for a particular target, we and Takeda will share equally the development and commercialization costs, and, if applicable, the profits, for each collaboration

program. However, for each collaboration program, we may elect not to continue sharing development and commercialization costs, or Takeda may elect to terminate our cost-profit sharing rights and obligations if, following notice from Takeda and a cure period, we fail to satisfy our cost sharing obligations with respect to the relevant collaboration program. After such an election by us or termination by Takeda becomes effective, we will no longer be obligated to share in the development and commercialization costs for the relevant collaboration program, and we will not share in any profits from that collaboration program. Instead we will be entitled to receive tiered royalties. The royalty rates will be in the low- to mid-teen percentages on net sales, or low- to high-teen percentages on net sales if we have met a certain co-funding threshold at the time of our election to opt out of co-development or Takeda's termination of our cost-profit sharing rights and obligations, and, in each case, these royalty rates will be subject to certain reductions specified in the Collaboration Agreement. Takeda will pay these royalties to us for each biologic product included in the relevant collaboration program, on a country-by-country basis, until the latest of (i) the expiration of certain patents covering the relevant biologic product, (ii) the expiration of all regulatory exclusivity for that biologic product, and (iii) an agreed period of time after the first commercial sale of that biologic product in the applicable country, unless biosimilar competition in excess of a significant level specified in the Collaboration Agreement occurs earlier, in which case Takeda's royalty obligations in the applicable country would terminate.

For each collaboration program for which we are sharing costs and profits with Takeda, we will lead the conduct of clinical activities for each indication up to the first Phase 2 trial with a clinical outcomes-based efficacy endpoints, and Takeda will lead the conduct of all subsequent clinical activities for that indication. For each collaboration program for which we are sharing costs and profits with Takeda, we and Takeda will jointly commercialize biologic products included in the relevant collaboration program in the United States and China. Unless we have opted out of cost-sharing for two collaboration programs, we have the right to lead commercialization activities in the United States for one collaboration program and Takeda will lead commercialization activities in the United States for all collaboration programs for which we do not lead commercialization activities. Further, Takeda will lead commercialization activities in China and will solely conduct commercialization activities in all other countries.

We have the right to lead all manufacturing activities for all collaboration programs for which the parties are sharing costs and profits.

Exclusivity

During the option period for a particular target and, if the applicable option is exercised by Takeda (unless the Collaboration Agreement is terminated earlier), until expiration of an agreed period of time after the first regulatory approval in the United States or Europe of a biologic product within the applicable collaboration program, neither party may conduct clinical or commercial activities involving antibodies or protein-based therapeutic products directed to the same target (or in the case of a bi-specific program, the same combination of targets) that have an intended therapeutic effect in diseases and conditions of the CNS (including lysosomal storage diseases), except to the extent permitted under the Collaboration Agreement.

Termination

Each party may terminate the Collaboration Agreement in its entirety, or with respect to a particular collaboration program, as applicable, if the other party remains in material breach of the Collaboration Agreement following a cure period to remedy the material breach. Takeda may terminate the Collaboration Agreement in its entirety or with respect to any particular collaboration program, for convenience and after giving a specified amount of prior notice to us, but Takeda may not do so for a

certain period of time after the Effective Date of the Collaboration Agreement. Takeda may also terminate the Collaboration Agreement with respect to any collaboration program if the joint steering committee established under the Collaboration Agreement unanimously agrees that a material safety event has occurred with respect to the applicable collaboration program. We may terminate the Collaboration Agreement with respect to a particular collaboration program if Takeda fails to conduct material development and commercial activities for a specified period of time with respect to a collaboration program, unless Takeda cures such failure within a certain period of time. We and Takeda may each terminate the Collaboration Agreement in its entirety if the other party is declared insolvent or in similar financial distress or if, subject to a specified cure period, the other party challenges any patents licensed to it under the Collaboration Agreement.

Following any termination of the Collaboration Agreement with respect to a particular collaboration program or the Collaboration Agreement in its entirety, our rights to each terminated collaboration program will revert to us, Takeda will grant us a license to intellectual property owned by Takeda with respect to such collaboration program (which could be subject to certain royalty payments that would be negotiated at the time of such a termination) and, unless the termination was by Takeda on the basis of a material safety event, Takeda will conduct certain development, manufacturing and commercialization wind-down activities.

Common Stock Purchase Agreement

Pursuant to the terms of the Collaboration Agreement, we entered into a common stock purchase agreement (the “Purchase Agreement”) with Takeda on January 3, 2018, pursuant to which we agreed to issue and sell, and Takeda agreed to purchase, 4,214,559 shares of our common stock (the “Shares”) for an aggregate purchase price of $110.0 million pursuant to the terms and conditions thereof. We closed the sale of the Shares to Takeda on February 23, 2018.

We and Takeda also entered into a standstill and stock restriction agreement (the “Standstill Agreement”). Pursuant to the terms of the Standstill Agreement, Takeda agreed to certain transfer and standstill restrictions, including a restriction on acquiring more than 10% of our capital stock, for a specified period of time following the closing of the sale of the Shares to Takeda, or earlier upon our change of control or, with respect to the transfer restrictions, termination of the Collaboration Agreement. In addition, Takeda is entitled to certain registration rights with respect to the Shares following termination of the transfer restrictions if the Shares cannot be resold without restriction pursuant to Rule 144 promulgated under the Securities Act of 1933, as amended.

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 (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.

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 LRRK2 small molecule program. Under the agreement, Genentech granted us (i) an exclusive, worldwide, sublicensable 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, sublicensable 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.

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 ("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, including Lonza Sales AG, or Lonza. Effective September 2017, we entered into a development and manufacturing services agreement with Lonza, which agreement we have subsequently amended to add the scope of work under this agreement. We refer to this agreement, as amended, as the DMSA or the Lonza agreement. Pursuant to the Lonza agreement, Lonza agreed to provide clinical development and manufacturing services with respect to certain of our biologic products on a fee-for-service basis.

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, Voyager Therapeutics, 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.

As of February 28, 2018, our owned and licensed patent portfolio includes over 650 patents and patent applications, including over 20 licensed U.S. issued patents, over 15 licensed U.S. pending patent applications, 2 owned U.S. issued patents, and over 30 owned U.S. pending patent applications, covering certain aspects of our proprietary technology, our product candidates, and related inventions and improvements. The patent portfolio also includes over 200 licensed patents issued in jurisdictions outside of the United States, over 85 licensed patent applications pending in jurisdictions outside of the United States, and over 10 owned patent applications pending in jurisdictions outside of the United States that, in many cases, are counterparts to the foregoing U.S. patents and patent applications. For our product candidates and our BBB platform technology, we generally pursue or in-license patent protection covering compositions of matter, methods of use and manufacture. For example, we own patent applications in the United States and internationally that are directed to the composition of matter of certain antibodies and small molecule product candidates that we intend to develop or are developing, as well as the Fc domain portion of our BBB platform technology.

For our BBB platform technology and ATV/ETV programs, we license multiple patent families from F-star, the earliest issued patents of which are expected to expire in 2026, not including any patent term adjustments and any patent term extensions. Furthermore, we own pending patent applications directed to the composition and sequences of our TfR-binding ATVs and other BBB platform technology. For our ATV:BACE1/Tau program, we license patents from VIB, which are expected to expire in 2030, not including any patent term adjustments and any patent term extensions. Furthermore, we own patent applications directed to our ATV:BACE1/Tau, ATV:aSyn, ATV:TREM2, and ETV:IDS programs. For our LRRK2 program, we license multiple patent families from Genentech directed to, among other things, our LRRK2 program, including DNL201, DNL151 and other related compounds, which are expected to expire in 2031, not including any patent term adjustments and any patent term extensions; and we own pending patent applications directed to the composition of matter of DNL151. For our RIPK1 program, we own two issued U.S. patents, which are expected to expire in 2037, not including any patent term adjustments and any patent term extensions and pending patent applications, which are directed to the composition of matter of DNL747 as well as other RIPK1 inhibitor compounds.

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 ("FDCA"), and its implementing regulations, and biologics under the FDCA, the Public Health Service Act ("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 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 ("NDA"), or a biologics license application ("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 ("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 ("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 ("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 ("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 ("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 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 PK and PD 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 ("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 ("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 ("PPACA"), Affordable Care Act ("ACA"), signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("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 PK or PD) 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 (“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 ACA 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 ACA. 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 Act. The Hatch-Waxman Act permits 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 ("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 (“NCA”), and one or more Ethics Committees (“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 (“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 ("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 ("CHMP"), of the European Medicines Agency ("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 ("RMS"). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics ("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 ACA 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 ACA 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 ("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 ACA 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 ("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 ("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 ACA 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.

Research and Development

We recognized $74.5 million, $75.7 million, and $11.6 million of research and development expenses in the years ended December 31, 2017, 2016 and 2015, respectively. The majority of these research and development expenses have related to the development of our RIPK1 and LRRK2 programs and our BBB platform technology.

Financial Information about Segments

We manage our operations as a single reportable segment for the purposes of assessing performance and making operating decisions. See “Note 1 - Significant Accounting Policies” in the notes to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Employees

As of December 31, 2017, we had approximately 130 employees, all of whom were full-time and around 110 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 is represented by a labor union or covered by a collective bargaining agreement.

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. We also use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.

We file, or will file, electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.denalitherapeutics.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read

or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov. The information in or accessible through the SEC and our website or social media sites does not constitute part of this Annual Report on Form 10-K or any other report or document we file with the SEC, and any references to our website and social media sites are intended to be inactive textual references only.

We use Denali Therapeutics®, the Denali Therapeutics logo, and other marks as trademarks in the United States and other countries. This Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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.

ITEM 1A. 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 Annual Report on Form 10-K, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." 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 and the market price of our common stock.

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 ("ALS"). We commenced operations in May 2015, have no products approved for commercial sale and have not generated any product revenue. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have recently initiated clinical trials for our LRRK2 and RIPK1 core programs 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 $88.2 million, $86.7 million, and $16.8 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $191.7 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 ("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;

- 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 product 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 three product candidates, DNL201, DNL151 and DNL747, 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.

As of December 31, 2017, we had $467.0 million in cash, cash equivalents and marketable securities. 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 13 programs. We designate certain programs as core programs and others as seed programs. Together, these programs require significant capital investment. We currently have seven core programs and six seed programs which are at various stages of research, discovery, preclinical and early clinical 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 five 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.

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 drug delivery platform technology designed 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, and two product candidates, DNL151 and DNL747, in Phase 1 clinical trials in healthy volunteers in the Netherlands. 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 six 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 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, which are biological molecules found in blood, other bodily fluids or tissues that are signs of a normal or abnormal process or of a condition or disease, 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, is currently in a Phase 1 clinical trial in healthy volunteers. This program was previously subject to a partial clinical hold due to preclinical toxicity data

that was removed in December 2017 based on additional clinical and preclinical data. Our second most advanced product candidate, DNL151, is currently in a Phase 1 clinical trial in healthy volunteers. Our third most advanced product candidate, DNL747, is currently in a Phase 1 clinical trial in healthy volunteers. In the nonclinical safety studies for DNL201, DNL151, and DNL747, toxicities were observed at high doses in rat and/or cynomologus monkey above doses and exposures that will be tested in the clinic. We cannot assure you that DNL201, DNL151, DNL747 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, more advanced or more 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, 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 candidates, DNL201, DNL151, and DNL747 are currently our only clinical stage product candidates. In 2017, we initiated Phase 1 clinical trials of DNL201 and DNL151 in healthy volunteers and, to date, both have been well tolerated. We initiated a Phase 1 clinical trial of DNL747 in healthy volunteers in March 2018. Adverse events and other side effects may result from higher dosing, repeated dosing and/or longer-term exposure to DNL201, DNL151 and/or DNL747 and could lead to delays and/or termination of the development of these product candidates.

In 2016, we initiated a Phase 1 clinical trial in a former RIPK1 inhibitor product candidate, DNL104, which we subsequently discontinued based on liver function 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 collaborations with F-star, Takeda and 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;
- collaborators may control certain interactions with regulatory authorities, which may impact on our ability to obtain and maintain regulatory approval of our products candidates;
- 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 may restrict us from researching, developing or commercializing certain products or technologies without their involvement;
- 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 grant sublicenses to our technology or product candidates or undergo a change of control and the sublicensees or 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;
- If our collaborators do not satisfy their obligations under our agreements with them, or if they terminate our collaborations with them, we may not be able to develop or commercialize product candidates as planned;
- collaborations may require us to share in development and commercialization costs pursuant to budgets that we do not fully control and our failure to share in such costs could have a detrimental impact on the collaboration or our ability to share in revenue generated under the collaboration;
- collaborations may be terminated in their entirety or with respect to certain product candidates or technologies and, if so terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates or technologies, including 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 or for our BBB platform technology, our competitors could develop and commercialize products or 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, as of February 28, 2018, 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 United States patents covering the composition of matter of the Fc domain portion of our BBB platform technology that binds to transferrin receptor, or any issued United States patents that cover the composition of matter of antibodies or enzymes being developed in our 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 a 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. 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. For additional information, see "Business - Licenses and Collaborations."

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 December 31, 2017, we had approximately 130 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.

We have engaged in and may in the future engage in acquisitions or strategic partnerships, which 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 strategic partnerships, 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. For instance, in January 2018 we entered into the Collaboration Agreement with Takeda, and in connection therewith we issued and sold to Takeda 4,214,559 shares of our common stock for an aggregate purchase price of $110.0 million in February 2018. 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, 2017, we had federal net operating loss carryforwards of approximately $134.1 million, and federal research and development tax credit carryforwards of approximately

$2.9 million which will begin to expire in 2035. Under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, or the 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 initial public offering ("IPO") in December 2017 and recent private placements and other transactions that have occurred since our incorporation, we may have experienced 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 Ownership of Our Common Stock

An active trading market for our common stock may not be sustained.

Prior to our initial public offering in December 2017, there was no public market for our common stock. Although our common stock is listed on the NASDAQ Global Select Market, the market for our shares has demonstrated varying levels of trading activity. Furthermore, an active trading market may not be sustained in the future. The lack of an active market may impair investors' ability to sell their shares at the time they wish to sell them or at a price that they consider reasonable, may reduce the market value of their shares and may impair our ability to raise capital.

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

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors 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 to achieve development, regulatory or commercialization milestones under our collaborations;
- 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; and
- general economic, industry, and market conditions.

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. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of any such lawsuits could be costly and divert the time and attention of our management and harm our operating results, regardless of the merits of such a claim.

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 and trading volume 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. 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 or trading volume 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. As of December 31, 2017, we had 90,143,972 shares of common stock outstanding. Of these shares, the 15,972,221 shares sold in our initial public offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining 74,171,751 shares, or 82.3% of our outstanding shares as of December 31, 2017, 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 of our initial public offering; 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 as early as June 6, 2018.

In addition, on December 8, 2017, we filed a registration statement on Form S-8 registering 14,156,836 shares of our common stock reserved for future issuance under our equity compensation plans. As a result, shares registered under this registration statement on Form S-8 will be available for sale in the public market subject to the satisfaction of applicable vesting arrangements and the exercise of such options, the lock-up arrangements described above and, in the case of our affiliates, the restrictions of Rule 144.

Moreover, as of December 31, 2017, certain holders of approximately 64,913,502 shares of our common stock 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. Registration of these shares under the Securities Act would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. In addition, Takeda is entitled to certain registration rights with respect to the 4,214,559 shares of our common stock it purchased following termination of the transfer restrictions if such shares cannot be resold without restriction pursuant to Rule 144 promulgated under the Securities Act of 1933, as amended. 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.

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.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

As of December 31, 2017, our directors, executive officers, holders of more than 5% of our outstanding stock and their respective affiliates beneficially own shares representing approximately 84.2% of our outstanding common stock. As a result, these stockholders, if they act together, may significantly influence 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 that our other stockholders may believe is in their best interests. This in turn could have a material adverse effect on our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

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. 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, or December 31, 2022. References herein to "emerging growth company" are intended to have the meaning associated with it in 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. 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, are be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has been and will continue to be required to devote substantial time to new compliance initiatives and corporate governance practices, including maintaining an effective system of internal controls over financial reporting.

As a public company, and particularly after we are no longer an emerging growth company, we have incurred and will continue to 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 NASDAQ, 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 efforts to comply with the requirements of being, a public company, and our management and other personnel will need to continue to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements have and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. 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 are 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 not paid and do not expect to pay any dividends for the foreseeable future. Any return on investment may be limited to the value of our common stock.

We have never paid cash dividends on our common stock and do not anticipate that we will pay any dividends in the foreseeable future. We currently intend to retain our future earnings, if any, to maintain and expand our existing operations. If we do not pay dividends, our common stock may be less valuable because a return on your investment will only occur if our stock price appreciates

Delaware law and provisions in our charter documents 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 amended and restated bylaws 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:

- 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 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 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

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 five 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 to accommodate our anticipated growth. We believe that suitable additional or alternative space would be available as required in the future on commercially reasonable terms.

ITEM 3. 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.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock has been listed on The NASDAQ Global Select Market under the symbol "DNLI" since December 8, 2017. Prior to that date, there was no public trading market for our common stock. The following table sets forth for the periods indicated the high and low intraday sales price per share of our common stock as reported on The NASDAQ Global Select Market for the period indicated:

Year ended December 31, 2017:	High	Low
Fourth quarter (from December 8, 2017)	$ 22.95	$ 14.72

Holders of Common Stock

As of March 12, 2018, there were 156 holders of record of our common stock. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial owners of our common stock represented by these record holders.

Dividend Policy

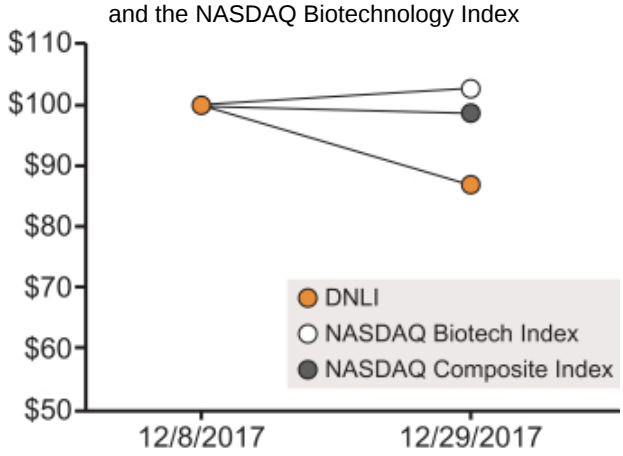
We have never declared or paid any cash dividends on our common stock or any other securities. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Payment of future cash dividends, if any, will be at the discretion of the board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of current or then-existing debt instruments and other factors the board of directors deems relevant.

Performance Graph

This graph is not "soliciting material" or deemed "filed" with the SEC for purposes of Section 18 of the Exchange Act, or otherwise subject to liabilities under that Section, and shall not be deemed incorporated by reference into any filing of Denali Therapeutics Inc. under the Securities Act of 1933, as amended (the "Securities Act"), whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following graph compares the cumulative total return to stockholder return on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of $100 is assumed to have been made in our common stock and each index on December 8, 2017 (the first day of trading of our common stock) and its relative performance is tracked through December 31, 2017. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder returns shown on the graph below are based on historical results and are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

COMPARISON OF CUMULATIVE TOTAL RETURN
among Denali Therapeutics Inc., the NASDAQ Composite Index
and the NASDAQ Biotechnology Index



	12/8/2017	12/31/2017
Denali Therapeutics Inc.	$ 100.00	$ 87.03
NASDAQ Composite Index	100.00	98.65
NASDAQ Biotechnology Index	100.00	102.71

Recent Sales of Unregistered Securities

The following list sets forth information regarding all unregistered securities sold by us from January 1, 2017 through March 12, 2018. 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. The share numbers have been adjusted, as appropriate, for the 4-for-1 reverse stock split that occurred on November 28, 2017.

(a) In November 2017, we issued 1,764,705 shares of our Series B-2 convertible preferred stock at $17.00 per share, for aggregate proceeds of $30.0 million, to a total of three accredited investors.

(b) In December 2017, we issued 81,164 shares of our common stock to one accredited investor, which we were obligated to issue upon certain milestones in relation to the acquisition of Incro Pharmaceuticals, Inc. (“Incro”). The milestones were satisfied and the shares were issued on December 20, 2017.

(c) From January 2017 through December 8, 2017 (the date of the filing of our registration statement on Form S-8, File No. 333-221956), we granted stock options to purchase an aggregate of 1,816,625 shares of common stock to certain employees, directors and consultants under our 2015 Stock Incentive Plan (the “2015 Plan”), at exercise prices per share ranging from $5.28 to $11.64, for an aggregate exercise price of approximately $12.8 million. From December 1, 2017 through December 8, 2017, we granted stock options to purchase an aggregate of 282,990 shares of common stock to certain employees, directors and consultants under our 2017 Equity Incentive Plan (the “2017 Plan”), at an exercise price per share of $18.00, for an aggregate exercise price of approximately $5.1 million.

(d) From January 2017 through December 8, 2017, we issued and sold an aggregate of 695,192 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 $0.68 to $5.28, for an aggregate exercise price of approximately $1.0 million.

(e) On February 23, 2018, we issued and sold 4,214,559 shares of common stock to Takeda for aggregate proceeds of $110.0 million in connection with the Collaboration Agreement.

The offer, sale and issuance of the securities described in clauses (a), (b) and (e) 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 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 clauses (c) and (d) 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.

Use of Proceeds from Registered Securities

On December 7, 2017, our Registration Statement on Form S-1 (File No. 333-221522) was declared effective by the SEC for our initial public offering of common stock. We started trading on The NASDAQ Global Select Market on December 8, 2017, and the transaction formally closed on December 12, 2017. In connection with the initial public offering, we sold an aggregate of 15,972,221 shares of common stock, including 2,083,333 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a price to the public of $18.00 per share. The aggregate offering price for shares sold in the offering was $287.5 million. The joint book-running managers for the initial public offering were Goldman, Sachs & Co, Morgan Stanley & Co. LLC, and J.P. Morgan Securities LLC. After deducting underwriting discounts, commissions and offering expenses paid or payable by us of approximately $23.2 million, the net proceeds from the offering were approximately $264.3 million. No offering expenses were paid or are payable, directly or indirectly, to our directors or officers, to persons owning 10% or more of any class of our equity securities or to any of our affiliates.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC on December 8, 2017 pursuant to Rule 424(b)(4). We invested the funds received in short-term, interest-bearing investment-grade securities and government securities.

Issuer Purchases of Equity Securities

Not applicable.

ITEM 6. SELECTED 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, 2017, 2016, and 2015 from our audited consolidated financial statements and related notes included elsewhere in this report.

Our historical results are not necessarily indicative of the results that may be expected in the future. 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 report.

	Year Ended December 31,		
	2017	2016	2015
	(In thousands, except share and per share amounts)		
Consolidated Statements of Operations and Comprehensive Loss Data:			
Operating expenses:			
Research and development	$ 74,460	$ 75,702	$ 11,571
General and administrative	15,680	11,731	5,108
Total operating expenses	90,140	87,433	16,679
Loss from operations	(90,140)	(87,433)	(16,679)
Interest income (expense), net	1,955	781	(109)
Net loss	(88,185)	(86,652)	(16,788)
Other comprehensive income (loss)	5	(373)	—
Comprehensive loss	$ (88,180)	$ (87,025)	$ (16,788)
Net loss per share, basic and diluted (1)	$ (5.89)	$ (13.49)	$ (5.58)
Weighted average number of shares outstanding, basic and diluted (1)	14,964,144	6,424,720	3,006,379

(1) See the consolidated statements of operations and Note 12 to our 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.

	As of December 31,		
	2017	2016	2015
	(in thousands)		
Consolidated Balance Sheets Data:			
Cash, cash equivalents and marketable securities	$ 466,976	$ 250,911	$ 30,740
Working capital (1)	395,443	172,849	29,950
Total assets	486,721	271,067	36,683
Total liabilities	20,925	16,548	4,009
Convertible preferred stock	—	348,673	48,308
Accumulated deficit	(191,697)	(103,512)	(16,860)
Total stockholders' equity (deficit)	465,796	(94,154)	(15,634)

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

ITEM 7. 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 Financial and Other Data" and our consolidated financial statements and the related notes to those statements included elsewhere in this report. This discussion and analysis and other parts of this report 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 report.

Overview

Our goal is to 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 genes that, when mutated, cause, or are major risk factors for, neurodegenerative diseases, which we refer to as degenogenes.
- **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 thirteen programs. To prioritize the allocation of our resources, we designate certain programs as core programs and others as seed programs, and we currently have seven core programs and six seed programs. 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 is currently in a Phase 1 clinical trial in healthy volunteers in the Netherlands. 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. We submitted a CTA for DNL747 to the Netherlands Health Authority in February 2018 and initiated a Phase 1 clinical trial in healthy volunteers in March 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 deep scientific, clinical, business and leadership experience and expertise.

- In May 2015, we entered into a preferred stock purchase agreement, which was subsequently amended, pursuant to which we raised aggregate gross 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 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 aggregate gross proceeds of $130.0 million 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 (“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.

- In October 2017, we submitted a CTA for DNL151 to the Netherlands Health Authority, and we initiated a Phase 1 clinical trial of DNL151 in healthy volunteers in the United States in December 2017.

- In November 2017, we further amended our preferred stock purchase agreement, pursuant to which we raised aggregate gross proceeds of $30.0 million from issuances of our Series B-2 convertible preferred stock in multiple closings.

- In December 2017, we completed our IPO pursuant to which we issued 15,972,221 shares of our common stock at a price of $18.00 per share. We received $264.3 million from the IPO, net of underwriting discounts and commissions, and offering expenses incurred by us.

- In January 2018, we entered into an option and collaboration agreement with Takeda pursuant to which we granted Takeda an option with respect to three of our programs to develop and commercialize, jointly with us, certain biologic products that are enabled by our BBB delivery technology and intended for the treatment of neurodegenerative disorders. Pursuant to this agreement, we received an upfront payment of $40.0 million in February 2018, as well as the first preclinical milestone payment of $5.0 million. Further, under the associated stock purchase agreement, we received proceeds of $110.0 million for the sale of 4,214,559 shares of our common stock which were issued on February 23, 2018.

- In February 2018, we submitted a CTA for DNL747 to the Netherlands Health Authority, and we initiated a Phase 1 clinical trial of DNL747 in healthy volunteers in the Netherlands in March 2018.

We do not have any products approved for sale and have not generated any product revenue since our inception. We have funded our operations primarily from the issuance and sale of convertible preferred stock, and the proceeds from our IPO.

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 $88.2 million, $86.7 million and $16.8 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $191.7 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.

License and Collaboration Agreements

Takeda

On January 3, 2018, we entered into the Collaboration Agreement with Takeda pursuant to which we granted Takeda an option with respect to three of our programs to develop and commercialize, jointly with us, certain biologic products that are enabled by our BBB delivery technology and intended for the treatment of neurodegenerative disorders. The three programs are Denali's ATV:BACE1/Tau and ATV: TREM2 programs, and a third identified, but yet undisclosed discovery stage program. The Collaboration became effective on February 12, 2018 when the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976 were satisfied.

Under the terms of the Collaboration Agreement, Takeda paid us a $40.0 million upfront payment, and is obligated to pay us up to an aggregate of $25.0 million with respect to each program under the Collaboration Agreement directed to a target and based upon the achievement of certain preclinical milestone events, up to $75.0 million in total, of which $5.0 million became due when the Collaboration Agreement became effective and was subsequently paid to us. Takeda is also obligated to pay us a $5.0 million option fee for each target for which Takeda exercises its option, up to $15.0 million in total.

Pursuant to the terms of the Collaboration Agreement, we entered into the Purchase Agreement with Takeda on January 3, 2018, pursuant to which we agreed to issue and sell, and Takeda agreed to

purchase, 4,214,559 shares of our common stock for an aggregate purchase price of $110.0 million. We closed the sale of the 4,214,559 shares of our common stock to Takeda on February 23, 2018.

After Takeda exercises its option for a particular target, we and Takeda will share equally the development and commercialization costs, and, if applicable, the profits, for each collaboration program. However, for each collaboration program, we may elect not to continue sharing development and commercialization costs, or Takeda may elect to terminate our cost-profit sharing rights and obligations if, following notice from Takeda and a cure period, we fail to satisfy our cost sharing obligations with respect to the relevant collaboration program. After such an election by us or termination by Takeda becomes effective, we will no longer be obligated to share in the development and commercialization costs for the relevant collaboration program, and we will not share in any profits from that collaboration program. Instead we will be entitled to receive tiered royalties. The royalty rates will be in the low- to mid-teen percentages on net sales, or low- to high-teen percentages on net sales if we have met a certain co-funding threshold at the time of our election to opt out of co-development or Takeda's termination of our cost-profit sharing rights and obligations, and, in each case, these royalty rates will be subject to certain reductions specified in the Collaboration Agreement. Takeda will pay these royalties to us for each biologic product included in the relevant collaboration program, on a country-by-country basis, until the latest of (i) the expiration of certain patents covering the relevant biologic product, (ii) the expiration of all regulatory exclusivity for that biologic product, and (iii) an agreed period of time after the first commercial sale of that biologic product in the applicable country, unless biosimilar competition in excess of a significant level specified in the Collaboration Agreement occurs earlier, in which case Takeda's royalty obligations in the applicable country would terminate.

Takeda will be obligated to pay us up to an aggregate of $707.5 million upon achievement of certain clinical and regulatory milestone events if Takeda exercises its option for all three collaboration programs. Furthermore, Takeda will be obligated to pay us up to $75.0 million per biologic product upon achievement of a certain sales-based milestone, or an aggregate of $225.0 million if one biologic product from each program achieves the milestone.

F-star

In August 2016, we entered into a License and Collaboration Agreement ("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 expenses incurred by F-star in conducting activities under each agreed development plan, for up to 24 months. These research expenses 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 ("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.

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 $1.1 million and $0.3 million of research and development expense related to the funding of F-star Gamma research costs for the years ended December 31, 2017 and 2016, respectively.

Genentech

On June 17, 2016, we entered into an Exclusive License Agreement with Genentech. The agreement gives us access to Genentech's LRRK2 small molecule program. 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 during the year ended December 31, 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 studies.

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 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 years ended December 31, 2017 and 2016

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

	Year Ended December 31,		Change	
	2017	2016	$	%
Operating expenses:				
Research and development	$ 74,460	$ 75,702	$ (1,242)	(2) %
General and administrative	15,680	11,731	3,949	34
Total operating expenses	90,140	87,433	2,707	3
Loss from operations	(90,140)	(87,433)	(2,707)	3
Interest income, net	1,955	781	1,174	150
Net loss	$ (88,185)	$ (86,652)	$ (1,533)	2 %

Research and development expenses. Research and development expenses were $74.5 million for the year ended December 31, 2017 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,		Change	
	2017	2016	$	%
LRRK2 program external expenses (1)	$ 13,515	$ 16,770	$ (3,255)	(19) %
RIPK1 program external expenses (2)	10,426	19,106	(8,680)	(45)
BBB platform external expenses (3)	3,294	8,016	(4,722)	(59)
Other external research and development expenses	10,428	8,020	2,408	30
Personnel related expenses (4)	23,466	14,974	8,492	57
Other unallocated research and development expenses	13,331	8,816	4,515	51
Total research and development expenses	$ 74,460	$ 75,702	$ (1,242)	(2) %

(1) Payments under the license agreement with Genentech for a milestone payment of $2.5 million and an upfront payment and technology transfer fee totaling $10.0 million are included in the amounts for the year ended December 31, 2017 and 2016, respectively.
(2) The amount for the year ended December 31, 2016 includes $5.3 million in expenses related to contingent stock consideration 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 $2.9 million and $2.1 million for the years ended December 31, 2017 and 2016, respectively, reflecting an increase of $0.8 million.

The decrease in total research and development expenses of $1.2 million was primarily attributable to an $8.7 million decrease in RIPK1 program external expenses and a $4.7 million decrease in BBB platform external expenses. The decrease in RIPK1 is primarily due to the $5.3 million expense associated with the issuance of our common stock to former shareholders of Incro as contingent consideration for our acquisition of Incro in the year ended December 31, 2016, as well as the termination of the Phase 1 clinical trial for DNL104 in April 2017. The decrease in BBB

platform expenses is due to the payment of $5.5 million made under our license and collaboration agreement with F-star in the year ended December 31, 2016, partially offset by increased expenses incurred in the year ended December 31, 2017 to support preclinical development of our BBB platform.

These decreases in external research and development expenses were partially offset by a $8.5 million increase in personnel related expenses due to an increase in our research and development headcount and a $4.5 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 $2.3 million and an increase in facilities related expenses of $2.5 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.

General and administrative expenses. General and administrative expenses were $15.7 million for the year ended December 31, 2017 compared to $11.7 million for the year ended December 31, 2016. The increase of $3.9 million was primarily attributable to a $1.9 million increase in personnel related expenses due to an increase in our general and administrative headcount, a $1.3 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 $2.0 million for the year ended December 31, 2017 compared to $0.8 million for the year ended December 31, 2016. The increase of $1.2 million reflects that the marketable securities balances were higher in 2017 than in 2016, and the increased interest rates in 2017.

Comparison of the years ended December 31, 2016 and 2015

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

	Year Ended December 31,		Change	
	2016	2015	$	%
Operating expenses:				
Research and development	$ 75,702	$ 11,571	$ 64,131	554 %
General and administrative	11,731	5,108	6,623	130
Total operating expenses	87,433	16,679	70,754	424
Loss from operations	(87,433)	(16,679)	(70,754)	424
Interest income (expense), net	781	(109)	890	*
Net loss	$ (86,652)	$ (16,788)	$ (69,864)	416 %

* Percentage is not meaningful.

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

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

	Year Ended December 31,		Change	
	2016	2015	$	%
LRRK2 program external expenses (1)	$ 16,770	$ 777	$ 15,993	* %
RIPK1 program external expenses (2)	19,106	2,256	16,850	747
BBB platform external expenses (3)	8,016	33	7,983	*
Other external research and development expenses	8,020	3,305	4,715	143
Personnel related expenses (4)	14,974	2,943	12,031	409
Other unallocated research and development expenses	8,816	2,257	6,559	291
Total research and development expenses	$ 75,702	$ 11,571	$ 64,131	554 %

(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, 2016 and 2015 include $5.3 million and $1.5 million in expenses related to contingent and initial 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 $2.1 million and $0.1 million in the years ended December 31, 2016 and 2015 respectively, with the increase driven by higher headcount and a higher estimated fair value of our common stock.

* Percentage is not meaningful.

The increase in total research and development expenses of $64.1 million was primarily attributable to a $16.9 million increase in RIPK1 program external expenses and a $16.0 million increase in 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. Further, there was an 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 $11.7 million for the year ended December 31, 2016 compared to $5.1 million for the year ended December 31, 2015. 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 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 income, net was $0.8 million for the year ended December 31, 2016 compared to interest expense, net of $(0.1) million for the year ended December 31, 2015. 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

We have funded our operations primarily from the issuance and sale of convertible preferred stock, and the proceeds from our IPO. In December 2017, we completed our IPO pursuant to which we issued 15,972,221 shares of our common stock, including 2,083,333 shares sold pursuant the underwriters' full exercise of their option to purchase additional shares, at a price of $18.00 per share. We received $264.3 million from our IPO, net of underwriting discounts and commissions, and offering expenses incurred by us. As of December 31, 2017, we had cash, cash equivalents and marketable securities in the amount of $467.0 million.

Pursuant to the Collaboration Agreement with Takeda, we received a $40.0 million upfront payment and a $5.0 million preclinical milestone in February 2018. Further, under the associated Purchase Agreement we received $110.0 million in February 2018 for the sale and issuance of 4,214,559 shares of our common stock.

Future Funding Requirements

To date, we have not generated any product revenue. We do not expect to generate any product revenue unless and until we obtain regulatory approval of and commercialize any of our product candidates, 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. Further, we expect general and administrative expenses to increase as we will now incur additional costs associated with operating as a public company. 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. 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 the Collaboration Agreement, or future agreements with other 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 $191.7 million through December 31, 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. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including:

- 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,		
	2017	2016	2015
Cash used in operating activities	$ (76,635)	$ (72,359)	$ (15,052)
Cash used in investing activities	(41,166)	(219,004)	(3,062)
Cash provided by financing activities	296,323	300,476	48,854
Net increase in cash and cash equivalents	$ 178,522	$ 9,113	$ 30,740

Cash Used in Operating Activities

During the year ended December 31, 2017, cash used in operating activities was $76.6 million, which consisted of a net loss of $88.2 million, adjusted by non-cash expenses of $8.2 million and cash provided by changes in our operating assets and liabilities of $3.3 million. The non-cash expenses consisted primarily of stock-based compensation expense of $4.4 million and depreciation expense of $3.1 million. The change in our operating assets and liabilities was primarily due to an increase of $3.6 million in accrued and other current liabilities, mainly attributable to an increase in accrued compensation due to our continued growth, and accruals for legal expenses incurred in connection with our IPO and negotiation of the Collaboration Agreement with Takeda.

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 expenses of $10.0 million and cash provided by changes in our operating assets and liabilities of $4.3 million. The non-cash expenses 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 expenses of $1.3 million and cash provided by changes in our operating assets and liabilities of $0.4 million. The non-cash expenses 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 Used in Investing Activities

During the year ended December 31, 2017, cash used in investing activities was $41.2 million, which consisted of $179.8 million of purchases of short-term marketable securities, partially offset by

$141.5 million in proceeds from the maturity of marketable securities, and $2.9 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 year ended December 31, 2017, cash provided by financing activities was $296.3 million, which primarily consisted of net proceeds from our IPO of $265.6 million and net proceeds from issuance of shares of our Series B-2 convertible preferred stock of $30.0 million.

During the years ended December 31, 2016 and 2015, cash provided by financing activities was $300.5 million and $48.9 million, respectively, which primarily consisted 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. During the year ended December 31, 2016, net proceeds from our sale of Series A and Series B-1 convertible preferred stock were $300.4 million. During the year ended December 31, 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, 2017 (in thousands):

	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease obligations (1)	$ 18,529	$ 2,586	$ 5,409	$ 5,744	$ 4,790
Obligations under license and other contractual agreements (2)	2,017	1,048	329	140	500
Purchase Commitments	1,032	1,032	—	—	—
Total contractual obligations	$ 21,578	$ 4,666	$ 5,738	$ 5,884	$ 5,290

(1) Represents future minimum lease payments under our operating lease. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Represents non-cancellable fees due in connection with license and other contractual agreements, including the Lonza agreement.

In the normal course of business, we enter into various firm purchase commitments primarily related to research and development activities. As of December 31, 2017, we had noncancelable purchase commitments of $1.0 million and obligations under license and other contractual agreements of $1.6 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.

Effective September 2017, we entered into a development and manufacturing services agreement, as amended (the “DMSA” or the “Lonza agreement”), with Lonza Sales AG (“Lonza”), for the development and manufacture of biologic products. Under the DMSA, we will execute purchase orders based on project plans authorizing Lonza to provide development and manufacturing services with respect to certain of our antibody and enzyme products, and will pay for the services provided and batches delivered in accordance with the DMSA and project plan. Unless earlier terminated, the Lonza agreement will expire on September 6, 2022. As of December 31, 2017, we had executed the First Amendment to the DMSA (“First Amendment”), totaling $0.7 million for the development and manufacture of biologic products, the activities under which commenced in January 2018 and are expected to be completed in May 2019. As of December 31, 2017, we had not incurred any amounts or made any payments for the manufacturing services rendered and we have total non-refundable purchase commitments of $0.4 million under the First Amendment.

In January 2018, we executed the Second Amendment to the DMSA (“Second Amendment”), which included services totaling $11.4 million for the development and manufacture of biologic products, the activities under which commenced in January 2018 and are expected to be completed in December 2020. As of March 12, 2018, we had total non-refundable purchase commitments of $2.8 million related to the Second Amendment.

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 (“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 report, 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.

We estimate the fair value of stock options granted to our employees and directors on the grant date, and rights to acquire stock granted under our Employee Stock Purchase Plan (“ESPP”), 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 we have very limited 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.

Determination of the estimated fair value of our common stock on grant dates prior to our IPO

As there was no public market for our common stock prior to our IPO, the estimated fair value of our common stock was 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.

We 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* ("Practice Aid"). In accordance with the Practice Aid, our board of directors considered the following methods:

- *Current Value Method.* Under the Current Value Method ("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 ("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 ("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 board of directors and management developed 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.

Determination of the fair value of our common stock on grant dates following our IPO

The fair value of each share of underlying common stock is based on the closing price of our common stock as reported by The NASDAQ Global Select Market on the date of grant.

Stock-based compensation expense was $4.4 million, $3.0 million and $0.5 million for the years ended December 31, 2017, 2016, and 2015, respectively. As of December 31, 2017, we had $17.7 million of total unrecognized stock-based compensation expenses which we expect to recognize over a weighted-average period of 3.2 years.

We have not recognized, and we do not expect to recognize in the near future, any tax benefit related to employee stock-based compensation expense as a result of the full valuation allowance on our deferred tax assets including deferred tax assets related to our net operating loss carryforwards.

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, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Subject to certain conditions set forth in the JOBS Act, as an emerging growth company, we intend to rely on certain exemptions and reduced reporting requirements provided by the JOBS Act,

including those relating to (i) providing an auditor's attestation report on our system of internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying 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, known as the auditor discussion and analysis.

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) December 31, 2022.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") 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. There will be no impact to the consolidated financial statements upon adoption of ASU 2014-09 as we have not generated revenue through December 31, 2017.

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, 2018, including interim periods within those fiscal years, with early adoption permitted. We plan to adopt this standard on January 1, 2019. 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 No. 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.

We plan to adopt this standard on January 1, 2018. 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 No. 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 plan to adopt this standard on January 1, 2018. 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.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business, primarily related to interest rate and foreign currency sensitivities.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $467.0 million as of December 31, 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 British Pounds, Swiss Francs and the Euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies 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.

ITEM 8. FINANCIALSTATEMENTS AND SUPPLEMENTARY DATA

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Denali Therapeutics Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Denali Therapeutics Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting 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.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.
Redwood City, California
March 19, 2018

Denali Therapeutics Inc.

Consolidated Balance Sheets
(In thousands, except share amounts)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 218,375	$ 39,853
Short-term marketable securities	187,851	138,478
Prepaid expenses and other current assets	3,381	3,624
Total current assets	409,607	181,955
Long-term marketable securities	60,750	72,580
Property and equipment, net	14,923	15,262
Other non-current assets	1,441	1,270
Total assets	$ 486,721	$ 271,067
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 2,716	$ 1,963
Accrued liabilities	5,364	3,850
Accrued compensation	5,166	2,592
Deferred rent	855	538
Other current liabilities	63	163
Total current liabilities	14,164	9,106
Deferred rent	6,294	7,045
Other non-current liabilities	467	397
Total liabilities	20,925	16,548
Commitments and contingencies (Note 7)		
Convertible preferred stock, $0.01 par value; 40,000,000 and 63,288,466 shares authorized as of December 31, 2017 and 2016, respectively; 0 and 58,600,315 shares issued and outstanding as of December 31, 2017 and 2016, respectively; aggregate liquidation preference of $0 and $370,071 as of December 31, 2017 and 2016, respectively	—	348,673
Stockholders' equity (deficit):		
Common stock, $0.01 par value; 400,000,000 and 83,587,362 shares authorized as of December 31, 2017 and 2016, respectively; 87,480,362 shares and 8,597,316 shares issued and outstanding as of December 31, 2017 and 2016, respectively	1,201	344
Additional paid-in capital	656,660	9,387
Accumulated other comprehensive loss	(368)	(373)
Accumulated deficit	(191,697)	(103,512)
Total stockholders' equity (deficit)	465,796	(94,154)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 486,721	$ 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,		
	2017	2016	2015
Operating expenses:			
Research and development	$ 74,460	$ 75,702	$ 11,571
General and administrative	15,680	11,731	5,108
Total operating expenses	90,140	87,433	16,679
Loss from operations	(90,140)	(87,433)	(16,679)
Interest income (expense), net	1,955	781	(109)
Net loss	(88,185)	(86,652)	(16,788)
Other comprehensive gain (loss):			
Net unrealized gain (loss) on marketable securities, net of tax	5	(373)	—
Comprehensive loss	$ (88,180)	$ (87,025)	$ (16,788)
Net loss per share, basic and diluted	$ (5.89)	$ (13.49)	$ (5.58)
Weighted average number of shares outstanding, basic and diluted	14,964,144	6,424,720	3,006,379

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2014	—	$ —	887,324	$ 35	$ —	$ —	$ (70)	$ (35)
Issuance of common stock	—	—	2,815,787	113	(1)	—	(2)	110
Issuance of common stock as consideration in asset acquisition	—	—	472,942	19	581	—	—	600
Issuance of series A-1 convertible preferred stock, net of issuance costs of $484	12,197,880	48,308	—	—	—	—	—	—
Vesting of restricted stock awards	—	—	84,507	3	(3)	—	—	—
Stock-based compensation	—	—	—	—	479	—	—	479
Net loss	—	—	—	—	—	—	(16,788)	(16,788)
Balance at December 31, 2015	12,197,880	48,308	4,260,560	170	1,056	—	(16,860)	(15,634)
Issuance of series A-1 convertible preferred stock, net of issuance costs of $23	33,916,543	135,643	—	—	—	—	—	—
Issuance of series A-2 convertible preferred stock, net of issuance costs of $7	4,361,527	34,885	—	—	—	—	—	—
Issuance of series B-1 convertible preferred stock, net of issuance costs of $153	8,124,365	129,837	—	—	—	—	—	—
Issuance of common stock as contingent consideration in asset acquisition	—	—	945,880	38	5,242	—	—	5,280
Issuance of common stock upon exercise of stock options	—	—	162,665	6	105	—	—	111
Vesting of early exercised common stock	—	—	239,580	10	153	—	—	163
Vesting of restricted stock awards	—	—	2,988,631	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	58,600,315	348,673	8,597,316	344	9,387	(373)	(103,512)	(94,154)
Issuance of series B-2 convertible preferred stock for cash, net of issuance costs of $73	1,764,705	29,927	—	—	—	—	—	—
Conversion of Series A and B convertible preferred stock into common stock	(60,365,020)	(378,600)	60,365,020	604	377,996	—	—	378,600
Issuance of common stock upon initial public offering, net of issuance costs of $23,612	—	—	15,972,221	160	264,101	—	—	264,261
Issuance of common stock upon exercise of stock options	—	—	648,317	25	708	—	—	733
Issuance of reserved common stock as consideration in asset acquisition	—	—	81,164	1	(1)	—	—	—
Vesting of early exercised common stock	—	—	187,500	6	121	—	—	127
Vesting of restricted stock awards	—	—	1,628,824	61	(61)	—	—	—
Stock-based compensation	—	—	—	—	4,409	—	—	4,409
Net loss	—	—	—	—	—	—	(88,185)	(88,185)
Other comprehensive income	—	—	—	—	—	5	—	5
Balance at December 31, 2017	—	$ —	87,480,362	$ 1,201	$ 656,660	$ (368)	$ (191,697)	$ 465,796

See accompanying notes to consolidated financial statements.

Denali Therapeutics Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Operating activities			
Net loss	$ (88,185)	$ (86,652)	$ (16,788)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	3,082	1,469	121
Stock-based compensation expense	4,409	2,951	479
Non-cash interest expense	—	—	110
Net amortization of premiums and discount on marketable securities	753	304	—
Loss on disposal of property and equipment	1	3	—
Fair value of common stock issued in connection with asset acquisition	—	5,280	600
Changes in operating assets and liabilities:			
Restricted cash	—	(451)	(84)
Prepaid expenses and other assets	73	(533)	(2,691)
Accounts payable	207	161	1,678
Accrued and other current liabilities	3,578	5,357	1,607
Non-current liabilities	(553)	(248)	(84)
Net cash used in operating activities	(76,635)	(72,359)	(15,052)
Investing activities			
Purchase of marketable securities	(179,789)	(226,370)	—
Purchase of property and equipment	(2,875)	(6,134)	(3,062)
Purchase of other investments	—	(500)	—
Maturities and sales of marketable securities	141,498	14,000	—
Net cash used in investing activities	(41,166)	(219,004)	(3,062)
Financing activities			
Proceeds from convertible promissory note received from a related party	—	—	5,000
Proceeds from exercise of common stock options	733	111	510
Proceeds from issuance of common stock, net of issuance costs	265,619	—	110
Proceeds from issuance of convertible preferred stock, net of issuance costs	29,971	300,365	43,234
Net cash provided by financing activities	296,323	300,476	48,854
Net increase in cash and cash equivalents	178,522	9,113	30,740
Cash and cash equivalents at beginning of year	39,853	30,740	—
Cash and cash equivalents at end of year	$ 218,375	$ 39,853	$ 30,740
Supplemental disclosures of cash flow information			
Convertible preferred stock issuance costs incurred but not yet paid	$ 44	$ —	$ 36
Property and equipment purchases accrued but not yet paid	$ 103	$ 233	$ 126
Conversion of convertible promissory note and interest into convertible preferred stock	$ —	$ —	$ 5,110
Deferred IPO costs incurred but not yet paid	$ 1,358	$ —	$ —

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 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").

Reverse Stock Split

In November 2017, the Company's board of directors and stockholders approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of its common stock and convertible preferred stock on a 4-to-1 basis (the "Reverse Stock Split"). The par values and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split. The Reverse Stock Split became effective on November 28, 2017. All issued and outstanding common stock and convertible preferred stock and related per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented.

Initial Public Offering

On December 7, 2017, the Company's Registration Statement on Form S-1 was declared effective by the SEC for our initial public offering ("IPO") of common stock. The Company's shares started trading on the NASDAQ Global Select Market on December 8, 2017, and the transaction formally closed on December 12, 2017. In connection with the IPO, the Company sold an aggregate of 15,972,221 shares of common stock, including 2,083,333 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares, at a price to the public of $18.00 per share. The aggregate net proceeds received by the Company from the offering, net of underwriting discounts and commissions and offering expenses, were $264.3 million. Upon the closing of the IPO, all then-outstanding shares of Company convertible preferred stock converted into 60,365,020 shares of common stock. The related carrying value of $378.6 million was reclassified to common stock and additional paid-in capital. Additionally, the Company amended and restated its certificate of incorporation effective December 7, 2017 to, among other things, change the authorized number of shares of common stock to 400,000,000 shares and the authorized number of shares of preferred stock to 40,000,000 shares.

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.

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.

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, 2017 and 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.

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.

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.

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 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.

Income Taxes

Income taxes are accounted for using the liability method, under which deferred tax assets and liabilities are determined based on the temporary 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.

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. Previously recognized tax positions that no longer meet the more-likely-than-not threshold are derecognized in the first subsequent financial reporting period in which that threshold is no longer met.

The Company's policy is to recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the "Tax Act"). The Tax Act makes broad and complex changes to the U.S. tax code, including reducing the U.S. federal corporate tax rate from 35 percent to 21 percent and changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss, primarily unrealized gains or 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. 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. There will be no impact to the consolidated financial statements upon adoption of ASU 2014-09 as the Company has not generated revenue through December 31, 2017.

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 Company plans to adopt this standard on January 1, 2019. 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 No. 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 plans to adopt this standard on January 1, 2018. 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 No. 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 plans to adopt this standard on January 1, 2018. 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.

2. Fair Value Measurements

Assets measured at fair value at each balance sheet date are as follows (in thousands):

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 212,868	$ —	$ —	$ 212,868
Short-term:				
U.S. government treasuries	42,587			42,587
U.S. government agency securities		106,139		106,139
Corporate debt securities		39,125		39,125
Long-term:				
U.S. government treasuries	39,848	—	—	39,848
U.S. government agency securities		19,911		19,911
Corporate debt securities	—	991	—	991
Total marketable securities	82,435	166,166	—	248,601
Total fair value measurements	$ 295,303	$ 166,166	$ —	$ 461,469

	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

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 years ended December 31, 2017 or 2016.

3. Marketable Securities

All marketable securities were considered available-for-sale at December 31, 2017 and 2016. The amortized cost, gross unrealized holding gains or losses, and fair value of the Company's marketable securities by major security type at each balance sheet date are summarized in the tables below (in thousands):

	December 31, 2017			
	Amortized Cost	Unrealized Holding Gains	Unrealized Holding Losses	Aggregate Fair Value
Short-term marketable securities:				
U.S. government treasuries	$ 42,614	$ —	$ (27)	$ 42,587
U.S. government agency securities	106,368	—	(229)	106,139
Corporate debt securities	39,197	—	(72)	39,125
Total short-term marketable securities	188,179	—	(328)	187,851
Long-term marketable securities:				
U.S. government treasuries	39,868	—	(20)	39,848
U.S. government agency securities	19,931	—	(20)	19,911
Corporate debt securities	991	—	—	991
Total long-term marketable securities	60,790	—	(40)	60,750
Total	$ 248,969	$ —	$ (368)	$ 248,601

	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

As of December 31, 2017 and December 31, 2016, 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 years ended December 31, 2017, 2016 or 2015. 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.

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 research 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 472,942 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 27,054 shares of common stock, valued at $32,466 to a former Incro stockholder. The deemed fair value (see Note 8) of the Company's common stock was $1.20 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 945,880 shares of common stock to the former Incro stockholders, and to recognize an obligation to issue 54,110 shares of common stock to a former Incro shareholder ("Milestone Shares"), upon acceptance of an investigational new drug ("IND") application by the U.S. FDA or an equivalent in the EU, Canada, Australia, or New Zealand within six years of the date of the acquisition. Of these shares, 350,000 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 595,880 shares of common stock, recognized an obligation to issue 54,110 shares of common stock, and recorded a liability of $1.8 million for the 350,000 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 $5.28 per share during the year ended December 31, 2016. In December 2016, the 350,000 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. In December 2017, the Company issued 81,164 shares of common stock related to an obligation to a former Incro shareholder.

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 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. 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.

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 years ended December 31, 2017, 2016 and 2015.

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 $1.1 million and $0.3 million of research and development expense related to the funding of F-star Gamma research costs during the years ended December 31, 2017 and 2016, respectively.

The $0.5 million other non-current asset is the only asset or liability recorded in the Company's consolidated balance sheets that relates to the Company's variable interest in F-star Gamma at

December 31, 2017 and December 31, 2016. The upfront payments of $0.5 million and $5.5 million, along with 1) the obligation to fund certain future research costs, 2) any future Fcab selection fee, technical milestone payments or monthly exclusivity fees and 3) any future license fees or pre-commercial milestone payments represent the Company's maximum exposure to loss under the arrangements with F-star. The ultimate expense that the Company incurs under the arrangements with F-Star cannot be quantified at this time as the amount will vary based on the timing and outcome of future research activities.

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 LRRK2 small molecule program. Under the agreement, Genentech granted the Company (i) an exclusive, worldwide, sublicensable 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, sublicensable 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 recognized as research and development expense for the year ended December 31, 2016.

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 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 expense in the year ended December 31, 2017.

6. Balance Sheet Components:

Property and Equipment, Net

	December 31,	
	2017	2016
	(in thousands)	
Lab equipment	$ 11,351	$ 8,868
Leasehold improvements	7,737	7,543
Computers equipment and purchased software	439	373
Furniture and fixtures	65	66
	19,592	16,850
Less: accumulated depreciation	(4,669)	(1,588)
Total property and equipment, net	$ 14,923	$ 15,262

Depreciation expense was $3.1 million, $1.5 million and $0.1 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Prepaid Expenses and Other Current Assets

	December 31,	
	2017	2016
	(in thousands)	
Prepaid research and development expenses	$ 946	$ 2,396
Prepaid insurance	927	—
Accrued interest on short-term marketable securities	464	438
Prepaid employee bonuses	—	234
Other prepaid and current assets	1,044	556
Total prepaid expenses and other current assets	$ 3,381	$ 3,624

Other Non-Current Assets

	December 31,	
	2017	2016
	(in thousands)	
Other investments	$ 500	$ 500
Restricted cash	451	451
Other prepaid and non-current assets	490	319
Total other non-current assets	$ 1,441	$ 1,270

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.

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 expired in December 2017 (the "First Lease"). The First Lease provided for 9,855 of rentable square feet at a base rent that increased 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 and terminated on December 31, 2017. The Company received sublease payments totaling $0.4 million and $0.1 million for the years ended December 31, 2017 and 2016, respectively, 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 December 31, 2017, the future minimum lease payments under non-cancelable operating leases are as follows (in thousands):

Year Ended December 31:	
2018	$ 2,586
2019	2,664
2020	2,745
2021	2,829
2022	2,915
2023 and later	4,790
	$ 18,529

Rent expense for the years ended December 31, 2017, 2016 and 2015 was $2.2 million, $1.0 million and $0.2 million, respectively.

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

Effective September 2017, the Company entered into a Development and Manufacturing Services Agreement as amended ("DMSA") with Lonza Sales AG ("Lonza") for the development and manufacture of biologic products. Under the DMSA, the Company will execute purchase orders based on project plans authorizing Lonza to provide development and manufacturing services with respect to certain of our antibody and enzyme products, and will pay for the services provided and batches delivered in accordance with the DMSA and project plan. As of December 31, 2017, the Company had executed one purchase order totaling $0.7 million for the development and manufacture of biologic products, the activities under which commenced in January 2018 and are expected to be completed in May 2019. The Company had not incurred any amounts or made any payments for the manufacturing services rendered under the agreement as of December 31, 2017. As of December 31, 2017, the Company had total non-refundable purchase commitments of $0.4 million under the DMSA.

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, 2017, the Company had non-cancellable purchase commitments of $1.0 million and contractual obligations under license agreements of $1.6 million. Pursuant to certain license and collaboration agreements, the Company had 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 Preferred Stock

The Company entered into a preferred stock purchase agreement ("Preferred Stock Purchase Agreement"), with certain investors in May 2015 (the "Initial Closing"), under which the Company agreed to sell up to 45,223,973 shares of Series A-1 convertible preferred stock and 4,361,532 shares of Series A-2 convertible preferred stock. Additionally, at the Initial Closing, the Company concurrently issued 6,295,805 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 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.

In May 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 456,250 shares of Series A-1 convertible preferred stock. Additionally, at the First Additional Closing, the Company issued 3,481,250 shares of Series A-1 convertible preferred stock for net proceeds of $13.9 million and in July 2015 ("Second Additional Closing"), the Company issued an additional 2,420,825 shares of Series A-1 convertible preferred stock for net proceeds of $9.6 million.

In January 2016 (the "Third Additional Closing"), the Company issued 500,000 shares of Series A-1 convertible preferred stock, for net proceeds of $2.0 million, and also issued 11,249,997 shares of Series A-1 convertible preferred stock (the "first Tranche Closing"), for net proceeds of $45.0 million. In June 2016 (the "Second Tranche Closing and Series A-2 Closing"), the Company issued 22,166,546 shares of Series A-1 convertible preferred stock and 4,361,527 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.

In June 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 7,646,241 shares of Series B-1 convertible preferred stock at a price of $16.00 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 81,787,362 shares and the authorized shares of its preferred stock to 63,288,466 shares, each with a par value of $0.01 per share. The authorized preferred shares consisted of 46,114,433 designated as Series A-1 convertible preferred stock, 4,361,533 designated as Series A-2 convertible preferred stock, 8,125,000 designated Series B-1 convertible preferred stock and 4,687,500 designated Series B-2 convertible preferred stock.

In August 2016, (the "Second Series B-1 Closing"), the Company sold 478,124 shares of Series B-1 convertible preferred stock at a price of $16.00 per share for net proceeds of $7.6 million.

In November 2017, the Company sold 1,764,705 shares of Series B-2 convertible preferred stock at a price of $17.00 per share for net proceeds of $29.9 million.

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	46,114,433	46,114,423	$ 4.00	$ 183,951	$ 198,264
Series A-2	4,361,533	4,361,527	8.00	34,885	36,483
Series B-1	8,125,000	8,124,365	16.00	129,837	135,324
Series B-2	4,687,500	—		—	—
	63,288,466	58,600,315		$ 348,673	$ 370,071

Prior to the conversion of the convertible preferred stock upon closing of the IPO, the rights, preferences and privileges of the convertible preferred stock were as follows:

Dividend Rights

The holders of preferred stock were 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, $0.32 per share per annum for Series B-1, and $0.34 per share per annum for Series B-2, from and after the date of issuance of such shares. As of December 31, 2016 and 2015, and through the date of conversion, no such dividends were declared or accrued.

Dividends on any other class of capital stock could not be paid unless the holders of the preferred stock first received, or simultaneously received, the preferred stock dividend. The holders of preferred stock also participated in dividends paid on common stock as if the shares of preferred stock had been converted into shares of common stock and were considered participating securities.

Conversion Rights

The holders of preferred stock had right to convert at any time into shares of common stock initially at a one-for-one ratio. All shares of the preferred stock would have been 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 was subject to an adjustment in the event of stock split, combination, common stock dividend or distribution, reclassification, exchange, substitution, or reorganization.

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 were entitled to be paid out of the assets of the Company available for distribution to its stockholders, before any payment could have been 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 were insufficient to pay holders of Preferred Stock the full amount they are entitled to, the holders of preferred stock would have shared 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 would have been 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 classified its convertible preferred stock outside of stockholders' deficit as certain change in control events are outside the Company's control.

Redemption

Upon certain change in control events that were outside of the Company's control, including liquidation, sale or transfer of control of the Company, holders of the convertible preferred stock could have caused its redemption. Shares of preferred stock could have been 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 could have been 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 could have redeemed 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.

Voting Rights

Each share of preferred stock had voting rights equal to the number of shares of common stock into which the preferred stock could have been converted immediately after the close of business on the record date.

As long as certain investors in Series A convertible preferred stock held 100,000 or more shares of convertible preferred stock purchased pursuant to the Preferred Stock Purchase Agreement, they were entitled to elect individually one member of the Board totaling five Series A Directors. Series B convertible preferred stockholders were 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 were entitled to elect two additional members of the Board that were not otherwise an affiliate of the Company or of any investor.

Upon the closing of the IPO, all outstanding shares of convertible preferred stock converted into 60,365,020 shares of common stock. As of December 31, 2017, the Company does not have any convertible preferred stock issued or outstanding.

9. Stock-Based Awards

2017 Equity Incentive Plan

In December 2017, the Company adopted the 2017 Equity Incentive Plan (the "2017 Plan"), which initially reserved 6,379,238 shares for the issuance of stock options, non-qualified stock options, stock appreciation rights, 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 2017 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. Options granted typically vest over a four-year period but may be granted with different vesting terms.

2015 Stock Incentive Plan

In May 2015, the Company adopted the 2015 Stock Incentive Plan (the "2015 Plan"), which as amended, reserved 8,325,000 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 $0.68, a deemed fair value of $1.20 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.

Upon adoption of the 2017 Plan, no new awards or grants are permitted under the 2015 Plan, and the 169,238 shares that were then unissued and available for future award under the 2015 Plan became available under the 2017 Plan. The 2015 Plan will continue to govern restricted stock awards and option awards previously granted thereunder.

As of December 31, 2017, there were 6,012,498 shares available for the Company to grant under the 2017 Plan. As of December 31, 2016, there were 1,813,321 shares available for the Company to grant under the 2015 Plan.

Stock Option Activity

The following table summarizes option award activity under the 2017 Plan and 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, 2015	3,525,121	$ 0.68	9.73	
Options granted	2,112,808	3.45		
Options exercised	(162,665)	0.68		
Options forfeited	(101,250)	0.82		
Balance at December 31, 2016	5,374,014	$ 1.77	9.03	$ 18,873
Options granted	2,183,365	8.78		
Options exercised	(695,192)	1.41		
Options forfeited	(172,708)	2.21		
Balance at December 31, 2017	6,689,479	$ 4.08	8.37	$ 77,317
Options vested and expected to vest at December 31, 2017	4,944,747	$ 5.28	8.62	$ 51,216
Options exercisable at December 31, 2017	1,190,088	$ 3.17	8.23	$ 14,837

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 $3.5 million, $0.7 million and $0.4 million for the years ended December 31, 2017, 2016 and 2015, respectively. During the years ended December 31, 2017 and 2016, the weighted-average grant-date fair value of the options vested was $1.94 and $1.36 per share, respectively. 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, 2017, 2016 and 2015 was $6.41, $2.83 and $2.03 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,		
	2017	2016	2015
Expected term (in years)	6.08	6.00 - 6.08	6.08
Volatility	81.9% - 91.3%	91.2% - 92.2%	85.7% - 90.2%
Risk-free interest rate	1.8% - 2.3%	1.2% - 2.1%	1.7% - 1.9%
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 uses 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 sufficient trading history for its common stock. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

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.

Early Exercise of Stock Options

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 750,000 and options exercised prior to vesting for total proceeds of $0.5 million to the Company, all of which was recognized within other non-current liabilities as of December 31, 2015. A total of 187,497 and 239,580 shares vested relating to these exercises in the years ended December 31, 2017 and 2016, respectively, resulting in a reclassification of $0.1 million and $0.2 million of liability to stockholders' equity (deficit) during the years ended December 31, 2017 and 2016, respectively. The remaining proceeds included in other non-current liabilities related to these unvested options was $0.2 million and $0.3 million as of December 31, 2017 and 2016, respectively.

In 2017, there were 46,875 options exercised prior to vesting for total proceeds of $0.3 million to the Company which was recognized within other non-current liabilities as of December 31, 2017. No shares vested relating to these exercises in the year ended December 31, 2017.

Performance Contingent Stock Options Granted to Employees

In August and November 2015, the Board of Directors granted 250,000 and 500,000 of stock option awards to certain executive officers, respectively. These awards have an exercise price of $0.68

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 1,619,738 and 125,000 of performance- and market- contingent awards to members of the senior management team, respectively. These awards have an exercise price of $0.68 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, 2017 and 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 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 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:

	Year Ended December 31,		
	2017	2016	2015
Expected term (in years)	7.50 - 8.09	8.50 - 9.70	9.50 - 9.84
Volatility	86.1% - 88.1%	95.3% - 98.2%	88.6% - 89.3%
Risk-free interest rate	2.3% - 2.4%	2.4%	2.0% - 2.3%
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	3,922,638	$ 0.18
Granted	—	0
Vested	(1,628,850)	0.18
Forfeited	—	—
Unvested at December 31, 2017	2,293,788	$ 0.18
Vested and expected to vest – December 31, 2017	2,293,788	$ 0.18

At December 31, 2017, there was $0.3 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 1.0 years.

Employee Stock Purchase Plan

In December 2017, the Company adopted the 2017 Employee Stock Purchase Plan (the “2017 ESPP”), which initially reserved 1,000,000 shares of our common stock for employee purchases under terms and provisions established by the Board of Directors. Under the 2017 ESPP, employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of common stock on the first trading day of each offering period or on the exercise date. The 2017 ESPP provides for consecutive, overlapping 12-month offering periods. The offering periods are scheduled to start on the first trading day on or after May 31 or November 30 of each year, except for the first offering period which commenced on December 8, 2017, the first trading day after the effective date of the Company’s registration statement. Contributions under the 2017 ESPP are limited to a maximum of 15% of an employee’s eligible compensation.

The fair values of the rights granted under the 2017 ESPP were calculated using the following assumptions:

	Year Ended December 31, 2017
Expected term (in years)	0.48 - 0.98
Volatility	50.0% - 51.3%
Risk-free interest rate	1.5% - 1.7%
Dividend yield	—

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,		
	2017	2016	2015
Research and development	$ 2,852	$ 2,078	$ 94
General and administrative	1,557	873	385
Total	$ 4,409	$ 2,951	$ 479

As of December 31, 2017, total unamortized stock-based compensation expense related to unvested employee and non-employee awards that are expected to vest was $17.2 million and $0.5 million, respectively. The weighted-average period over which such stock-based compensation expense will be recognized is approximately 3.2 years.

The Company recorded stock-based compensation expense for options issued to non-employees of $0.7 million, $1.0 million and $0.1 million for the years ended December 31, 2017, 2016 and 2015, respectively.

10. Defined Contribution Plan

In January 2017, the Company began to sponsor a 401(k) retirement savings plan for the benefit of its 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. The Company made contributions to the Plan for eligible participants, and recorded contribution expenses of $0.5 million for the year ended December 31, 2017.

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, 2017 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,	
	2017	2016
Taxes at the U.S. statutory tax rate	34.0%	34.0%
Effect of Tax Act	(26.6)	—
Change in valuation allowance	(7.3)	(32.0)
Contingent consideration issued in tax-free reorganization	—	(2.1)
Research tax credits	1.0	0.6
Stock-based compensation	(1.0)	(0.5)
Other	(0.1)	—
Total provision for income taxes	0.0%	0.0%

The components of the Company's net deferred tax assets are as follows (in thousands):

	December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 37,606	$ 26,044
Tax credit carryforwards	4,072	1,486
Reserves and accruals	3,328	4,038
Capitalized start-up costs	6,248	5,128
Intangibles	5,300	6,565
Share based compensation	733	390
Other	7	—
Gross deferred tax assets	57,294	43,651
Valuation allowance	(54,650)	(40,113)
Net deferred tax assets	2,644	3,538
Deferred tax liabilities:		
Property and equipment	(2,618)	(3,379)
Stock-based compensation	(26)	(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, 2017 and 2016.

On December 22, 2017, the U.S. government enacted the Tax Act. The Act reduces the corporate tax rate to 21 percent, effective January 1, 2018. The Company has calculated its best estimate of the impact of the Tax Act in accordance with our understanding of the Tax Act and guidance available as of the date of this filing as provisional amount. The tax rate decrease resulted in a reduction of $23.5 million in our deferred tax assets, and a corresponding decrease of the same amount in the valuation allowance, as substantially all of our deferred tax assets, net of deferred tax liabilities, are subject to a full valuation allowance. We will continue to examine the impact the Tax Act may have on our business.

As of December 31, 2017, the Company has federal net operating loss ("NOL") carryforwards of approximately $134.1 million, which are available to reduce future taxable income, and has federal tax credits of approximately $2.9 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 $135.1 million, which are available to reduce future taxable income, and has state tax credits of approximately $3.1 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. Annual limitations may result in expiration of net operating loss and tax credit carryforwards before some or all of such amounts have been utilized.

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.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

	December 31,	
	2017	2016
Gross unrecognized tax benefits at January 1	$ 531	$ 122
Additions for tax positions taken in a prior year	—	7
Additions for tax positions taken in the current year	640	411
Reductions for tax positions taken in the prior year	(25)	(9)
Gross unrecognized tax benefits at December 31	$ 1,146	$ 531

If recognized, none of the unrecognized tax benefits as of December 31, 2017 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, 2017, 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 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,		
	2017	2016	2015
Numerator:			
Net loss	$ (88,185)	$ (86,652)	$ (16,788)
Denominator:			
Weighted average common shares outstanding	14,964,144	6,424,720	3,006,379
Net loss per share, basic and diluted	$ (5.89)	$ (13.49)	$ (5.58)

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 as the inclusion of all potential dilutive securities 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:

	Year Ended December 31,	
	2017	2016
Series A-1 convertible preferred stock	—	46,114,423
Series A-2 convertible preferred stock	—	4,361,527
Series B-1 convertible preferred stock	—	8,124,365
Options issued and outstanding and ESPP shares issuable and outstanding	6,835,313	5,374,014
Restricted shares subject to future vesting	2,293,788	3,922,638
Early exercised common stock subject to future vesting	369,796	510,417
Shares to be issued under Incro acquisition agreement	—	81,164
Total	9,498,897	68,488,548

13. Subsequent events

Takeda

On January 3, 2018, the Company entered into an Option and Collaboration Agreement with Takeda Pharmaceutical Company Limited (“Takeda”), pursuant to which the Company granted Takeda an option with respect to three programs to develop and commercialize, jointly with the Company, certain biologic products that are enabled by Denali’s blood-brain barrier (“BBB”) delivery technology and intended for the treatment of neurodegenerative disorders. The three programs are Denali’s ATV:BACE1/Tau and ATV: TREM2 programs, and a third identified, but yet undisclosed discovery stage program. The Collaboration Agreement became effective on February 12, 2018 when the requirements of the Hart-Scott-Rodino Antitrust Improvements Act of 1976 were satisfied.

Pursuant to this agreement, an upfront payment of $40.0 million was received in February 2018, as well as the first preclinical milestone payment of $5.0 million. Further, under the associated stock purchase agreement, the Company received $110.0 million for the sale of 4,214,559 shares of its common stock which were issued on February 23, 2018.

Lonza

On January 26, 2018, the Company executed a second amendment to the DMSA with Lonza for approximately $11.4 million, which covers activities that will take place through the end of 2020.

14. Selected Quarterly Financial Data (Unaudited)

The following table provides the selected quarterly financial data for the years 2017 and 2016 (in thousands, except per share amounts):

	Quarter Ended			
	December 31, 2017	September 30, 2017	June 30, 2017	March 31, 2017
Loss from operations	$ (23,540)	$ (22,288)	$ (22,568)	$ (21,744)
Net loss	$ (22,887)	$ (21,844)	$ (22,134)	$ (21,320)
Net loss per share, basic and diluted	$ (0.74)	$ (2.14)	$ (2.29)	$ (2.36)

	Quarter Ended			
	December 31, 2016	September 30, 2016	June 30, 2016	March 31, 2016
Loss from operations	$ (19,776)	$ (30,932)	$ (23,453)	$ (13,272)
Net loss	$ (19,354)	$ (30,611)	$ (23,418)	$ (13,269)
Net loss per share, basic and diluted	$ (2.41)	$ (4.51)	$ (3.82)	$ (2.80)

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

As of December 31, 2017, management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2017, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required by this item will be contained in our definitive proxy statement to be filed with the SEC on Schedule 14A in connection with our 2018 Annual Meeting of Stockholders (the “Proxy Statement”), which is expected to be filed not later than 120 days after December 31, 2017, and is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required by this item will be contained in the Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITSAND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements in Part II Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

The documents listed in the Exhibit Index are incorporated by reference or are filed with this report, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Number	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-38311	3.1	12/12/2017
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-38311	3.2	12/12/2017
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.	S-1	333-221522	4.1	11/13/2017
4.2	Specimen common stock certificate of the Registrant.	S-1/A	333-221522	4.2	11/27/2017
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1/A	333-221522	10.1	11/27/2017
10.2+	2015 Stock Incentive Plan, as amended, and forms of agreement thereunder.	S-1	333-221522	10.2	11/13/2017
10.3+	2017 Equity Incentive Plan and forms of agreements thereunder.	S-1/A	333-221522	10.3	11/27/2017
10.4+	2017 Employee Stock Purchase Plan and form of agreement thereunder.	S-1/A	333-221522	10.4	12/7/2017
10.5+	Offer Letter between the Registrant and Ryan J. Watts, Ph.D., dated November 10, 2017.	S-1	333-221522	10.5	11/13/2017
10.6+	Offer Letter between the Registrant and Alexander O. Schuth, M.D., dated November 10, 2017.	S-1	333-221522	10.6	11/13/2017
10.7+	Offer Letter between the Registrant and Steve E. Krognes, dated November 10, 2017.	S-1	333-221522	10.7	11/13/2017
10.8+	Offer Letter between the Registrant and Carole Ho, M.D., dated November 10, 2017.	S-1	333-221522	10.8	11/13/2017
10.9	Lease Agreement between the Registrant and HCP Oyster Point III LLC, dated September 24, 2015.	S-1	333-221522	10.9	11/13/2017

10.10Ü	Exclusive License Agreement between the Registrant and Genentech, Inc., dated June 17, 2016.	S-1	333-221522	10.10	11/13/2017
10.11Ü	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.	S-1	333-221522	10.11	11/13/2017
10.12Ü	Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 6, 2017, as amended by Amendment No. 1 on October 18, 2017.	S-1	333-221522	10.12	11/13/2017
10.12.1#	Amendment No. 2 to Development and Manufacturing Services Agreement between the Registrant and Lonza Sales AG, dated September 6, 2017, as amended by Amendment No. 1 on October 18, 2017, dated January 18, 2018.				
10.13+	Key Executive Change in Control and Severance Plan.	S-1	333-221522	10.13	11/13/2017
10.14+	Executive Incentive Compensation Plan.	S-1	333-221522	10.14	11/13/2017
10.15+	Outside Director Compensation Policy.	S-1	333-221522	10.15	11/13/2017
10.16#	Option and Collaboration Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated January 3, 2018.				
10.17	Common Stock Purchase Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated January 3, 2018.				
10.18	Standstill and Stock Restriction Agreement between the Registrant and Takeda Pharmaceutical Company Limited, dated February 23, 2018.				
23.1	Consent of Independent Registered Public Accounting Firm.				
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act.				
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act.				
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act.				
32.2*	Certification of Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act.				

* The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are deemed furnished and not filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.
Ü Portions of the exhibit have been omitted pursuant to an order granted by the Securities and Exchange Commission for confidential treatment.
\# Portions of this exhibit have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.
\+ Indicates management contract or compensatory plan.

ITEM 16. FORM10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 19, 2018

DENALI THERAPEUTICS INC.

By: /s/ Ryan J. Watts

Ryan J. Watts, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Ryan J. Watts, Ph.D. and Steve E. Krognes, and each of them acting individually, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and 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 connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Ryan J. Watts Ryan J. Watts, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 19, 2018
/s/ Steve E. Krognes Steve E. Krognes	Chief Financial Officer and Treasurer *(Principal Financial and Accounting Officer)*	March 19, 2018
/s/ Vicki Sato Vicki Sato, Ph.D.	Chairperson of our Board of Directors	March 19, 2018
/s/ Marc Tessier-Lavigne Marc Tessier-Lavigne, Ph.D.	Director	March 19, 2018
/s/ Douglas Cole Douglas Cole, M.D.	Director	March 19, 2018
/s/ Jay Flatley Jay Flatley	Director	March 19, 2018
/s/ Robert Nelsen Robert Nelsen	Director	March 19, 2018
/s/ David Schenkein David Schenkein, M.D.	Director	March 19, 2018

Confidential

SPECIFIC TERMS IN THIS EXHIBIT HAVE BEEN REDACTED BECAUSE CONFIDENTIAL TREATMENT FOR THOSE TERMS HAS BEEN REQUESTED. THE REDACTED MATERIAL HAS BEEN SEPARATELY FILED WITH THE SECURITIES AND EXCHANGE COMMISSION, AND THE TERMS HAVE BEEN MARKED AT THE APPROPRIATE PLACE WITH THREE ASTERISKS [***].

Amendment No. 2

to the

DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT

Dated 6th September 2017

Between

LONZA SALES AG

and

DENALI THERAPEUTICS lNC.

Appendix A2 – Project Plan

Confidential

Confidential

THIS Amendment is made the 18th day of January, 2018

BETWEEN

LONZA SALES AG, of Muenchensteinerstrasse 38, Ch-4002 Basel, Switzerland (herein after referred to as “Lonza”) and

DENALI THERAPEUTICS INC., of 151 Oyster Point Blvd, 2nd Floor, South San Francisco, CA 94080, U.S.A (hereinafter referred to as “Customer”)

WHEREAS

A. Customer and Lonza are Parties to a development and manufacturing services agreement dated 6th September 2017, as amended (the “Agreement”), pursuant to which Lonza is required to perform Services for Customer relating to the Cell Line and Product described (all terms as defined in the Agreement); and

B. The Parties now wish to amend and supplement the terms of the Agreement.

NOW THEREFORE in consideration of the mutual promises and covenants contained herein and other good and valuable consideration the sufficiency of which is acknowledged, it is hereby agreed by and between the Parties to amend the Agreement as follows:

1. The Project Plan attached to this Amendment No. 2 shall be inserted as Appendix A2 to the Agreement.

2. All capitalised terms used herein shall have the meanings set forth in the Agreement unless otherwise defined herein.

3. Save as herein provided all other terms and conditions of the Agreement shall remain in full force and effect.

IN WITNESS WHEROF the Parties have caused this Amendment No.2 to be executed by their representatives thereunto duly authorised as of the day and year first written.

Signed for and on behalf of LONZA SALES AG	/s/ Cordula Altekrüger Cordula Altekrüger Senior Legal Counsel	 TITLE
Signed for and on behalf of LONZA SALES AG	/s/ Bart A. M. van Aarnhem Bart A. M. van Aarnhem Senior Legal Counsel	 TITLE
Signed for and on behalf of DENALI THERAPEUTICS INC.	/s/ Ryan Watts Ryan Watts, CEO	

Appendix A2

Project Plan

[***]

Confidential

*** Certain information in this agreement has been omitted and filed separately with the Securities and Exchange Commission. [***] indicates that text has been omitted and is the subject of a confidential treatment request.

Exhibit 10.16

CONFIDENTIAL
Execution Version

SPECIFIC TERMS IN THIS EXHIBIT HAVE BEEN REDACTED BECAUSE CONFIDENTIAL TREATMENT FOR THOSE TERMS HAS BEEN REQUESTED. THE REDACTED MATERIAL HAS BEEN SEPARATELY FILED WITH THE SECURITIES AND EXCHANGE COMMISSION, AND THE TERMS HAVE BEEN MARKED AT THE APPROPRIATE PLACE WITH THREE ASTERISKS [***].

OPTION AND COLLABORATION AGREEMENT

between

DENALI THERAPEUTICS INC.

and

TAKEDA PHARMACEUTICAL COMPANY LIMITED

TABLE OF CONTENTS

TABLE OF CONTENTS
(cont'd)

TABLE OF CONTENTS
(cont'd)

OPTION AND COLLABORATION AGREEMENT

This Option and Collaboration Agreement (the "**Agreement**") is made and entered into effective as of January 3, 2018 (the "**Execution Date**") by and between Denali Therapeutics, Inc., a Delaware corporation ("**Denali**"), and Takeda Pharmaceutical Company Limited, a corporation organized under the laws of Japan ("**Takeda**"). Denali and Takeda are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, Denali has developed the ATV Platform (as defined herein) and certain Biologics and Products (each, as defined herein) and Controls (as defined herein) certain intellectual property and other rights with respect to such ATV Platform, Biologics and Products in the Territory (as defined herein);

WHEREAS, the Parties wish to collaborate in the research and development of Biologics Directed (as defined herein) to Designated Targets (as defined herein) and Denali wishes to grant to Takeda an exclusive option to obtain a license under Denali's intellectual property with respect to such Biologics Directed to such Designated Targets, and Takeda wishes to obtain such option, for purposes of developing, manufacturing and commercializing Optioned Products (as defined herein) in the Territory, in each case in accordance with the terms and conditions set forth below; and

WHEREAS, on even date herewith, Denali and Takeda (or one of its Affiliates) are entering into a stock purchase agreement ("**Stock Purchase Agreement**") providing for Takeda's (or one of its Affiliate's) purchase of stock of Denali, all in accordance with the terms and conditions set forth in such Stock Purchase Agreement.

NOW, THEREFORE, in consideration of the premises and the mutual promises and conditions hereinafter set forth, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

ARTICLE 1
DEFINITIONS

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.1 "**Acceptance**" of an IND shall be deemed to have occurred: (a) subject to subsection (b), in the United States and any other applicable country or regulatory jurisdiction, on the date of expiration of any required waiting period following the filing of such IND; *provided* that, if prior to the expiration of such required waiting period, the applicable Regulatory Authority notifies the sponsor of such IND that a clinical study may not begin upon the expiration of such required waiting period, then "Acceptance" shall be deemed to occur as of the date a clinical study may legally begin; and (b) if required in a particular country or regulatory jurisdiction (including the United States and any such other applicable country or regulatory

jurisdiction in the event such approval becomes required therefor during the Term due to any change in Applicable Law), the date of receipt of any required approval from the applicable Regulatory Authority to conduct a clinical study; in each case whichever occurs first.

1.2 "**Accounting Standards**" means, with respect to Denali, the United States Generally Accepted Accounting Principles, and, with respect to Takeda, the International Financial Reporting Standards, in each case, as consistently applied.

1.3 "**Acquisition**" means, with respect to a Party, an acquisition by such Party of a Third Party (whether by merger or acquisition of all or substantially all of the stock or of all or substantially all of the assets of a Third Party or of any operating or business division of a Third Party or similar transaction), other than a Change in Control of the Party.

1.4 "**Additional Development Costs**" means those Out-of-Pocket Costs and FTE Costs incurred by the Proposing Party in performing the relevant Additional Development Activities, which costs shall be determined using the same manner of calculating Development Costs and Allowable Expenses as if such Additional Development Activities had been incorporated into the Development Plan.

1.5 "**Affiliate**" means, with respect to a Person, any other Person that, directly or indirectly, through one (1) or more intermediaries, controls, is controlled by or is under common control with such Person. For purposes of this definition, "control" and, with correlative meanings, the terms "controlled by" and "under common control with" means (a) the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract relating to voting rights or corporate governance, or otherwise; or (b) the ownership, directly or indirectly, of more than fifty percent (50%) of the voting securities or other ownership interest of a Person (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity). The Parties acknowledge that in the case of certain entities organized under the laws of certain countries outside of the United States, the maximum percentage ownership permitted by law for a foreign investor may be less than fifty percent (50%), and that, in such case, such lower percentage shall be substituted in the preceding sentence, *provided* that such foreign investor has the power to direct the management or policies of such entity.

1.6 "**Allowable Expenses**" means, with respect to a Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option, all FTE Costs and Out-of-Pocket Costs incurred by, or on behalf of, a Party after the Option Exercise Date for such Collaboration Program that are specifically identifiable or reasonably allocable to:

1.6.1 the Commercialization of Optioned Products within such Collaboration Program in the Territory in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget, including to the extent consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget: sales, pricing, activities relating to obtaining and managing reimbursement from payers and reimbursement authorities, contracting, launch timing, distribution (including order handling, transportation and storage), activities directed to advertising and marketing (including marketing messaging, product positioning, development and distribution of selling, advertising

and promotional materials), sales tracking and auditing, market research, marketing studies and product usage surveys, provision of medical affairs support staff and conduct of activities by such medical affairs support staff, and scientific and medical advisory boards (including any global medical conferences and other seminars and conventions), peer-to-peer activities and speakers programs;

1.6.2 the sales force costs for Optioned Products within such Collaboration Program incurred in a manner consistent with such Commercialization Plan and in accordance with associated Commercialization Budget and calculated in accordance with Section 6.4.5;

1.6.3 the training, operation and management of sales representatives and medical affairs support staff in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget;

1.6.4 activities pertaining to preparation for and the conduct of Phase IV Studies of Optioned Products within such Collaboration Program in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget;

1.6.5 the preparation of Regulatory Documentation as reasonably necessary to conduct Commercialization activities for Optioned Products within such Collaboration Program, including any Regulatory Documentation pertaining to pricing and reimbursement approvals for such Optioned Products and any filing fees incurred in connection therewith, all in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget;

1.6.6 any product liability claims for Optioned Products within the applicable Collaboration Program;

1.6.7 any recalls and withdrawals of such Optioned Products to the extent treated as an Allowable Expense pursuant to Section 6.10;

1.6.8 payment made by (i) Denali to a Third Party under an In-License Agreement or (ii) a Party to a Third Party in order to obtain a license or right under a Patent or other intellectual property owned or controlled by such Third Party, in each case, to the extent such payments will be shared by the Parties as Allowable Expenses in accordance with Sections 7.5.1 or 7.5.2;

1.6.9 the defense, enforcement and cooperation activities (including any freedom to operate analysis, intellectual property clearance or similar activities) incurred in connection with the Optioned Products and to be shared by the Parties to the extent provided in Sections 9.3, 9.4, and 9.5;

1.6.10 Indemnified Losses and other Out-of-Pocket Costs incurred in connection with Third Party Claims described in Section 13.3 solely to the extent such Indemnified Losses and other Out-of-Pocket Costs are specified in Section 13.3 as to be included in Allowable Expenses;

1.6.11 Prosecution and Maintenance of Patents pertaining to such Collaboration Program to the extent provided in Section 9.2 and of trademarks to the extent provided in Section 9.6;

1.6.12 the Manufacturing Costs for any samples of the Optioned Products within such Collaboration Program, for any Commercial supply of such Optioned Product for sale and for use in any Phase IV Study, all conducted and incurred in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget;

1.6.13 the Manufacturing related activities pertaining to such Optioned Products not otherwise included in Manufacturing Costs, including stability testing and other CMC support costs for such Optioned Products, but only to the extent such costs are not included in Development Costs and all conducted and incurred in a manner consistent with the applicable Commercialization Plan and in accordance with associated Commercialization Budget; and

1.6.14 any other FTE Costs and Out-of-Pocket Costs agreed to be shared by the Parties as set forth in this Agreement that are not otherwise covered as a Development Cost.

For clarity, Allowable Expenses are exclusive of and do not include Development Costs.

1.7 "**Alzheimer's Disease**" means an Indication [***]

1.8 "**Annual Net Sales**" means the total Net Sales throughout the Territory of a particular Optioned Product in a given Calendar Year.

1.9 "**Antibody**" means an immunoglobulin (Ig) molecule or fragment thereof that includes (a) a [***] and (b) an [***].

1.10 "**Applicable Law**" means federal, state, local, national and supra-national laws, statutes, rules, and regulations, including any rules, regulations, regulatory guidelines, or other requirements of the Regulatory Authorities, major national securities exchanges or major securities listing organizations, that may be in effect from time to time during the Term and applicable to a particular activity or country or other jurisdiction hereunder.

1.11 "**Aspect**" means, with respect to any molecule, the structure or functionality thereof.

1.12 "**ATV Platform**" means the proprietary platform technology owned or in-licensed by Denali [***].

1.13 "**ATV Platform Claim**" means a Patent claim that (a) Covers the [***] or (b) is deemed to be an ATV Platform Claim pursuant to Section 9.1.1.

1.14 "**ATV Platform Know-How**" means any Information [***].

1.15 "**ATV Platform Patent**" means [***].

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1.16 "**ATV Platform Technology**" means ATV Platform Know-How and ATV Platform Patents.

1.17 "**Biologic**" means an Antibody or Non-Antibody Protein.

1.18 "**Biosimilar Competition Percentage**" means, with respect to each Optioned Product in a given country in the Territory in a given Calendar Quarter, the total number of units of all Biosimilar Products sold by one or more Third Parties divided by the sum of: (a) the total number of units of the applicable Optioned Product sold by Takeda, its Affiliates and Sublicensees, and (b) the total number of units of all Biosimilar Products sold by one or more Third Parties, where, in each case, the number of units of the Optioned Product and each Biosimilar Product sold in the relevant country and Calendar Quarter shall be as reported by IMS America Ltd. or any successor thereto and normalized to equivalent units ("**IMS**") (or based on equivalent data reported by any other independent sales auditing firm mutually agreed upon by the Parties if IMS data is not available).

1.19 "**Biosimilar Product**" means, with respect to a particular Optioned Product and a particular country, a biologic therapeutic that (a) containing [***]; or (b) is otherwise determined by the FDA or other Regulatory Authority outside of the United States to be [***] with such Optioned Product, as set forth in 42 U.S.C. 262(k) or other analogous Applicable Law outside the United States. An Optioned Product licensed, marketed, sold, manufactured or produced by Takeda, its Affiliates or Sublicensees shall not constitute a Biosimilar Product.

1.20 "**Business Day**" means a day, other than a Saturday or Sunday, on which banking institutions in San Francisco, California, U.S.A. or Tokyo, Japan are open for business.

1.21 "**Calendar Quarter**" means each successive period of three (3) calendar months commencing on January 1, April 1, July 1 and October 1, except that the first Calendar Quarter shall commence on the Effective Date and end on the day immediately prior to the first to occur of January 1, April 1, July 1 or October 1 after the Effective Date, and the last Calendar Quarter shall end on the last day of the Term.

1.22 "**Calendar Year**" means each successive period of twelve (12) calendar months commencing on January 1 and ending on December 31, except that the first Calendar Year shall commence on the Effective Date and end on December 31 of the year in which the Effective Date occurs and the last Calendar Year of the Term shall commence on January 1 of the year in which the Term ends and end on the last day of the Term.

1.23 "**Centralized Approval Procedure**" means the procedure through which an MAA filed with the EMA results in a single marketing authorization valid throughout the European Union (or at least all continental Major European Countries that are within the European Union).

1.24 "**Change in Control**," with respect to a Party, shall be deemed to have occurred if any of the following occurs after the Execution Date:

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1.24.1 any "person" or "group" (as such terms are defined below) (a) becomes the "beneficial owner" (as defined below), directly or indirectly, of shares of voting capital stock (or similar interests (for instance partnership interests) if a Party is not a corporation) ("Voting Stock") of such Party representing a majority of the total voting power of all outstanding classes of Voting Stock of such Party or (b) acquires the power, directly or indirectly, to elect a majority of the members of the Party's board of directors (or similar governing body if a Party is not a corporation); or

1.24.2 such Party enters into a merger, consolidation or similar transaction with a Third Party (whether or not such Party is the surviving entity) and as a result of such merger, consolidation or similar transaction the Persons that beneficially owned, directly or indirectly, the shares of Voting Stock of such Party immediately prior to such transaction cease to beneficially own, directly or indirectly, shares of Voting Stock representing at least a majority of the total voting power of all outstanding classes of Voting Stock of the surviving Person or the parent entity of the surviving Person; or

1.24.3 such Party sells or transfers to any Third Party, in one (1) or more related transactions, properties or assets representing all or substantially all of such Party's consolidated total assets; or

1.24.4 the holders of capital stock of such Party approve a plan or proposal for the liquidation or dissolution of such Party.

For the purpose of this definition of Change in Control, (a) "person" and "group" have the meanings given such terms under Section 13(d) and 14(d) of the United States Securities Exchange Act of 1934 and the term "group" includes any group acting for the purpose of acquiring, holding or disposing of securities within the meaning of Rule 13d-5(b)(1) under the said Act; (b) a "beneficial owner" shall be determined in accordance with Rule 13d-3 under the aforesaid Act; and (c) the terms "beneficially owned" and "beneficially own" shall have meanings correlative to that of "beneficial owner." Notwithstanding the foregoing, a bona fide financing transaction (including any public offering of a Party's capital stock) shall not be deemed a Change in Control.

1.25 "**Clinical Data**" means the original source patient data and case report forms (CRFs) collected or generated with respect to Clinical Studies of any Optioned Biologic or Optioned Product, together with all analysis, reports, and results with respect thereto.

1.26 "**Clinical Studies**" means any Phase I Trial, Phase II Trial, Phase III Trial, Phase IV Study or any such other test or study in human subjects that is performed pursuant to a Development Plan, Commercialization Plan or an Additional Development Proposal.

1.27 "**CNS Field**" means [***].

1.28 "**Co-Commercialization Plan**" means, for each applicable Collaboration Program, a detailed plan and detailed budget for the Commercialization in the Field in the United States and/or China, as applicable, of Optioned Products included in such Collaboration Program for which the Non-Commercial Lead has exercised the co-commercialization option under

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Section 6.2.4, which shall include for each of the United States and China, as applicable: (a) [***]; (b) [***]; (c) the allocation of Commercialization activities between the Parties to be undertaken with respect to the Optioned Products within such Collaboration Program in the applicable country, including the allocation of responsibility for the [***]; (d) an estimated annual sales forecast in each of the United States and China; and (e) the corresponding Commercialization Budget.

1.29 "**Co-Commercialization Territory**" means the United States and China.

1.30 "**Collaboration Program**" means, with respect to an Optioned Target, all Optioned Biologics and Optioned Products Directed to such Optioned Target, and the Development activities, Manufacturing activities and Commercialization activities with respect to such Optioned Biologics and Optioned Products.

1.31 "**Collaboration Program Annual Net Sales**" means the total Net Sales throughout the Territory of all Optioned Products included in a particular Collaboration Program in a given Calendar Year.

1.32 "**Combination Product**" means an Optioned Product that is comprised of or contains one (1) or more Optioned Biologics as an active ingredient together with one (1) or more Other Active Ingredients, whether in the same or different formulations, so long as both the Optioned Biologic(s) and Other Active Ingredient(s) are sold as a single unit or for a single price.

1.33 "**Commercial Lead**" means the Party specified as the "Commercial Lead" pursuant to the terms of Section 6.2.3.

1.34 "**Commercialization**" means any and all activities directed to the preparation for sale of, offering for sale of, or sale of an Optioned Product in each case, as performed in a manner consistent with the applicable Commercialization Plan, including activities related to conducting Phase IV Studies, marketing, promoting, distributing, medical affairs, obtaining pricing and reimbursement approval for an Optioned Product, Manufacturing Optioned Products for commercial sale, samples and Phase IV Studies, importing and exporting such Optioned Product, and the preparation and submission of Regulatory Documentation and interacting with Regulatory Authorities regarding any of the foregoing. When used as a verb, "**Commercialize**" and "**Commercializing**" means to engage in Commercialization, and "**Commercialized**" has a corresponding meaning. When used as an adjective, "**Commercial**" modifies the following noun to allow for the foregoing activities.

1.35 "**Commercialization Budget**" means a rolling [***] Calendar Year budget setting forth the budgeted amounts estimated to be incurred in performance of the related Commercialization Plan in the first Calendar Year (or part thereof) of such budget and the overall estimated budget to be incurred in performance of the related Commercialization Plan next [***] successive Calendar Years thereafter. For each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option, each such Commercialization Budget shall include a reasonably detailed budget for FTE Costs and Out-of-Pocket Costs, broken down by Calendar Quarter for the first Calendar Year (or part thereof) and a then current estimate of such FTE Costs and Out-of-Pocket Costs for the next [***] successive Calendar

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Years. For each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option, the Global Commercialization Plan shall also include a breakout of costs by functional area or category as determined by the JPT. For each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option and for each country for which the Non-Commercial Lead has exercised the co-commercialization option under Section 6.2.4, each Co-Commercialization Plan shall also include a breakout of costs by functional area or category as determined by the JPT.

1.36 "**Commercialization Plans**" means, collectively, (a) for each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option, the Co-Commercialization Plan, Exclusive Market Commercialization Plan, and Global Commercialization Plan, and (b) for each Collaboration Program for which Denali has exercised the Denali Worldwide Royalty Option, the Global Commercialization Plan, in each case including the corresponding budgets for each such plan.

1.37 "**Commercially Reasonable Efforts**" means, with respect to the efforts to be expended by a Party in connection with a particular activity or objective to be conducted under this Agreement, that level of efforts that [***] would normally use, in the exercise of its prudent scientific and business judgment, for the development and commercialization of a bio-pharmaceutical product that it is actively developing or commercializing for a similar patient population at a similar stage of its development or commercialization, taking into account all [***] factors that such Party would reasonably take into account, including [***], but not taking into account [***].

1.38 "**Confidential Information**" means any Information or data provided orally, visually, in writing or other form by or on behalf of one (1) Party (or an Affiliate or representative of such Party or such Party's Affiliate) to the other Party (or to an Affiliate or representative of such Party or such Party's Affiliate) in connection with this Agreement, whether prior to, on, or after the Execution Date, including Information pertaining to the terms of this Agreement, a Research Biologic, Optioned Biologic or any Optioned Product (including the Regulatory Documentation and Regulatory Data), any Exploitation of an Optioned Biologic or Optioned Product, any know-how with respect thereto developed by or on behalf of the disclosing Party or its Affiliates (including Takeda Know-How and Denali Know-How), or the scientific, regulatory or business affairs or other activities of either Party. Notwithstanding the foregoing, Joint Program Know-How and all Regulatory Documentation generated after the Execution Date and owned by a Party pursuant to this Agreement shall be deemed to be the Confidential Information of both Parties, and the restrictions on use and disclosure in Sections 11.1 and 11.2 shall be deemed to apply to each Party as a receiving Party, regardless of which Party initially generated or disclosed the relevant Joint Program Know-How or Regulatory Documentation, as applicable, to the other Party in connection with this Agreement.

1.39 "**Consent Matter**" means:

1.39.1 [***] and

1.39.16 any other matter that is explicitly identified as a Consent Matter in this Agreement.

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1.40 "**Control**" or "**Controlled**" means, with respect to any item of Information, Regulatory Documentation, material, Patent, or other property right, the possession of the right, whether directly or indirectly, and whether by ownership, license, covenant not to sue or otherwise (other than by operation of the license and other grants in Sections 7.1 and 7.2), to grant access to or a license, sublicense or other right (including the right to reference Regulatory Documentation) to or under such Information, Regulatory Documentation, material, Patent, or other property right as provided in this Agreement, without violating the terms of any agreement or other arrangement with any Third Party.

1.41 "**Controlling Party**" means the Party specified as the "Controlling Party" in Section 9.2.1.

1.42 "**Corporate Names**" means the Trademarks and logos identified on Schedule 1.42 and such other names and logos, in each case as Denali or Takeda may designate in writing from time to time.

1.43 "**Cover**" "**Cover**", "**Covering**" or "**Covered**" means, with respect to a product, technology, process or method, that, in the absence of ownership of or a license granted under a Valid Claim, the practice or Exploitation of such product, technology, process or method would infringe such Valid Claim (or, in the case of a Valid Claim that has not yet issued, would infringe such Valid Claim if it were to issue).

1.44 "**Data Package**" means, with respect to a Designated Target and the applicable Research Biologics Directed to such Designated Target, [***] set forth in Schedule 1.44 or that are otherwise set forth in the applicable Research Plan or approved by the JSC in accordance with Section 2.3.6 (which, for clarity, shall be a Consent Matter and not subject to either Party's final decision making authority), which shall include:

1.44.1 for the then-lead Research Biologics Directed to such Designated Target, [***]; and

1.44.2 other [***] from the activities conducted under the applicable Research Plan for such Designated Target with respect any other (a) Antibody that is a Research Biologic Directed to such Designated Target and for which [***] and/or (b) Non-Antibody Protein that is a Research Biologic Directed to such Designated Target and for which [***].

1.45 "**Denali Business Partner**" means any Third Party to which, as of the Execution Date or during the Term, [***].

1.46 "**Denali Know-How**" means Information, including any related Regulatory Documentation and Clinical Data, Controlled by Denali or any of its Affiliates during the Term that is reasonably necessary or actually used to Exploit a Biologic or a Product, in each case, Directed to one (1) or more Designated Target(s), in the Field in the Territory.

1.47 "**Denali Patents**" means Patents Controlled by Denali or any of its Affiliates during the Term that: (i) claim the composition of matter of, or the method of making or using, a Biologic or a Product, in each case, Directed to one (1) or more Designated Target(s); or (ii) are otherwise reasonably necessary or actually used to Exploit a Biologic or a Product, in each case, Directed to one (1) or more Designated Target(s), in the Field in the Territory.

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1.48 "**Denali Technology**" means, collectively, the Denali Patents and the Denali Know-How.

1.49 "**Designated Target**" means any Target specified in Schedule 1.49, or otherwise selected by the Parties during the Term in accordance with the procedures set out in Section 3.1.3 and with respect to which the Parties intend to develop Biologics and Products and to potentially commercialize Products pursuant to this Agreement.

1.50 "**Detail**" means a face-to-face meeting, between a sales representative of the applicable Party, and a health care professional, during which a presentation of the Optioned Product's attributes is presented in a manner consistent with Applicable Law and industry standards and with the quality of similar presentations made by a Party's sales representatives for such Party's other products, if applicable. A Detail does not include a sample drop made by a sales representative. The Parties may agree in the Commercialization Plan to include real-time, electronic Detailing by means of information technology (*e.g.*, Skype).

1.51 "**Development**" means any and all activities related to research, pre-clinical, other non-clinical testing and Clinical Studies (other than Phase IV Studies), including test method development and stability testing, toxicology, formulation, process development, Manufacturing in support of the foregoing activities and manufacturing scale-up, qualification and validation, quality assurance/quality control, any statistical analysis and report writing, the preparation and submission of Regulatory Documentation pertaining to seeking and obtaining Regulatory Approval for a therapeutic product (excluding any activities required solely for obtaining pricing and reimbursement approval but not for other elements of the Regulatory Approval) and interacting with Regulatory Authorities regarding any of the foregoing. When used as a verb, "**Develop**" means to engage in Development and "**Developed**" has a corresponding meaning.

1.52 "**Development Costs**" means, with respect to a particular Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option:

1.52.1 all Out-of-Pocket Costs and FTE Costs incurred by or on behalf of a Party in a manner consistent with the applicable Development Plan and in accordance with associated Development Budget that are specifically identifiable or reasonably allocable to Development of the applicable Collaboration Program in the Territory. Subject to the foregoing, Development Costs shall include such Out-of-Pocket Costs and FTE Costs incurred in connection with the following activities for the relevant Collaboration Program, as applicable, to the extent performed under and in a manner consistent with the applicable Development Plan and in accordance with the associated Development Budget:

(a) pre-clinical and non-clinical activities such as toxicology and formulation development, test method development, stability testing, quality assurance, quality control development, and statistical analysis;

(b) Clinical Studies for an Optioned Biologic or Optioned Product within such Collaboration Program, including (i) the preparation for and conduct of such Clinical Studies; (ii) data collection and analysis and report writing; (iii) clinical laboratory work; (iv) regulatory activities in direct connection with such studies, including adverse event recordation and reporting; and (v) advisory meetings in connection with such an Optioned Biologic or Optioned Product;

(c) the preparation of Regulatory Documentation as reasonably necessary to conduct Development activities in a manner consistent with then-current Development Plan and in accordance with the associated Development Budget, including any Regulatory Documentation reasonably necessary to obtain or maintain any Regulatory Approval for an Optioned Product within such Collaboration Program and, in all cases, any filing fees incurred in connection therewith, but excluding any Regulatory Documentation pertaining to pricing and reimbursement approvals and any filing fees associated therewith;

(d) the Manufacturing Costs for any Optioned Biologic, Optioned Product, comparators or placebo reasonably necessary to conduct Development activities in a manner consistent with the then-current Development Plan and in accordance with the associated Development Budget;

(e) the disposal of Biologics, Products and other supplies used in the conduct of Development activities in a manner consistent with the then-current Development Plan and in accordance with the associated Development Budget;

(f) the development of the manufacturing process for an Optioned Biologic or Optioned Product included in such Collaboration Program, manufacturing process validation, including validation batches, and qualification and validation of manufacturing Third Party Providers; and

(g) Indemnified Losses and other Out-of-Pocket Costs incurred in connection with Third Party Claims described in Section 13.3 solely to the extent such Indemnified Losses and other Out-of-Pocket Costs are specified in Section 13.3 as to be included in Development Costs;

1.52.2 All FTE Costs and Out-of-Pocket Costs incurred by either Party prior to the Option Exercise Date for such Collaboration Program to the extent such activities: [***] (such activities, the "**Pre Opt-In Development Activities**"), including such corresponding payments to clinical trial sites and clinical research organizations, Manufacturing Costs for an Optioned Product or Optioned Biologic intended for use in such Clinical Studies, manufacturing process development activities and qualification and validation of Third Party Providers for such Manufacturing activities; and

1.52.3 any other FTE Costs and Out-of-Pocket Costs agreed to be shared by the Parties as a Development Cost as expressly set forth in this Agreement.

Except as set forth in Section 1.52.2 and Section 1.52.3, Development Costs shall only include those costs incurred by or on behalf of a Party for those activities performed after the Option Exercise Date. For clarity, Development Costs are exclusive of and do not include Allowable Expenses.

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1.53 "**Development Lead**" means the Party specified as the "Development Lead" pursuant to the terms of Section 4.2.3.

1.54 "**Development Plan**" means, on a Collaboration Program-by-Collaboration Program basis, the plan for the Development of Optioned Biologics and Optioned Products under such Collaboration Program, which plan shall include (a) the activities within the Early Stage Development Activities and Late Stage Development Activities to be conducted by each Party to obtain Regulatory Approval for [***]; and (b) budgeted amounts estimated to be incurred for conducting activities to be undertaken in a manner consistent with the Development Plan (the "**Development Budget**"); and (c) the number of FTEs of each Party or its Affiliates to be allocated to the relevant Development activities. Each Development Plan and Development Budget shall be reasonably detailed with respect to the Development and Manufacturing activities and estimated FTE Costs and Out-of-Pocket Costs, broken down by Calendar Quarter for the first Calendar Year (or part thereof) and by Calendar Year for the next [***] successive Calendar Years.

1.55 "**Directed**" means (a) in the context of a protein-based therapeutic, including an antibody or portion thereof, and a Target that is a Binding Target, that the primary intended mechanism of action of such protein-based therapeutic is to [***] such Target or (b) in the context of a protein-based therapeutic, including an non-antibody protein or portion thereof, and a Target that is a Function Target, that the primary intended mechanism of action of such protein-based therapeutic is to [***] such Target.

1.56 "**Divestiture**" means (a) the divestiture of a Competing Product through (i) an outright sale or assignment of all material rights in such Competing Product to a Third Party or (ii) an exclusive out-license of all development and commercialization rights with respect to such Competing Product, in each case in the Field with no further material role, influence or authority of the applicable Party, directly or indirectly, with respect to such Competing Product in the Field or (b) the complete cessation of all development and commercialization activities with respect to such Competing Product in the Field. For clarity, the right of the applicable Party to receive royalties, milestones or other payments in connection with an acquiror, assignee or licensee's development or commercialization of a Competing Product pursuant to sub-section (a) above, shall be permitted for any such Divestiture. When used as a verb, "**Divest**" and "**Divested**" means to cause a Divestiture.

1.57 "**Dollars**" or "**$**" means United States Dollars.

1.58 "**Drug Approval Application**" means a Biologics License Application as defined in the FFDCA, or any corresponding application for regulatory approval in the Territory, including, with respect to the European Union, a Marketing Authorization Application (a "**MAA**") filed with the EMA pursuant to the Centralized Approval Procedure or an MAA filed with the PMDA, including, in each case, all supplements, amendments, variations, extensions and renewals thereof.

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1.59 "**Early Stage Development Activities**" means, with respect to an Optioned Product(s) within a Collaboration Program, [***].

1.60 "**Effective Date**" means the Business Day following the HSR Clearance Date.

1.61 "**EMA**" means the European Medicines Agency and any successor agency(ies) or authority having substantially the same function.

1.62 "**Enforcing Party**" means the Party specified as the "Enforcing Party" in Section 9.3.2.

1.63 "**European Union**" means the economic, scientific, and political organization of member states known as the European Union, as its membership may be altered from time to time, and any successor thereto.

1.64 "**Exclusive Market Commercialization Plan**" means the plan for commercializing an Optioned Product in each Major Market in which the Parties are not co-Commercializing such Optioned Product, which plan shall include a description of the material pre-launch, launch, and subsequent material commercialization activities to be undertaken in such Major Markets and a reasonably detailed budget for such activities.

1.65 "**Exclusivity Period**" means, with respect to each Designated Target, the time period: (i) beginning on: [***] and (ii) ending on the earlier of [***] whichever [***] occurs first.

1.66 "**Existing Regulatory Documentation**" means the Regulatory Documentation Controlled by Denali or any of its Affiliates as of the Execution Date.

1.67 "**Exploit**", "**Exploitation**", or "**Exploiting**" means to make, have made, import, export, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, modify, enhance, improve, Manufacture, have Manufactured, hold, or keep (whether for disposal or otherwise), or otherwise dispose of. "**Exploited**" has a corresponding meaning.

1.68 "**F-Star Agreements**" means those agreements listed on Schedule 1.68 between Denali and F-Star Gamma Limited, F-Star Biotechnology Limited, F-Star Biotechnologische Forschungs-Und Entwicklungsges M.B.H. or the shareholders of F-Star Gamma Limited, as applicable, and as may be amended from time to time.

1.69 "**FDA**" means the United States Food and Drug Administration and any successor agency(ies) or authority having substantially the same function.

1.70 "**FFDCA**" means the United States Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq.*, as amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions, and modifications thereto).

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1.71 "**Field**" means the diagnosis, treatment or prevention of any condition, disorder and/or disease in humans.

1.72 "**First Commercial Sale**" means, with respect to an Optioned Product and a country, the first sale for monetary value for use or consumption by the end user of such Optioned Product in such country after Regulatory Approval for such Optioned Product has been obtained in such country and where such sale results in a recordable Net Sale in accordance with the applicable Accounting Standards. Sales prior to receipt of Regulatory Approval for such Optioned Product, such as so-called "treatment IND sales," "named patient sales," and "compassionate use sales," in each case to the extent such Optioned Product is sold at or below cost, shall not be construed as a First Commercial Sale.

1.73 "**FTE**" means the equivalent of the work of one (1) employee full time for one (1) Calendar Year (consisting of at least a total of [***] hours per Calendar Year). Each employee utilized by a Party in connection with its performance under this Agreement may be less than or greater than one FTE based on the hours actually worked by such employee performing Development, Commercialization or Manufacturing activities with respect to a Collaboration Program and shall be treated as an FTE on a pro rata basis based upon the actual number of such hours worked divided by [***]. For the avoidance of doubt, FTE only applies to employees of a Party, and does not apply to contractors of a Party.

1.74 "**FTE Costs**" means, with respect to a Party for any period, the applicable FTE Rate multiplied by the applicable number of FTEs of such Party performing Development, Commercialization or Manufacturing activities during such period in accordance with the applicable Research Plan, Development Plan, Additional Development Proposal or Commercialization Plan, as the case may be.

1.75 "**FTE Rate**" means, for the period commencing on the Option Exercise Date, the rate agreed upon by the Parties for a particular category of FTE's activities conducted in the United States. For all other geographic locations outside the United States, the FTE Rate for such locations will be calculated by multiplying the agreed FTE Rate in the United States by a cost of living adjustment between the US and such other geographic location as set forth in [***]. The FTE Rate will be increased by a percentage equivalent to the change over the preceding twelve (12)-month period in [***].

1.76 "**Global Commercialization Plan**" means, for each Collaboration Program, a high-level global commercialization plan and high-level estimated budget for the Commercialization of Optioned Products included in such Collaboration Program in the Field in the Territory, which shall include: (a) an outline for the strategy for the Commercial launch of, and subsequent Commercialization of, such Optioned Product in the Territory; (b) a summary of pre-launch Commercialization activities to be taken by the Parties, including procurement of any necessary pricing and governmental reimbursement approvals; (c) general marketing and promotional plans for such Optioned Product; (d) an estimated annual sales forecast; and (e) the corresponding Commercialization Budget.

1.77 "**Good Clinical Practices**", "**GCP**" or "**cGCP**" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines

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adopted by the International Conference on Harmonization ("**ICH**"), titled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," (or any successor document) including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time.

1.78 "**Good Laboratory Practices**", "**GLP**", or "**cGLP**" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in 21 C.F.R. Part 58 (or any successor statute or regulation), including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority applicable to the Territory, as they may be updated from time to time, including applicable guidelines promulgated under the ICH.

1.79 "**Good Manufacturing Practice**" or "**GMP**" means the then-current good manufacturing practices required by the FDA, as set forth in the FFDCA, as amended, and the regulations promulgated thereunder, for the manufacture and testing of pharmaceutical materials, and comparable Applicable Law related to the manufacture and testing of pharmaceutical materials in jurisdictions outside the U.S., including the quality guideline promulgated by the ICH designated ICH Q7A, titled "Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients" and the regulations promulgated thereunder, in each case as they may be updated from time to time.

1.80 "**HSR Act**" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended.

1.81 "**Humanized**" means: (a) with respect to an Antibody, [***] (b) with respect to a Non-Antibody Protein [***] and "initiation of activities" to Humanize a Biologic shall be deemed to have occurred (x) with respect to an Antibody [***] (y) with respect to a Non-Antibody Protein, [***]. "**Humanize**" and "**Humanization**" have corresponding meanings.

1.82 "**In-License Agreement**" means the Product In-License Agreements and the Platform In-License Agreements.

1.83 "**IND"** means an application filed with a Regulatory Authority for authorization to commence Clinical Studies, including (a) an Investigational New Drug Application as defined in the FFDCA or any successor application or procedure filed with the FDA, (b) any equivalent of a United States IND in other countries or regulatory jurisdictions, (*e.g.*, Clinical Trial Application (CTA)) and (c) all supplements, amendments, variations, extensions and renewals thereof that may be filed with respect to the foregoing.

1.84 "**Indication**" means a disease or condition and all of its associated signs, symptoms**,** stages or progression (including precursor conditions). Notwithstanding the foregoing, [***] shall be deemed to be separate "Indications" for the purposes of this Agreement.

1.85 "**Information**" means all knowledge of a technical, scientific, business and other nature, including know-how, technology, methods, processes, practices, formulae, instructions,

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skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, Regulatory Data, and other biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and information, including study designs and protocols, reagents (*e.g.*, plasmids, proteins, cell lines, assays and compounds) and biological methodology; in each case (whether or not confidential, proprietary, patented or patentable, of commercial advantage or not) in written, electronic or any other form now known or hereafter developed.

1.86 "**Initiation**" means, with respect to any Clinical Study, the [***] in such Clinical Study. "**Initiate**" means to engage in Initiation and "**Initiated**" has a corresponding meaning.

1.87 "**Joint Committee**" means the JSC or a JPT, as applicable.

1.88 "**Late Stage Development Activities**" means, with respect to an Optioned Product(s) within a Collaboration Program, all Development activities that are not Early Stage Development Activities.

1.89 "**Limited Funding Cap**" means [***].

1.90 "**Major European Country**" means any of France, Germany, Italy, Spain or the United Kingdom.

1.91 "**Major Markets**" means the United States, Japan, and each Major European Country.

1.92 "**Manufacture**", "**Manufacturing**", and "**Manufactured**" means all activities related to the synthesis, making, production, processing, purifying, formulating, filling, finishing, packaging, labeling, shipping, and storage of a Biologic, any Product, or any intermediate thereof, including process development, process qualification and validation, scale-up, pre-clinical, clinical and Commercial production and analytic development, product characterization, stability testing, quality assurance, and quality control.

1.93 "**Manufacturing Cost**" means the costs that pertain to an Optioned Biologic or Optioned Product within a Collaboration Program in the Territory that is either (i) supplied by a Third Party, or (ii) manufactured directly by a Party or an Affiliate of a Party, determined as follows:

1.93.1 In the case of clause (i) above, Manufacturing Costs means [***].

1.93.2 In the case of clause (ii) above, Manufacturing Costs means [***].

1.94 "**Manufacturing Lead**" means the Party specified as the Manufacturing Lead in Section 5.2.

1.95 "**Net Revenues**" means, for each Collaboration Program with respect to which Denali has not exercised the Denali Worldwide Royalty Option: (a) the total Net Sales of all

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Optioned Products included in the applicable Collaboration Program plus (b) Other Income received in connection with the Optioned Products included in such Collaboration Program, minus (c) the following items, to the extent applicable, and subject to this Section 1.95:

1.95.1 the standard inventory cost (actual acquisition or manufacture cost) of devices used for dispensing or administering the applicable Optioned Product that are shipped with such Optioned Product and included in the gross invoiced sales prices;

1.95.2 any import or export duties or their equivalent borne by the relevant Party, Affiliate or Sublicensee and specifically attributable to the applicable Optioned Products; and

1.95.3 the actual insurance, packaging, shipping and freight costs directly related to the delivery of such Optioned Product and special packaging.

For clarity, a particular deduction may only be accounted for once in the calculation of Net Revenues and any deduction included in the calculation of Net Sales shall not be included in Net Revenues. For the avoidance of doubt, and for all purposes under this Agreement, Net Revenues shall be accounted for in accordance with the applicable Party's standard accounting practices, as practiced in the relevant country in the Territory, but in any event in accordance with the applicable Accounting Standards, as consistently applied by such Party in such country in the Territory.

1.96 "**Net Sales**" means, with respect to an Optioned Product for any period, the total amount billed or invoiced on sales of such Optioned Product during such period by a Party, its Affiliates, or Sublicensees in the Territory to Third Parties (including Third Party wholesalers or distributors), in bona fide arm's length transactions, less the following deductions, in each case related specifically to such Optioned Product and actually allowed and taken by such Third Parties and not otherwise recovered by or reimbursed to such Party, its Affiliates, or Sublicensees, to the extent deducted in accordance with the applicable Accounting Standards in calculating the "gross to net" revenue adjustment:

1.96.1 trade, cash and quantity discounts;

1.96.2 price reductions or rebates, retroactive or otherwise, imposed by, negotiated with or otherwise paid to governmental authorities or other payees;

1.96.3 taxes on sales (such as sales, value added, or use taxes) to the extent added to the sale price and set forth separately as such in the total amount invoiced and [***];

1.96.4 amounts repaid or credited by reason of rejections, defects, return goods allowance, recalls or returns, or because of retroactive price reductions, including rebates or wholesaler charge backs;

1.96.5 the portion of administrative fees paid during the relevant time period to group purchasing organizations, pharmaceutical benefit managers or Medicare Prescription Drug Plans relating to such Optioned Product;

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1.96.6 any invoiced amounts from a prior period which are not collected and are written off by a Party or its Affiliates, [***]; and

1.96.7 freight, insurance, import/export, and other transportation charges to the extent added to the sale price and set forth separately as such in the total amount invoiced, as well as any fees for services provided by wholesalers and warehousing chains related to the distribution of such Optioned Product.

Net Sales shall not include transfers or dispositions without charge or for a price less than Manufacturing Cost for charitable, promotional, pre-clinical, clinical, regulatory, or governmental purposes. Net Sales shall include the amount or fair market value of all other consideration received by a Party, its Affiliates or Sublicensees in respect of the Optioned Product, whether such consideration is in cash, payment in kind, exchange or other form. Net Sales shall not include sales of Optioned Product between or among a Party, its Affiliates, or Sublicensees for resale, but the subsequent resale of such Optioned Product to a Third Party shall be included within the computation of Net Sales. For purposes of determining Net Sales, an Optioned Product shall be deemed to be sold when recorded as a sale in accordance with the applicable Accounting Standards. For clarity, a particular deduction may only be accounted for once in the calculation of Net Sales. For the avoidance of doubt, and for all purposes under this Agreement, Net Sales shall be accounted for in accordance with the applicable Commercial Lead's accounting principles, as practiced in the relevant country in the Territory, but in any event in accordance with the applicable Accounting Standards, as consistently applied by such Party in such country in the Territory.

In the event an Optioned Product is a Combination Product, the Net Sales for such Combination Product shall be calculated as follows:

(x) If a Party, its Affiliate, or Sublicensee separately sells in substantial volumes in such country or other jurisdiction in the same reporting period, (A) a product containing as its sole active ingredient an Optioned Biologic contained in such Combination Product (the "**Mono Product**") and (B) products containing as their sole active ingredients the Other Active Ingredients in such Combination Product ("**Other Product**"), the Net Sales attributable to such Combination Product shall be calculated by [***].

(y) If a Party, its Affiliates, and Sublicensees do not separately sell in such country or other jurisdiction as described above [***].

1.97 "**Non-Antibody Protein**" means a protein molecule that is not an Antibody or fragment of such protein molecule that includes (a) [***] ("**Functional Moiety**") and (b) [***].

1.98 "**Non-Commercial Lead"** means the Party that is not the Commercial Lead.

1.99 "**Non-Controlling Party**" means the Party that is not the Controlling Party.

1.100 "**Non-Enforcing Party**" means the Party that is not the Enforcing Party.

1.101 "**Non-Manufacturing Lead**" means the Party that is not the Manufacturing Lead.

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1.102 "**Non-Regulatory Lead**" means the Party that is not the Regulatory Lead.

1.103 "**Option Deadline**" means, with respect to a Designated Target and subject to Section 3.2.3(g), the earlier of (a) [***] days following Takeda's receipt of [***], or (b) (i) for each Initial Designated Target, the [***] anniversary of the Effective Date or (ii) for any Replacement Designated Target, the [***] anniversary of the date that the applicable Proposed Target was deemed, pursuant to Section 3.1.3, a Replacement Designated Target, as applicable.

1.104 "**Optioned Biologic**" means: (a) the lead Research Biologic at the time of the applicable Option Exercise Date that is Directed to a Designated Target(s) Developed under a Research Program for such Designated Target(s), (b) [***], (c) if [***] and (d) any derivatives or fragments of any Biologic that is an Antibody described in subsections (a), (b), and (c) (if any), so long as [***]. Notwithstanding the foregoing, "Optioned Biologic", with respect to a Designated Target that is [***].

1.105 "**Optioned Product**" means any Product which contains an Optioned Biologic.

1.106 "**Optioned Target**" means any Designated Target for which Takeda has exercised the Option.

1.107 "**Other Active Ingredient**" means any standalone active pharmaceutical ingredient, which active pharmaceutical ingredient is not covered by any Denali Patents or Takeda Patents. For purposes of clarity, specifically excluded from "Other Active Ingredients" are (a) delivery technologies that increase delivery or exposure of therapeutic proteins in the brain or provide for tissue or cell targeting, and (b) components or modifications to a Biologic that provide additional pharmacological activity (*e.g.*, addition of components or introduction of mutations that would render it bi-specific or multi-specific) or altered pharmacokinetic qualities (*e.g.*, PEGylation).

1.108 "**Other Income**" means any payment (other than Net Sales) when recognized as income or an offset to an expense in accordance with the applicable Accounting Standards by a Party or its Affiliate from a Third Party that is attributable to an Optioned Biologic or Optioned Product within a particular Collaboration Program, including any such payment received in connection with the grant of a sublicense or other right or activity with respect to an Optioned Biologic or Optioned Product, including the grant of an option to obtain such sublicense or other right with respect to an Optioned Biologic or Optioned Product. For clarity, any portion of such payment that is recognized by a Party as an offset to an expense and recorded as Other Income as part of the quarterly reconciliation and true-up process in accordance with Section 8.6.3, shall not also be recorded as an offset against Development Costs or Allowable Expenses for the purposes of such reconciliation and true-up.

1.109 "**Out-of-Pocket Costs**" means amounts actually paid to Third Party vendors or contractors, for services or materials: (a) provided by such Person directly in the performance of activities under and in a manner consistent with a Development Plan or Commercialization Plan and in accordance with the associated Development Budget or Commercialization Budget, as applicable, or (b) to the extent such services or materials apply directly to an Optioned Biologic, an Optioned Product or a Collaboration Program and for which this Agreement provides that

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such costs are sharable between the Parties as a Development Cost or Allowable Expense. For clarity, out-of-pocket costs do not include payments for internal: salaries or benefits; facilities; utilities; general office or facility supplies; insurance; information technology, capital expenditures or the like.

1.110 "**Parkinson's Disease**" means an Indication [***].

1.111 "**Patents**" means: (a) all national, regional and international patents and patent applications, including provisional patent applications; (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from either of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals and continued prosecution applications; (c) any and all patents that have issued or in the future issue from the foregoing patent applications (*i.e.*, described in clauses (a) and (b) above), including utility models, petty patents and design patents and certificates of invention; (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications (*i.e.*, described clauses (a), (b), and (c) above); and (e) any similar rights, including so-called pipeline protection.

1.112 "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

1.113 "**Phase I Trial**" means a human clinical trial of an Optioned Biologic or Optioned Product, the principal purpose of which is a preliminary determination of safety, tolerability and/or pharmacokinetics in healthy individuals or patients or similar clinical study prescribed by the Regulatory Authorities, including the trials referred to in 21 C.F.R. §312.21(a), as amended. Phase I Trial shall include [***].

1.114 "**Phase II Trial**" means a human clinical trial of an Optioned Biologic or Optioned Product, the principal purpose of which is to explore efficacy, Target engagement, pharmacodynamics and/or biological activity in one (1) or more specified doses in the target patient population, or a similar clinical study recommended by the Regulatory Authorities, from time to time, pursuant to Applicable Law or otherwise, including the trials referred to in 21 C.F.R. §312.21(b), as amended. For the purpose of Section 8.3.1, a Phase II Trial shall be [***].

1.115 "**Phase III Trial**" means a human clinical trial of an Optioned Biologic or Optioned Product on a sufficient number of subjects in an indicated patient population that is designed to establish that an Optioned Biologic or Optioned Product is safe and efficacious for its intended use and to determine the benefit/risk relationship, warnings, precautions, and adverse reactions that are associated with such product in the dosage range to be prescribed, which trial is intended to support a Drug Approval Application for such Optioned Biologic or Optioned Product, including all tests and studies that are required by the applicable Regulatory Authority from time to time, pursuant to Applicable Law or otherwise, including the trials referred to in 21 C.F.R. §312.21(c), as amended.

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1.116 "**Phase IV Study**" means: (a) a post-approval clinical study for an Optioned Product with respect to any Indication for which Regulatory Approval has been received or that is required or agreed to be conducted as a condition of receiving Regulatory Approval in a country; as well as (b) any marketing study, epidemiological study, modeling and pharmacoeconomic study, investigator-initiated clinical trial or post-marketing surveillance study of an Optioned Product, in each case (for this clause (b)) that is not intended for use as a basis for obtaining Regulatory Approval (including expanded labeling) with respect to such Optioned Product.

1.117 "**PHSA**" means the United States Public Health Service Act, as amended from time to time.

1.118 "**Platform In-License Agreement**" means any agreement between a Party and a Third Party existing as of the Execution Date or entered into during the Term pursuant to which such Party obtains rights to any intellectual property that is [***]. Those Platform In-License Agreements as of the Execution Date are listed on Schedule 1.118, and include the F-Star Agreements.

1.119 "**PMDA**" means Japan's Pharmaceuticals and Medical Devices Agency and any successor agency(ies) or authority having substantially the same function.

1.120 "**Post-Grant Proceedings**" means proceedings conducted with respect to a Patent before a patent office or other administrative agency that is not a court of law following the grant or issuance of such Patent and pursuant to which the validity, enforceability or scope of such Patent is challenged by a Third Party, including a post-grant opposition proceeding, *ex parte* re-examination (but only if such re-examination is requested by a Third Party), *inter partes* review and other post-grant review proceedings. An appeal, including to a court of law, from such Post-Grant Proceeding, shall be understood to be encompassed by the term Post-Grant Proceedings.

1.121 "**Product**" means any pharmaceutical product containing a Biologic, including all forms, presentations, strengths, doses and formulations (including any method of delivery).

1.122 "**Product Claim**" means a Patent claim that (a) Covers [***].

1.123 "**Product In-License Agreement**" means any agreement between a Party and a Third Party pursuant to which such Party has obtained rights to any Third Party intellectual property which is [***], but excluding in all cases any Platform In-License Agreement. Those Product In-License Agreements existing as of the Execution Date are listed in Schedule 1.123.

1.124 "**Product Labeling**" means, with respect to an Optioned Product in a country or other jurisdiction in the Territory, (a) the full prescribing information for such Optioned Product for such country or other jurisdiction, including any required patient information, approved by the applicable Regulatory Authority and (b) all labels and other written, printed, or graphic matter upon a container, wrapper, or any package insert utilized with or for such Optioned Product in such country or other jurisdiction.

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1.125 "**Product Patent**" means (a) any Denali Patent or Joint Program Patent that includes a Product Claim or (b) any Takeda Patent that includes only Product Claims that are specifically directed to [***].

1.126 "**Product Trademarks**" means the product specific Trademark(s) to be used by a Party or its Affiliates or its or their respective Sublicensees for the Development or Commercialization of Optioned Products in the Territory and any registrations thereof or any pending applications relating thereto in the Territory (excluding, in any event, any trademarks, service marks, names or logos that include any corporate name or logo of the Parties or their Affiliates, including the Corporate Names of the Parties).

1.127 "**Proposed Target**" means a Target that has been nominated by a Party after the Effective Date for consideration by the Parties to replace a Designated Target in accordance with the procedures in Section 3.1.3.

1.128 "**Prosecution and Maintenance**" (including variations such as "**Prosecute and Maintain**") means, with respect to a Patent, the preparing, filing, prosecuting and maintenance of such Patent, including paying all maintenance and/or governmental fees to maintain such Patent in force, and requests for patent term extensions and the like with respect to such Patent, together with the conduct of interferences, Post-Grant Proceedings and other similar proceedings with respect to a Patent, but excluding any Post-Grant Proceedings arising in connection with prosecution of any Product Infringement.

1.129 "**Regulatory Approval**" means, with respect to a country or other jurisdiction in the Territory, all approvals (including Drug Approval Applications), licenses, registrations, or authorizations of any Regulatory Authority necessary to Commercialize an Optioned Biologic or Optioned Product in such country or other jurisdiction, including, where applicable, (a) pricing or reimbursement approval in such country or other jurisdiction, (b) pre-and post-approval marketing authorizations (including any prerequisite Manufacturing approval or authorization related thereto), and (c) approval of Product Labeling.

1.130 "**Regulatory Authority**" means any applicable supra-national, federal, national, regional, state, provincial, or local governmental or regulatory authority, agency, department, bureau, commission, council, or other entities (*e.g.*, the FDA, EMA and PMDA) regulating or otherwise exercising authority with respect to activities contemplated in this Agreement, including the Exploitation of the Optioned Biologic or Optioned Products in the Territory.

1.131 "**Regulatory Documentation**" means all (a) applications (including all INDs and Drug Approval Applications and other Major Regulatory Filings), registrations, licenses, authorizations, and approvals (including Regulatory Approvals) and designations (including designations of a product as an "orphan" drug or its equivalent outside of the United States), (b) correspondence, materials and reports submitted to or received from Regulatory Authorities (including pre-meeting submissions and minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect

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thereto, including all regulatory drug lists, advertising and promotion documents, adverse event files, and complaint files, and (c) Clinical Data and data contained or relied upon in any of the foregoing, in each case (*i.e.*, clauses (a), (b), and (c) above), to the extent pertaining to an Optioned Biologic or Optioned Product.

1.132 "**Regulatory Exclusivity**" means, with respect to any country or jurisdiction, any exclusive marketing rights or data exclusivity protection conferred by an applicable Regulatory Authority or other governmental body in such country or jurisdiction with respect to a biologic or pharmaceutical product, including any regulatory data protection exclusivity and any extensions to such exclusivity rights.

1.133 "**Regulatory Lead**" means the Party specified as the "Regulatory Lead" in Section 4.4.1.

1.134 "**Research Biologic**" means any Biologic Directed to a Designated Target that is Developed by or on behalf of Denali (or, if applicable, Takeda) in the performance of the Research Program for such Designated Target under this Agreement.

1.135 "**Research Milestone Criteria**" means, with respect to each Research Program and a particular Research Milestone Event, the criteria to be satisfied prior to the payment of the milestone payment corresponding to such particular Research Milestone Event, subject to the terms of Section 3.2.3(f).

1.136 "**Research Plan**" means, with respect to a Research Program, an individualized research plan, which will include (a) all key Development, Manufacturing and regulatory activities (if any) to be conducted to advance [***] to be ready for [***]; (b) target criteria for the advancement of activities with respect to each Designated Target, including the Research Milestone Criteria with respect to each Research Milestone Event; (c) the Information to be included in the Data Package and (d) the allocation of responsibilities between Parties for such activities; and in the case of each such research plan, that has been agreed to by the Parties or approved by the JSC in accordance with Section 2.3.6.

1.137 "**Research Program**" means, with respect to a Designated Target, all Research Biologics Directed to such Designated Target and the Development activities with respect to such Research Biologics under the Research Plan.

1.138 "**Research Term**" means, with respect to a Designated Target, the period: (a) beginning on (i) Effective Date for the Initial Designated Targets or (ii) for a Replacement Designated Target, the date the applicable Proposed Target was deemed a Replacement Designated Target in accordance with Section 3.1.3; and (b) ending on the earlier of (i) Takeda's exercise of the Option with respect to such Designated Target, or (ii) the Option Deadline with respect to such Designated Target.

1.139 "**Segregate**" means, with respect to a Denali Competing Product or Takeda Competing Product, as applicable, to use Commercially Reasonable Efforts to segregate the Development, Manufacture and Commercialization activities relating to such product, as applicable, in the Field from Development, Manufacture and Commercialization activities with

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respect to Optioned Biologics and Optioned Products under this Agreement, including using Commercially Reasonable Efforts to ensure that: (a) [***]; and (b) [***]; *provided*, that, in either case of (a) or (b), [***].

1.140 "**Small Patient Population Indication**" means an Indication [***].

1.141 "**Subcontract Agreement**" means, with respect to a Third Party Provider, a written agreement between a Party and such Third Party Provider.

1.142 "**Sublicensee**" means a Person that is granted (directly or indirectly) a sublicense by a Party or its Affiliate under the grants in Section 7.1 or Section 7.2, as applicable and as provided in Section 7.3 or other rights to Develop and/or Commercialize an Optioned Biologic or Optioned Product.

1.143 "**Takeda Know-How**" means Information Controlled by Takeda during the Term that is necessary or actually used to Exploit a Biologic or a Product, in each case, Directed to a Designated Target, in the Field in the Territory, including any related Regulatory Documentation and Clinical Data.

1.144 "**Takeda Patents**" means Patents Controlled by Takeda during the Term that are necessary or actually used to Exploit a Biologic or a Product, in each case, Directed to a Designated Target, in the Field in the Territory.

1.145 "**Takeda Technology**" means, collectively, the Takeda Patents and the Takeda Know-How.

1.146 "**Target**" means any biological target(s) (a) to which an antibody, protein or other pharmaceutical product binds in order to elicit a therapeutic or other pharmacodynamic response (any such biological target, a "**Binding Target**") or (b) that is a protein molecule, such as non-antibody protein molecule, the level of which may be modulated, including by supplementation or replacement, to elicit a therapeutic or other pharmacodynamic response (any such biological target, a "**Function Target**"). Notwithstanding the foregoing, [***] shall not be a Target for purposes of this Agreement. [***].

1.147 "**Tax**" or "**Taxes**" means any form of tax or taxation, levy, duty, charge, social security charge, contribution or withholding of whatever nature (including any related fine, penalty, surcharge or interest) imposed by, or payable to, any government, state or municipality, or any local, state, federal or other fiscal, revenue, customs, or excise authority, body or official in the Territory.

1.148 "**Terminated Program**" means (a) with respect to the termination of this Agreement for a Collaboration Program, all Optioned Biologics and Optioned Products within such Collaboration Program subject to such termination, (b) upon expiration of the Option Period for a Designated Target for which Takeda does not deliver an Option Exercise Notice on or prior to the applicable Option Deadline, all Research Biologics within such Research Program, and (c) with respect to termination of this Agreement in its entirety, all Research Biologics, Optioned Biologics and Optioned Products for each Collaboration Program.

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1.149 "**Territory**" means the entire world.

1.150 "**TfR**" means [***].

1.151 "**Third Party**" means any Person other than Denali, Takeda and their respective Affiliates.

1.152 "**Third Party Provider**" means a Third Party service provider to which a Party has subcontracted its activities under and in accordance with this Agreement.

1.153 "**Trademark**" means any word, name, symbol, color, designation or device or any combination thereof that functions as a source identifier, including any trademark, trade dress, brand mark, service mark, trade name, brand name, logo, business symbol or domain names, whether or not registered.

1.154 "**Transition Plan**" means the plan, approved by the Parties, for the transfer of the Development Lead and Regulatory Lead from one Party to the other Party, which plan will set forth those activities necessary to transition relevant responsibilities related to such Optioned Product or such Collaboration Program, as the case may be, including the transfer of regulatory responsibilities and pharmacovigilance responsibilities.

1.155 "**United States**" or "**U.S.**" means the United States of America and its territories and possessions (including the District of Columbia and Puerto Rico).

1.156 "**Valid Claim**" means (a) a claim of an issued and unexpired Patent to the extent such claim has not been revoked, held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final order, from which no further appeal can be or has been taken, and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer or otherwise; or (b) a claim within a patent application to the extent such claim has not been pending for more than [***] years from the earliest filing date to which such claim or the applicable patent application is entitled to claim priority and which claim has not been revoked, cancelled, withdrawn, held invalid or abandoned.

1.157 Additional Definitions. In addition, each of the following terms shall have the meaning described in the corresponding Section of this Agreement identified below.

Term	Section	Term	Section
Additional Development Activities	4.2.4	Agreement	Preamble
Additional Event Payment	8.3.3	Aggregate Stock Purchase Price	8.1.1
Additional Development Opt-In Notice	4.2.4(e)(i)	Alliance Manager	2.4
Additional Development Proposal	4.2.4(a)	Bankruptcy Code	14.11
Additional Upfront Consideration	8.1.2	Biosimilar Application	9.3.3
Adverse Ruling	14.2	Binding Target	1.146
AEs	10.1	Breaching Party	14.2
		CMO Supply Agreement	5.6.4
		Co-Funding End Date	8.7.1
		Co-Funding Termination	8.7.2
		Commercialization Wind-Down Period	14.8.2

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Term	Section
Competing Product	7.8.1
Consenting Party	3.1.3(c)
Covered ATV Platform Technology	9.1.1
Criteria Achievement Notice	3.2.3(f)
Declining Party	4.2.4(c)
Default Notice	14.2
Denali	Preamble
Denali Indemnitees	13.1
Denali New Technology	7.5.1(b)
Denali Worldwide Royalty Option	8.7.1
Development Budget	1.54
Development Milestone	8.3.1
Development Wind-Down Period	14.8.1
Dispute	16.6
DOJ	15.2
Excluded Target	3.1.3(a)
Execution Date	Preamble
Existing In-License Agreements	7.5.1(a)
Existing Patents	12.2.1
Fabs	1.9
Finance Working Group	8.6.5
Force Majeure Event	16.1
FTC	15.2
Function Target	1.146
Functional Moiety	1.97
HSR Clearance Date	15.1
HSR Conditions	15.1
ICH	1.77
IMS	1.18
Indemnification Claim Notice	13.4
Indemnified Losses	13.1
Indemnified Party	13.4
Indirect Taxes	8.10
Initial Designated Target / Initial Designated Targets	3.1.1
Joint Program Know-How	9.1.1
Joint Program Patents	9.1.1
JPT	2.2.1
JSC	2.1.1
MAA	1.58
Major Indication	8.3.1
Major Regulatory Filings	4.4.2(c)
Manufacturing Process	5.6.1
Manufacturing Technology Transfer	5.6.1
Manufacturing Transfer Plan	5.2
Material Safety Event	14.6
Minor Indication	8.3.1

Term	Section
Mono Product	1.96(x)
Neutral Expert	Schedule 16.6.4
Nominating Party	3.1.3(c)
Non-Breaching Party	14.2
Option	3.2.4(a)
Option Exercise Date	3.2.4(c)(ii)
Option Exercise Fee	8.2.2
Option Exercise Notice	3.2.4(c)
Option Period	3.2.4(c)
Other Product	1.96(x)
Partial Data Package	3.2.3(g)
Party / Parties	Preamble
Patent Working Group	9.2.4
Patient Samples	4.7
Payments	8.9.1
Pharmacovigilance Agreement	10.1
Phase 2 Update	4.2.4(e)(i)
Phase 3 Update	4.2.4(e)(ii)
Pre Opt-In Development Activities	1.52.2
Pre-Option Expenses	8.6.3
Product Infringement	9.3.1
Promotional Materials	6.5
Proposed Target Nomination Notice	3.1.3(c)
Proposed Target Response Notice	3.1.3(c)
Proposing Party	4.2.4(a)
Prosecuted Infringements	9.3.2
Regulatory Approval Update	4.2.4(e)(iii)
Regulatory Data	4.4.3
Replacement Designated Target	3.1.2
Representative Expert	Schedule 16.6.4
Required Assigned Technology	9.1.1
Research Milestone	8.2.1(a)
Royalty Term	8.7.5(c)
Sales Milestone	8.5
Significant Biopharmaceutical Company	7.3.2
Stock Purchase Agreement	Recitals
Supply and Quality Agreement	5.4
Takeda	Preamble
Takeda Indemnitees	13.2
Takeda New Technology	7.5.2
Term	14.1
Terminated Biologic	14.7.1(g)
Terminated Product	14.7.1(g)
Terminated Target	14.7.1(g)
Third Party Claims	13.1
Unavailable	3.1.3(e)
Working Group	2.6

ARTICLE 2
COLLABORATION MANAGEMENT

2.1 Joint Steering Committee.

2.1.1 Formation. As soon as practical, but no later than [***] days after the Effective Date, the Parties shall establish a joint steering committee (the "**JSC**"), which shall perform the functions set forth in Section 2.1.2, oversee the conduct of the Research Programs as set forth in Section 2.1.3, and, if applicable, oversee the conduct of the Collaboration Programs in the Territory. The JSC shall consist of an equal number of representatives from each of the Parties, unless otherwise agreed by the Parties in writing.

2.1.2 Specific Responsibilities. Prior to Takeda's exercise of the Option for a Collaboration Program, the JSC shall oversee the Development of the Research Biologics under the Research Programs. From and after Takeda's exercise of the Option for a Collaboration Program (or any subsequent Collaboration Program), the JSC shall oversee the Development and Commercialization of Optioned Biologics and Optioned Products in the Territory. The JSC shall serve as a forum for the coordination of Development and Commercialization activities for Research Biologics, Optioned Biologics, and Optioned Products in the Territory. In particular, the JSC shall:

(a) [***];

(b) review and approve any Additional Development Proposal in accordance with Section 4.2.4;

(c) form Working Groups as needed to fulfill the obligations of the JSC under this Agreement, including a Finance Working Group (unless Denali has exercised the Denali Worldwide Royalty Option for all Collaboration Programs) with responsibilities as provided in Section 8.6.5 and a Patent Working Group with responsibility as provided in Section 9.2.4;

(d) oversee the Working Groups created by the JSC on all significant strategic issues that fall within the purview of each such Working Group;

(e) except with respect to matters within the responsibility of the Patent Working Group or as otherwise agreed in writing by the Parties, resolve issues presented to the JSC by any Working Group established by such JSC;

(f) resolve issues presented to the JSC in accordance with this Agreement; and

(g) perform such other functions as are set forth herein or as the Parties may mutually agree in writing.

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2.1.3 Research-Specific Responsibilities. In addition to the responsibilities set forth above, during each Research Program, the JSC shall:

(a) review and approve the initial Research Plan for each Replacement Designated Target (if any), other than those Research Plans set forth in Schedule 3.2.1;

(b) serve as a forum for discussing the conduct of activities in connection with such Research Program and the results of such activities;

(c) for any Research Program, approve a change to Research Milestone Criteria, a change to the categories of data, or a material decrease to the scope of data, in each case that need to be included in any Data Package; and

(d) determine whether, for a particular Research Program, the applicable Research Milestone Criteria for Research Milestone Event 1 or Research Milestone Event 2 in the table in Section 8.2.1(a) have been satisfied.

2.2 Joint Program Teams.

2.2.1 Formation. Unless otherwise agreed by the Parties at the JSC, within [***] days after Takeda's receipt of notice from Denali that it has [***] (and Denali shall notify Takeda of such [***] within [***] Business Days), the Parties shall establish a joint program team for each Research Program (each, a "**JPT**"), which will become the JPT for the corresponding Collaboration Program if Takeda exercises its Option for such Research Program in accordance with Section 3.2.4; provided that the Parties may agree to appoint a single JPT for one (1) or more Collaboration Programs. References in this Agreement to "the JPT" with respect to activities or matters occurring in connection with a particular Collaboration Program shall mean the JPT established by the Parties for such Collaboration Program, as the case may be. The composition of each JPT shall be mutually agreed by the Parties, with the understanding that the number of representatives from each Party on a JPT may vary over time; *provided* that the JPT shall include at least one (1) representative from each Party at all times. For clarity, a representative from a Party may be a member of more than one (1) JPT.

2.2.2 Specific Responsibilities. Each JPT shall oversee the Development of a Research Biologic under the applicable Research Plan and the Development Plan and Commercialization of Optioned Biologics and Optioned Products under the applicable Collaboration Program, in each case, in the Territory. In particular, the JPT shall have the responsibilities set forth in this Section 2.2.2:

(a) General Activities and Pre-Option Exercise Development Activities. Each JPT shall:

(i) form Working Groups as needed to fulfill the obligations of such JPT under this Agreement;

(ii) review the budget for any activities conducted prior to the Option Exercise Date if the costs incurred in connection with such activities may be included in Development Costs or Allowable Expenses upon Option exercise for such Collaboration Program;

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(iii) oversee the Working Groups created by such JPT on all significant strategic issues that fall within the purview of each such Working Group;

(iv) resolve issues presented to such JPT for a decision by any Working Group established by such JPT; and

(v) perform such other functions as are set forth in this Agreement, or as the Parties may mutually agree in writing.

(b) Development Activities After Option Exercise. With respect to Development activities for a particular Collaboration Program following Takeda's exercise of its Option for such Collaboration Program (unless Denali exercises the Denali Worldwide Royalty Option for such Collaboration Program), the JPT shall:

(i) review and finalize, for the JSC's approval, the initial Development Plan and the associated Development Budget for such Collaboration Program;

(ii) review and finalize, for the JSC's approval (if applicable), any amendment to the Development Plan and the associated Development Budget for such Collaboration Program;

(iii) review and monitor the activities being conducted under the Development Plan and the progress of such activities;

(iv) review and discuss the selection of clinical trial sites, clinical research organizations and other key Third Party Providers for Clinical Studies included in the Development Plan;

(v) prepare and approve, the Parties' strategies related to:

(A) field-based medical education activities by either Party and grant-based medical education programs in each country within the Co-Commercialization Territory; and

(B) funding for any investigator-initiated clinical trials for the Territory, including Clinical Studies involving a safety issue or the head-to-head comparison of an Optioned Product with any other pharmaceutical agent; *provided*, that the decision to authorize the undertaking of such Clinical Study is subject to JSC approval;

(vi) review and finalize, for the JSC's approval, any Additional Development Proposal pertaining to such Collaboration Program; and

(vii) review and approve the overall strategies for obtaining Regulatory Approvals for Optioned Products included in such Collaboration Program.

(c) Commercialization Activities. With respect to Commercialization activities for a particular Collaboration Program in the Territory (unless Denali exercises the Denali Worldwide Royalty Option for such Collaboration Program), the JPT shall:

(i) discuss, review, and finalize for the JSC's approval each initial Global Commercialization Plan and each Co-Commercialization Plan (if any) for such Collaboration Program (including the associated Commercialization Budget);

(ii) approve the Exclusive Market Commercialization Plan (including the associated Commercialization Budget); *provided* that such approval shall only be withheld to the extent the Exclusive Market Commercialization Plan (if any) (including the associated Commercialization Budget) is inconsistent with the Global Commercialization Plan, the associated Commercialization Budget, or this Agreement;

(iii) discuss, review, and finalize for the JSC's approval (if applicable), any amendments to a Global Commercialization Plan or Co-Commercialization Plan and the associated Commercialization Budgets related thereto;

(iv) review and approve any decision to launch commercial sales of an Optioned Product in a region or country within the Territory; and

(v) discuss, review, and finalize reasonably in advance of the first Regulatory Approval for an Optioned Product, and annually thereafter, a non-binding [***] year estimated sales forecast for the Optioned Products within such Collaboration Program;

(vi) monitor the competitive landscape for the Optioned Products in the Territory;

(vii) discuss, review, and finalize the Parties' strategies related to Phase IV Studies;

(viii) discuss pricing of Optioned Products included in such Collaboration Program; and

(ix) establish a process for reviewing and approving (a) Promotional Materials and (b) training materials and programs for sales representatives, in each case (a) and (b), that are intended for use in any country within the Co-Commercialization Territory.

(d) Manufacturing Activities. With respect to Manufacturing activities for a particular Collaboration Program in the Territory following Takeda's exercise of its Option for such Collaboration Program, the JPT shall:

(i) oversee supply of the Optioned Biologics and Optioned Products as reasonably necessary to conduct Development activities in a manner consistent with the Development Plan and the conduct of Commercialization activities in a manner consistent with the Global Commercialization Plan in order to be able meet expected demand (as reflected in such Global Commercialization Plan);

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(ii) discuss the worldwide manufacturing, licensure, and sourcing strategies in support of the Manufacturing of the Optioned Biologics and Optioned Products;

(iii) review Manufacturing Costs of the Optioned Biologics and Optioned Products, including yields, success rates and other relevant production statistics;

(iv) review a supply forecast for the Optioned Products prepared by the applicable Commercial Lead;

(v) discuss and make recommendations to the Manufacturing Lead regarding results of regulatory inspections related to an Optioned Biologic or Optioned Product and review steps to be taken by either Party to address any deficiencies noted, it being understood that resolution of any such deficiency shall remain in the sole control of the Manufacturing Lead; and

(vi) discuss and make recommendations to the Manufacturing Lead regarding changes in manufacturing sites, testing sites, and responsibilities in the supply chain for each Optioned Biologic and Optioned Product, it being understood that decisions regarding selection of which of internal or Third Party manufacturing and testing sites shall be used to Manufacture the Optioned Biologics and Optioned Products shall remain in the sole control of the Manufacturing Lead, subject to the terms of Section 5.2.

2.3 General Provisions Applicable to Joint Committees.

2.3.1 Meetings and Minutes. The JSC shall meet at least [***], or as otherwise agreed to by the JSC. Upon formation, the JPT shall meet at least [***] per Calendar Quarter, or as otherwise agreed to by the JPT. Meetings of the JSC and each JPT may be conducted by telephone, video-conference, or in-person as determined by the JSC or JPT, as applicable. In-person meetings of each Joint Committee, unless otherwise agreed, shall be held at Denali's offices prior to Takeda's exercise of its Option with respect to each Collaboration Program and shall alternate between Denali's offices and Takeda's offices after Takeda exercises its Option with respect to the relevant Collaboration Program. Regularly scheduled meetings of each Joint Committee may be called by either Party on no less than [***] Business Days' notice, or such shorter time period as agreed by the members. Each Party shall make all proposals for agenda items for regularly scheduled meetings of a Joint Committee, and shall provide all appropriate information with respect to such proposed items, to the applicable meeting managers at least [***] Business Days in advance of the applicable meeting, or such shorter time period as agreed by the Parties. Each Party may also call a special meeting of a Joint Committee to resolve particular matters requested by such Party, on no less than [***] days' notice (or such shorter time period as may be appropriate under the circumstances, but in no event less than [***] Business Days' notice). In the case of a special meeting of a Joint Committee called by a Party, the proposed agenda items and appropriate information with respect to such proposed items shall be provided to the applicable meeting managers together with the notice calling for such special meeting to the other Party.

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2.3.2 Chairpersons. During the Research Programs, the chairperson for the JSC, and any JPT that has been created, shall be appointed by Denali. At the beginning of the first Calendar Year following Takeda's exercise of its Option for a Collaboration Program, the Joint Committees shall each have co-chairpersons. Denali and Takeda shall each select from their representatives a co-chairperson for each of the Joint Committees. Each Party may change any of its designated chairpersons from time to time upon written notice to the other Party. In the event Denali exercises the Denali Worldwide Royalty Option for all Collaboration Programs, the chairperson for the JSC shall be appointed by Takeda.

2.3.3 Meeting Managers. Unless otherwise agreed by the Joint Committee, each Joint Committee shall have meeting co-managers, who need not be a voting member of such Joint Committee. The co-managers will coordinate in good faith for an appropriate distribution of responsibilities between them. The meeting co-managers for the Joint Committees, with assistance and guidance from the Alliance Managers (as appropriate), shall be responsible for calling meetings and for preparing and circulating an agenda in advance of each meeting of such Joint Committee. The meeting co-managers shall prepare and circulate, for review and approval of the Parties, minutes of each meeting within [***] Business Days after such meeting. The Parties shall agree on the minutes of each meeting promptly, but in no event later than [***] days after such meeting.

2.3.4 Procedural Rules. Each Joint Committee shall have the right to adopt such standing rules as shall be necessary for its work, to the extent that such rules are not inconsistent with this Agreement; *provided* that such rules shall not be subject to a deciding vote of either Party having final decision-making authority for such committee. At least (1) representative from each Party on each Joint Committee shall have the requisite seniority to make decisions on behalf of the relevant Party with respect to the issues falling within the decision-making authority of the relevant Joint Committee. A quorum of the Joint Committee shall exist whenever there is present at a meeting at least [***] representative appointed by each Party with the requisite seniority to make decisions described in the second sentence of this Section 2.3.4. From time to time, each Party may substitute one (1) (or more, if applicable) of its representatives to a particular Joint Committee on written notice to the other Party, *provided* that the criteria in the second sentence of this Section 2.3.4 shall continue to be satisfied. Representatives of the Parties on a Joint Committee may attend a meeting either in person or by telephone, video conference, or similar means in which each participant can hear what is said by, and be heard by, the other participants.

2.3.5 Meeting Attendance. Employees of either Party (or a Party's Affiliate) that are not representatives of such Party on a Joint Committee may attend meetings of such Joint Committee; *provided*, that the Party wishing such persons to participate in a meeting has provided reasonable advance notice to the other Party. Non-employees may only attend meetings of a Joint Committee if such non-employee is bound by written obligations of confidentiality and non-disclosure substantially equivalent to those set forth in Article 11 and with the prior written approval of the other Party (such approval not to be unreasonably withheld, delayed or conditioned).

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2.3.6 Joint Committee Decision Making.

(a) The decisions of each Joint Committee shall be by unanimous agreement. Each Party shall have a single vote on a matter to be decided by the applicable Joint Committee irrespective of the number of representatives of such Party in attendance at the applicable Joint Committee meeting. Decisions of a Joint Committee may also be made by a written resolution unanimously agreed by the Parties and signed by at least one representative of each Party appointed to the applicable Joint Committee; it being understood that such unanimous written agreement may be provided by email if the Parties so agree.

(b) If a Joint Committee does not reach unanimous agreement on an issue for decision by the Joint Committee within [***] Business Days after the meeting at which such issue was first presented for decision by the Joint Committee, despite good faith efforts to do so, then, unless such issue is a Consent Matter or otherwise to be resolved in accordance with Section 2.3.6(c) below: (i) [***] shall have final decision making authority with respect to [***] respectively, (ii) the [***] shall have final decision making authority with respect to [***] matters, and (iii) the [***] for shall have final decision making authority with respect to [***] matters [***]. The decision of the applicable Party's representative on a Joint Committee with respect to an issue within such Joint Committee's decision making authority and for which such Party has the deciding vote shall become the decision of the applicable Joint Committee. All Consent Matters must be [***]. If the JSC does not reach unanimous agreement on a Consent Matter or any other matter within the decision-making authority of the JSC within [***] Business Days after the JSC meeting at which the applicable issue was first presented to the JSC for decision, such issue shall be resolved in accordance with Section 2.3.6(c) and the resolution of such issue in accordance with Section 2.3.6(c) below shall become the decision of the JSC with respect to such issue.

(c) With respect to any Consent Matter on which the JSC does not reach unanimous agreement within [***] Business Days after the first meeting of the JSC at which such issue or dispute is considered, or any other matter or dispute to be resolved in accordance with this Section 2.3.6(c), then, either Party may refer the dispute in writing to the senior executive officers of the Parties, who shall confer in good faith on the resolution of the dispute. Any final decision mutually agreed to by the senior executive officers shall be conclusive and binding on the Parties. If the senior executive officers are not able to agree on the resolution of any such dispute within [***] days after such issue was first referred to them, then such dispute shall be [***].

(d) Disputes arising between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith, and that are outside of the decision-making authority of the Joint Committees and not within a Party's sole decision-making authority shall be resolved pursuant to Section 16.6.

2.3.7 Limitations on Authority. Each Party shall retain the rights, powers, and discretion granted to it under this Agreement and no such rights, powers, or discretion shall be delegated to or vested in a Joint Committee unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing. No Joint Committee shall have the power to, and no deciding vote of a Party or decision of the Neutral Expert on a matter referred to such Person, shall, amend, modify, or waive compliance with this Agreement, which may only be amended or modified as provided in Section 16.8 or compliance

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with which may only be waived as provided in Section 16.11. No decision of any Joint Committee (including by a Party in the exercise of its deciding vote in accordance with Section 2.3.6 or a decision of the Neutral Expert on a matter referred to such Person,) shall (a) finally determine any interpretation of this Agreement or the Parties rights or obligations hereunder, or (b) conflict with any terms and conditions of this Agreement, nor be in contravention of Applicable Law in any material respect.

2.3.8 Discontinuation of Joint Committees. Each Joint Committee shall continue to exist until the first to occur of: (a) the Parties mutually agreeing to disband the Joint Committee; and (b) Denali providing to Takeda written notice of its intention to disband and no longer participate in such Joint Committee, *provided*, that Denali shall not give such written notice prior to Takeda's exercise of the Option or the expiration of the last-to-expire Option Period. Notwithstanding anything herein to the contrary, once one or more Joint Committees have been disbanded, such disbanded Joint Committee shall be terminated and thereafter (i) any requirement of a Party to provide Information or other materials to such Joint Committee shall be deemed a requirement to provide such Information or other materials to the other Party, and (ii) any matters previously delegated to the Joint Committee shall be resolved by unanimous agreement of the Parties, or, if the Parties do not reach unanimous agreement, in accordance with the decision making provisions of Sections 2.3.6(b)–2.3.6(c).

2.4 Alliance Manager. Each Party shall appoint a person(s) who shall be responsible for the overall coordination and facilitation of the communication, interaction, and cooperation between the Parties and shall have such other responsibilities as the Parties may agree in writing after the Effective Date (each, an "**Alliance Manager**"). Each Party may replace its Alliance Manager at any time by notice in writing to the other Party.

2.5 Denali Worldwide Royalty Option. Notwithstanding any of the foregoing provision in this Article 2, in the event Denali exercises the Denali Worldwide Royalty Option with respect to any Collaboration Program, the following shall apply with respect to such Collaboration Program from and after the Co-Funding End Date for such Collaboration Program:

2.5.1 Takeda shall be designated the Development Lead, Regulatory Lead, Manufacturing Lead (subject to Section 5.2), and Commercial Lead with respect to the such Collaboration Program.

2.5.2 The applicable JPT with respect to such Collaboration Program shall dissolve. On an at least an [***] basis thereafter, Takeda shall submit a revised Development Plan and Global Commercialization Plan (if appropriate based on the then-current Development stage of the Optioned Product) to the JSC for review and comment. Without limiting Section 2.5.3, Takeda shall consider any comments from Denali with respect to such Development Plan or Commercialization Plan in good faith. For clarity, such Development Plans and Global Commercialization Plans shall be limited to the Major Markets and shall only include a description of material activities and a corresponding high-level budget for such activities.

2.5.3 Takeda shall have the right to make decisions with respect to all matters pertaining to such Collaboration Program previously subject to the decision-making authority of the JSC, including all Consent Matters for such Collaboration Program other than those Consent

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Matters described in Sections 1.39.10–1.39.15, which such matters shall be resolved in accordance with Section 2.3.6(c) if the Parties are unable to reach unanimous agreement with respect to any such matter; *provided* that Takeda may only exercise such final decision making authority with respect to such Consent Matters after escalation to the JSC and if such decisions by Takeda are consistent with the terms and conditions of this Agreement.

2.5.4 The JSC shall no longer meet with respect to such Collaboration Program after the [***] anniversary of the First Commercial Sale of an Optioned Product from such Collaboration Program. Thereafter, Takeda shall provide Denali (via the JSC if still in operation with respect to other Collaboration Programs) [***] update of all [***] activities in the [***] that were completed [***] and those planned for the [***].

2.6 Working Groups. From time to time, a Joint Committee may establish and delegate duties to sub-committees or directed teams (each, a "**Working Group**") to oversee particular projects or activities (for example, joint finance group and/or joint intellectual property group), *provided* that in no event shall a Joint Committee have the right to, and no Joint Committee shall, delegate its respective decision-making authority to any such Working Group. Each such Working Group shall be constituted as the applicable Joint Committee determines and shall establish its own procedures, to the extent that such procedures are not inconsistent with this Agreement; *provided* that each Working Group shall have adequate functional representation from each Party. Members of a Working Group may also be members of a Joint Committee. Working Groups may be established on an ad hoc basis for purposes of a specific project or on such other basis as the applicable Joint Committee may determine. Each Working Group and its activities shall be subject to the oversight, review, and approval of, and shall report to, the Joint Committee that established such Working Group. In no event shall the authority of a Working Group exceed the authority specified for the Joint Committee that established the Working Group pursuant to this Article 2. All decisions of a Working Group shall be made by unanimous agreement. Any disagreement between the representatives of Takeda and Denali on a Working Group shall be referred to the Joint Committee that established the Working Group for resolution in accordance with Section 2.3.6. Employees of either Party (or a Party's Affiliate) that are not representatives of such Party on a Working Group may attend meetings of such Working Group; *provided*, that the Party wishing such persons to participate in a meeting has provided reasonable advance notice to the other Party. Non-employees may only attend meetings of a Working Group if such non-employee is bound by written obligations of confidentiality and non-disclosure substantially equivalent to those set forth in Article 11 and with the prior written approval of the other Party (such approval not to be unreasonably withheld, delayed or conditioned).

2.7 Information. Each Party shall keep the Joint Committees reasonably informed as to its efforts and activities with respect to the Development, Manufacture, and Commercialization of the Research Biologics, Optioned Biologics, and Optioned Products in the Territory, including by providing such Information as the other Party may reasonably request from time to time.

2.8 Expenses. Each Party shall be responsible for all travel and related costs and expenses for its representatives and, if applicable, its (or any of its Affiliate's) other personnel to attend meetings of, and otherwise participate in, a Joint Committee or other Working Group. All other Out-of-Pocket Costs incurred by the Joint Committees or Working Groups in furtherance

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of a meeting, such as expenses associated with off-site meetings, shall be (a) if the meeting is specific to a particular Collaboration Program prior to the first Regulatory Approval of an Optioned Product in such Collaboration Program, a Development Cost for such Collaboration Program, or (b) otherwise, an Allowable Expense; provided that if Denali has exercised the Denali Worldwide Royalty Option for all Collaboration Programs, such Out-of-Pocket Costs will be shared equally by the Parties.

ARTICLE 3
DESIGNATED TARGETS; RESEARCH ACTIVITIES

3.1 Designated Targets.

3.1.1 General. The Parties may select up to three (3) Designated Targets at any given time to be Developed and Commercialized under and in accordance with this Agreement. Schedule 1.49 sets forth the initial three (3) Designated Targets that have been mutually agreed by the Parties as of the Effective Date (each, an "**Initial Designated Target**" and together, the "**Initial Designated Targets**").

3.1.2 Replacement Designated Targets. A Party may propose to replace an Initial Designated Target with another Target in accordance with and subject to the terms of Section 3.1.3 (such replacement Designated Target, a "**Replacement Designated Target**"); *provided* that such proposal is provided in writing to the other Party prior to the earliest to occur of the following events: (a) the [***] year anniversary of the Effective Date; (b) the existence of a Biologic Directed to such original Designated Target [***]; or (c) initiation of activities under this Agreement to [***]. For avoidance of doubt, such replacement shall be allowed no more than [***] for each Designated Target without the Parties' mutual written agreement, and [***] pursuant to this Section 3.1.2 without the Parties' mutual written agreement. Effective on and after the date of selection of a Replacement Designated Target, (i) the previously selected Designated Target shall no longer be, or be deemed to be, a Designated Target for any purposes of this Agreement, (ii) the licenses granted by each Party to the other Party in the Territory pursuant to Section 7.1 and 7.2 shall terminate with respect to such previously selected Designated Target, and (iii) any exclusivity obligations of a Party with respect to such previously selected Designated Target pursuant to Section 7.8 shall terminate.

3.1.3 Selection and Replacement Procedures. The following procedure shall apply with respect to the selection of a Replacement Designated Target:

(a) Neither Party may nominate a Proposed Target that is identified on the excluded Target list set forth in Schedule 3.1.3(a) or that is otherwise not applicable to [***] (each such Target, an "**Excluded Target**").

(b) Prior to the nomination of any Proposed Target pursuant to Section 3.1.3(c), the Parties shall discuss any potential Proposed Target at the JSC and the each Party shall consider the other Party's comments on such Proposed Target in good faith.

(c) To nominate a Proposed Target as a Designated Target, a Party (such Party, the "**Nominating Party**") shall provide to the other Party (such Party, the

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"**Consenting Party**") a written description of the Proposed Target specifically referencing this Section 3.1.3(c), including to the extent available, the NCBI Entrez Gene Symbol and NCBI RefSeq accession (each, a "**Proposed Target Nomination Notice**"). Each Proposed Target Nomination Notice shall not include more than [***] Proposed Target. Within [***] Business Days following the Consenting Party's receipt of the Proposed Target Nomination Notice with respect to a Proposed Target, the Consenting Party shall notify the Nominating Party in writing of its acceptance or rejection of such Proposed Target as a Replacement Designated Target (each, a "**Proposed Target Response Notice**"), [***]. If the Proposed Target Response Notice indicates that the Consenting Party accepts the Proposed Target, Denali shall prepare, for the JSC's approval, a Research Plan with respect to such Proposed Target. Upon approval by the JSC of such Research Plan, such Proposed Target shall be deemed to be a Replacement Designated Target.

(d) If a Nominating Party provides a Proposed Target Nomination Notice to the Consenting Party, such Nominating Party shall not provide any other Proposed Target Nomination Notice to the Consenting Party until the earlier of receipt of a Proposed Target Response Notice from the Consenting Party or [***] Business Days following the Consenting Party's receipt of the Proposed Target Nominating Notice.

(e) For any of the first [***] Proposed Targets that is not Unavailable with respect to the Consenting Party, if the Consenting Party rejects any such Proposed Target under Section 3.1.3(c), then for a period beginning on the date of the applicable Proposed Target Response Notice and ending [***] months thereafter, the Consenting Party shall not, [***]. For avoidance of doubt, the provisions of this Section 3.1.3(e) shall not limit a Party's [***] Directed to (i) any Target that is Unavailable or (ii) any Target that is not Unavailable other than a Target that was one of the first [***] Proposed Targets that were not Unavailable. As used herein, "**Unavailable**" means that, with respect to the applicable Proposed Target and a Consenting Party, (A) such Proposed Target is an Excluded Target or (B) such Consenting Party has: (i) [***]; (ii) [***], or (iii) [***]. Where a Proposed Target comprises more than one Target, such Proposed Target shall be Unavailable if any of such Targets are Unavailable.

(f) For clarity, notwithstanding the provisions of this Section 3.1.3, the Parties could mutually agree to select a Proposed Target that is an Excluded Target or otherwise Unavailable as described in Section 3.1.3(e)(B)(ii) or (iii) as a Replacement Designated Target.

3.2 Research Plans and Activities.

3.2.1 Research Plans. The initial Research Plans for the Initial Designated Targets are set forth in Schedule 3.2.1. The initial Research Plan for a Designated Target (other than an Initial Designated Target) shall be prepared by Denali as provided in Section 3.1.3(c) and subject to the approval by the JSC in accordance with Section 2.1.3(a) and Section 2.3.6.

3.2.2 Amendments to a Research Plan. The JSC shall review the Research Plan for each Research Program on a regular basis, and in no event less frequently than [***] Calendar Year, and the progress of activities being conducted for each Research Program against the Research Plan. Either Party may propose amendments to the Research Plan for a given

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Research Program from time to time as appropriate, to take into account completion, commencement or cessation of activities contemplated in the then-current Research Plan for, as well as any newly available Information related to, such Research Program. Such amendments shall be effective upon JSC approval and subject to the decision making in accordance with Section 2.3.6.

3.2.3 Research Activities.

(a) **Efforts**. Each Party shall use Commercially Reasonable Efforts to [***]. Each Party shall perform any and all of its Development activities with respect to a Research Program in good scientific manner and in compliance with all Applicable Law, including applicable national and international (*e.g.*, ICH, GCP, GLP, and GMP) guidelines.

(b) **Allocation of Activities**. Each Party shall be responsible for day-to-day implementation of the research activities allocated to it under a Research Plan or for which it is otherwise responsible under the applicable Research Program pursuant to this Agreement. Denali shall be the Development Lead for each Research Plan. Takeda shall conduct or otherwise be responsible for activities under any Research Program only upon the mutual agreement of the Parties and to the extent reflected in the then-current Research Plan for such Research Program.

(c) **Research Reports**. For each Research Program, Takeda may designate internal subject matter experts with respect to such Research Program. For clarity, Takeda may designate the same subject matter experts for multiple Research Programs. Denali shall, on at least a [***] basis, informally communicate with such designated subject matter experts with respect to the ongoing Development activities for such Research Program. Without limiting the foregoing, at each meeting of the JSC, each Party shall report on the Development activities such Party has performed (or caused to be performed) under the applicable Research Plan since the last meeting of the JSC, and the results of such activities, all in accordance with reporting procedures reasonably determined by the JSC from time to time. The JSC will evaluate the progress of such Development activities and results in relation to the goals of the applicable Research Plan and may request a Party provide such other information as may be reasonably necessary to understand the status of the applicable Research Program and the progress towards achievement of the Research Milestones in such Research Program.

(d) **Research Plan Expenses**. Each Party shall be solely responsible for any Out-of-Pocket Costs or FTE Costs it incurs in furtherance of the activities assigned to it under an applicable Research Plan.

(e) **Regulatory Activities**. Denali shall be the Regulatory Lead for all Research Biologics Directed to a given Designated Target prior to the Option Exercise Date for such Designated Target. Prior to the Option Exercise Date for a particular Designated Target, Denali shall provide Takeda with a reasonable opportunity to review and comment on any material communications with the applicable Regulatory Authorities with respect to Research Biologics included in the Research Program for such Designated Target, including to the extent existing prior to the Option Exercise Date, any INDs and other Major Regulatory Filings. Denali shall consider in good faith any such comments of Takeda with respect to such communications.

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Denali shall also keep Takeda reasonably informed, via the JSC and/or Takeda's designated subject matter experts, regarding any substantive meetings with any Regulatory Authority regarding Research Biologics Directed to a particular Designated Target.

(f) **Achievement of Research Milestone Criteria**. For each Research Program, Denali shall notify Takeda and the JSC if Denali determines in good faith that the Research Milestone Criteria for a particular Research Milestone Event have been satisfied by a Research Biologic within such Research Program (each a "**Criteria Achievement Notice**") and shall provide Takeda and the JSC with [***]. If, within [***] Business Days after the Criteria Achievement Notice, Takeda does not notify the JSC in writing that it objects to Denali's determination that the applicable Research Milestone Criteria have been satisfied, such Research Milestone Criteria shall be deemed to have been satisfied. If Takeda issues an objection notice pursuant to the preceding sentence within the applicable [***]-Business Day period, the matter shall [***].

(g) **Data Package Disclosure**. For each Research Program, Denali shall deliver to Takeda the Data Package as soon as reasonably practicable after completion of the activities under the applicable Research Plan if such activities are completed prior to the expiration of the applicable Option Deadline. In the event Denali reasonably believes that [***], Denali shall, no later than [***] days before the applicable Option Deadline for such Research Program, provide Takeda with [***] (the "**Partial Data Package**"). Notwithstanding the foregoing, if at the time the Partial Data Package is delivered to Takeda, there are [***], Denali shall [***] and the applicable Option Deadline shall be extended by up to [***] months, or, if earlier, until [***] days after Takeda receives such Information. Along with the delivery of each of the Data Package, or Partial Data Package, as the case may be, Denali shall provide Takeda with [***]. To the extent Takeda has incurred or expects to incur, prior to the Option Exercise Date, any FTE Costs or Out-of-Pocket Costs to be included as a Development Cost under Section 1.52.2, Takeda shall provide to Denali details of such FTE Costs and Out-of-Pocket Costs promptly following Denali's disclosure of each of the Data Package, or Partial Data Package, as the case may be. For avoidance of doubt, the reference of the conduct of any specific Development activities under this Section 3.2.3(g) shall not be construed as altering either Party's obligations under Section 3.2.3(a).

3.2.4 Option Grants to Takeda.

(a) **The Option**. Subject to the terms and conditions of this Agreement, Denali hereby grants to Takeda, on a Designated Target-by-Designated Target basis, the exclusive right, but not the obligation, to obtain the licenses set forth in Section 7.1.2 with respect to the Collaboration Program for such Designated Target (each, an "**Option**").

(b) **Review of the Data Package**. Upon Takeda's receipt of the Data Package or Partial Data Package, as applicable, Takeda shall have the remaining Option Period to determine whether it will submit the Option Exercise Notice. During this review period, upon Takeda's reasonable request, Denali shall make reasonable efforts to promptly make available to Takeda: (i) its and its Affiliates' employees and consultants who performed the activities on behalf of Denali under the Research Plan, including the preparation of the Data Package; and (ii) any additional Information or data then-existing and under Denali's possession or control related to the Research Program that is reasonably necessary in evaluating such Data Package or Partial Data Package, including with respect to the then-current development CMC status.

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(c) **Option Exercise Mechanics**. Takeda shall have the right to exercise its Option with respect to a Designated Target by providing written notice of such election to Denali (the "**Option Exercise Notice**") at any time on or after the Effective Date and prior to the occurrence of the Option Deadline with respect to such Designated Target (the "**Option Period**"). Along with such Option Exercise Notice, Takeda shall specify in writing [***]. For the avoidance of doubt, Takeda's election to exercise its Option for a particular Research Program prior to Denali's delivery of a Data Package or Partial Data Package pursuant to Section 3.2.3(g) above, shall not otherwise affect the allocation of rights and responsibilities between the Parties under this Agreement with respect to such Research Program.

(i) **Option Exercise**. If Takeda submits the Option Exercise Notice to Denali with respect to a particular Designated Target, Takeda shall pay the Option Exercise Fee in accordance with Section 8.2.2; [***]. For clarity, in the event an approval from a governmental authority is required, the Parties shall seek such approval in accordance with Article 15.

(ii) **Option Exercise Date**. The exercise of the Option shall become effective, and the licenses granted under Sections 7.1.2 and 7.2.2 with respect to such Designated Target and the corresponding Collaboration Program shall be in full force and effect, immediately upon Takeda's payment of the Option Exercise Fee set forth in Section 8.2.2 to Denali (the "**Option Exercise Date**").

(iii) **Failure to Exercise Option**. If Takeda does not provide Denali with an Option Exercise Notice or if Takeda provides Denali with written notice of it decision not to exercise the Option with respect to a Collaboration Program for a Designated Target prior to the Option Deadline, then from and after the expiration of the Option Period or Denali's receipt of such notice not to exercise the Option, as applicable, each Party will be free itself or with or through an Affiliate or Third Party, to develop and commercialize any Biologics or Products Directed to such Terminated Target, and the Parties' respective rights and obligations with respect to such Target under Section 7.8 shall terminate. In such event, the provisions of Sections 14.7 and 14.8 shall apply with respect to the Terminated Program and Takeda shall grant licenses to Denali as provided in Section 14.7.1 (and subject to the procedures described therein), in each case to the extent applicable.

ARTICLE 4
DEVELOPMENT AND REGULATORY ACTIVITIES AFTER OPTION EXERCISE

4.1 General. Subject to the terms of this Agreement, the JPT and the JSC (as applicable) shall, following Takeda's exercise of its Option with respect to a particular Designated Target, oversee and coordinate the Development of Optioned Biologics and Optioned Products within the applicable Collaboration Program in the Field in the Territory.

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4.2 Development Plan and Activities.

4.2.1 Development Plan. Promptly after the formation of the JPT with respect to an applicable Designated Target, the applicable Development Lead shall prepare in consultation with the other Party, for the JPT's review and the JSC's approval, the portion of a Development Plan corresponding to the Development activities for which it is the Development Lead, for the Development of the Optioned Products within the Collaboration Program for such Designated Target. The Development Plan for each Collaboration Program shall reflect Commercially Reasonable Efforts [***]. Unless Denali has exercised the Denali Worldwide Royalty Option for a particular Collaboration Program, each Development Plan for a Collaboration Program shall include a role for Denali, as mutually agreed by the Parties. In the event Denali has exercised the Denali Worldwide Royalty Option with respect to a Collaboration Program, the Development Plan for such Collaboration Program shall be limited to [***]; provided that the foregoing limitations on specific content of the Development Plan shall not be construed as to limit (or be deemed to limit) Takeda's diligence obligations under this Agreement.

4.2.2 Amendments and Updates. The JPT shall review the Development Plan for each Collaboration Program on a regular basis, and in no event less frequently than [***] Calendar Year. Either Party, through its representatives on the JPT, may propose amendments to a Development Plan and the associated Development Budget for a given Collaboration Program from time to time. In any event, an updated Development Plan, including the associated Development Budget, for each Collaboration Program shall be provided by the JPT (and approved by the JSC as required) no later than December 1 of each Calendar Year. If such revised Development Plan (and associated Development Budget) is not approved by the JSC, then, until such time as an updated Development Plan for such Collaboration Program is approved by the JSC in accordance with Section 2.3.6: (a) the then-current Development Plan (and associated Development Budget) shall continue to govern the Parties' Development activities under this Agreement with respect to the applicable Collaboration Program; and (b) each Party shall be obligated to conduct Development activities allocated to such Party under such then-current Development Plan and shall be permitted to incur Development Costs consistent with such associated Development Budget, which Development Costs shall be shared by the Parties in accordance with Section 8.6.

4.2.3 Development Activities.

(a) **Efforts**. Each Party shall use Commercially Reasonable Efforts to [***]. Each Party shall perform any and all of its Development activities with respect to each Collaboration Program in good scientific manner and in compliance with all Applicable Law, including applicable national and international (*e.g.*, ICH, GCP, GLP, and GMP) guidelines, informed consent and institutional review board regulations, current standards for pharmacovigilance practice, and all applicable requirements relating to the protection of human subjects.

(b) **Allocation of Activities**. Each Party shall be responsible for day-to-day implementation of the Development activities allocated to it under a Development Plan. The Development Lead shall be responsible for preparing clinical trial designs and protocols, sponsoring Clinical Studies, engaging Third Party Providers, and shall be primarily responsible for the conduct of any such Early Stage Development Activities or Late Stage Development Activities, as the case may be, consistent with the then-current Development Plan for such Collaboration Program.

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(c) **Designation of Development Lead**. Unless otherwise agreed by the Parties, for each Collaboration Program, Denali shall be the Development Lead with respect to Early Stage Development Activities and Takeda shall be the Development Lead with respect to Late Stage Development Activities; *provided* that after initiation of Late Stage Development Activities with respect to any Optioned Biologic or Optioned Product for a particular Indication, Takeda shall be the Development Lead with respect to all subsequent Development of such Optioned Biologic or Optioned Product for such Indication, including any Clinical Study that is Initiated thereafter for such Indication, whether Early Stage Development Activities or Late Stage Development Activities. Notwithstanding the initiation of Late Stage Development Activities for a particular Optioned Product within a Collaboration Program for an Indication, unless otherwise agreed, Denali will continue to be Development Lead for [***]. In addition to any activities that the Parties agree the Non-Development Lead may conduct, the Non-Development Lead shall have the right to have one (1) or more of its employees attend, and participate in, all global advisory board meetings and other meetings with key opinion leaders regarding each Collaboration Program, or any Optioned Biologics or Optioned Products included in such Collaboration Program. Neither Party shall conduct, directly or indirectly, any Clinical Study or other Development of any Optioned Biologic or Optioned Product within a particular Collaboration Program in the Field in the Territory, except as expressly permitted in this Article 4.

(d) **Transition of Development Lead**. Reasonably in advance of the Initiation of Late Stage Development Activities for each Collaboration Program, the JPT will prepare a Transition Plan to be approved by the Parties for the transfer of the Development Lead with respect to such Optioned Product from Denali to Takeda.

(e) **Development Reports**. For each Collaboration Program, each Party shall report on the Development activities such Party has performed (or caused to be performed) under such Collaboration Program in accordance with the procedures established by the JPT. The JPT shall evaluate the work performed in relation to the goals of the applicable Development Plan. The Parties shall provide such other Information as may be reasonably requested by the JPT with respect to such Development activities.

4.2.4 Additional Development Activities. Each Party shall be permitted to undertake Development activities for an Optioned Product within a particular Collaboration Program for [***] (such activities, the "**Additional Development Activities**"); *provided* that such Party complies with the provisions of this Section 4.2.4.

(a) **Additional Development Proposals**. If a Party (such Party, the "**Proposing Party**") desires to undertake Additional Development Activities, such Party shall submit to the JPT a proposal for the addition of such Additional Development Activities to the Development Plan that includes a proposed work plan, timeline and budget for such Additional Development Activities (an "**Additional Development Proposal**"). The Additional Development Proposal shall be prepared in a similar scope and format of a Development Plan. The Proposing Party shall provide the JPT with any additional Information related to the Additional Development Proposal reasonably requested by the JPT.

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(b) **Inclusion of Additional Development Activities in the Development Plan**. The JPT shall review and decide on such Additional Development Proposal within [***] days after its receipt of such Additional Development Proposal; *provided* that such time shall be extended if the Proposing Party has not provided all available Information reasonably requested by the JPT. If the JPT approves an Additional Development Proposal, such Additional Development Proposal shall be submitted promptly to the JSC for review. If the JSC approves an Additional Development Proposal, the Development Plan shall be deemed to be amended to include the Additional Development Activities and associated budget upon approval of such Additional Development Proposal by the JSC. For the sake of clarity, all FTE Costs and Out-of-Pocket Costs incurred thereafter by the Parties in performing such Additional Development Activities shall be treated as Development Costs until the Co-Funding End Date after Denali exercises the Denali Worldwide Royalty Option for the applicable Collaboration Program. If the JSC does not approve the Additional Development Proposal, inclusion of the Additional Development Activities within the Development Plan shall not be subject to resolution under Section 2.3.6, and instead the provisions of Sections 4.2.4(c)–(e) shall apply.

(c) **Objection by the Other Party**. If the JPT and JSC do not timely approve an Additional Development Proposal within the time periods set forth in Section 4.2.4(b), the other Party (the "**Declining Party**") may, within [***] Business Days of the JSC's final vote with respect to the Additional Development Proposal, initiate the dispute resolution arbitration procedures set forth in Section 16.6.4, if, and only if, the Declining Party determines reasonably and in good faith that (i) [***] or (ii) [***]. Upon initiation of dispute resolution, the Proposing Party will be prohibited from [***] until such time that dispute is finally determined in accordance with Section 16.6.4.

(d) **Performance of Additional Development Activities**. If the JPT and JSC do not timely approve an Additional Development Proposal within the time periods set forth in Section 4.2.4(b) and either (i) the Declining Party does not timely initiate the dispute resolution arbitration procedures set forth in Section 16.6.4, or (ii) the dispute is finally determined in accordance with Section 16.6.4 in favor of the Proposing Party, the Proposing Party may, upon notice to the JSC, conduct the relevant Additional Development Activities described in the Additional Development Proposal. For clarity, an Optioned Product that is the subject of Additional Development Activities shall continue to be an Optioned Product for all purposes of this Agreement. The Proposing Party shall be the Development Lead and Regulatory Lead with respect to such Additional Development Activities, including with respect to obtaining any required Regulatory Approval, until the Proposing Party's receipt of an Additional Development Opt-In Notice for such Additional Development Activities, after which the provisions of Section 4.2.3 shall apply. In the event the Proposing Party is not the Manufacturing Lead for the applicable Optioned Biologic or Optioned Product, if a Party so requests, the Proposing Party and the Manufacturing Lead shall enter into a Supply and Quality Agreement in accordance with Section 5.4. Additional Development Activities undertaken by the Proposing Party shall be subject to the oversight of the JPT for the applicable Collaboration Program; *provided* that the Proposing Party will have final decision making authority with respect to any issue related to the Additional Development Activities. The Proposing Party shall bear all costs

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associated with the Additional Development Activities it undertakes and such costs shall not be taken into account as Development Costs or as Allowable Expenses. Except as expressly set forth in this Section 4.2.4(d), the conduct of the Additional Development Activities will be subject to all terms and conditions of this Agreement relating to Development of Optioned Products. At each meeting of the JPT, the Proposing Party shall report its progress with regard to the Additional Development Activities in the same manner as the Parties provide reports to the JPT with respect to activities covered by the Development Plan for the relevant Collaboration Program, including providing formal written reports of the results related to the Additional Development Activities, as well as the actual costs incurred by the Proposing Party, along with estimated future budgets.

(e) **Opt-In for Additional Development Activities**.

(i) **Completion of a Phase 2 Trial**. Within [***] days after the date of the database lock for the first Phase II Trial related to the Additional Development Activities, the Proposing Party shall furnish to the JPT and the Declining Party, a written report of the results of such Clinical Study and the Additional Development Costs incurred by the Proposing Party (the "**Phase 2 Update**"). The Proposing Party shall also provide the JPT with any other Information related to the Additional Development Activities which is reasonably requested by the JPT and available to the Proposing Party. If, within [***] days of the Declining Party's receipt of the Phase 2 Update, it notifies the JPT and the Proposing Party in writing that it desires to include the Additional Development Activities into the Development Plan (an "**Additional Development Opt-In Notice**"): (1) the Declining Party shall, subject the review rights set forth in to Section 8.6.1(b), pay to the Proposing Party an amount equal to [***] of the Additional Development Costs identified in the Phase 2 Update and (2) the terms of Section 4.2.4(e)(iv) shall apply.

(ii) **Completion of Phase 3 Trial**. In the event that the Declining Party does not submit the Additional Development Opt-In Notice in accordance with Section 4.2.4(e)(i), then within [***] days after the date of the database lock for the first Phase III Trial related to the Additional Development Activities, the Proposing Party shall furnish to the JPT and the Declining Party, a written report of the results of such Clinical Study and the Additional Development Costs incurred by the Proposing Party (the "**Phase 3 Update**"). The Proposing Party shall also provide the JPT with any other Information related to the Additional Development Activities which is reasonably requested by the JPT and available to the Proposing Party. If, within [***] days of the Declining Party's receipt of the Phase 3 Update, the Declining Party submits an Additional Development Opt-In Notice to the JPT and Proposing Party: (1) the Declining Party shall, subject the review rights set forth in to Section 8.6.1(b), pay to the Proposing Party an amount equal to [***] of the Additional Development Costs identified in the Phase 2 Update and Phase 3 Update and (2) the terms of Section 4.2.4(e)(iv) shall apply.

(iii) **Regulatory Approval**. In the event that the Declining Party does not submit the Additional Development Opt-In Notice in accordance with Section 4.2.4(e)(i) or (ii), and the Proposing Party receives Regulatory Approval in a Major Market country with respect to the Additional Development Activities, the Proposing Party shall promptly notify the Declining Party in writing of such Regulatory Approval and the Additional Development Costs incurred by the Proposing Party (the "**Regulatory Approval Update**").

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Promptly after receipt of a Regulatory Approval Update, the Declining Party shall be required to submit an Additional Development Opt-In Notice to the JPT and the Declining Party and the Declining Party shall, subject the review rights set forth in to Section 8.6.1(b), pay to the Proposing Party an amount equal to [***] of the Additional Development Costs identified in the Phase 2 Update, Phase 3 Update and Regulatory Approval Update and the terms of Section 4.2.4(e)(iv) shall apply; *provided* that such amount shall be reduced to [***] of such Additional Development Costs if [***].

(iv) **Additional Development Opt-In Notice**. Immediately upon the Proposing Party's receipt of the Additional Development Opt-In Notice: (i) the Additional Development Activities (if any) for such Optioned Product and the applicable Indication of the Additional Development Activities shall be deemed to be included in the Development Plan for the relevant Collaboration Program; (ii) the then-current plan and budget for such Additional Development Activities shall be deemed to be included within and part of the Development Plan, and shall control with respect to such Additional Development Activities unless and until an amendment to the Development Plan providing for a different or modified plan and budget is approved by the JSC in accordance with Section 4.2.2; (iii) all Out-of-Pocket Costs and FTE Costs incurred thereafter in connection with such Additional Development Activities shall be treated as Development Costs and shared by the Parties until the Co-Funding End Date after Denali exercises the Denali Worldwide Royalty Option for the applicable Collaboration Program; and (iv) to the extent one or more Commercialization Plans for such Optioned Product then-exist and the Phase 3 Update or Regulatory Approval Update has occurred, the JPT will update such Commercialization Plans in accordance with Section 6.3.4 to address Commercialization of such Optioned Product for the applicable Indication in any country for which Regulatory Approval is obtained.

(v) **Worldwide Royalty Option**. Notwithstanding the foregoing, in the event Denali exercises the Denali Worldwide Royalty Option with respect to any Collaboration Program, Denali shall not be permitted to undertake any Additional Development Activities pursuant to this Section 4.2.4, and Takeda shall have the right to conduct Additional Development Activities by amending the applicable Development Plan, and this Section 4.2.4 will not apply to such activities by Takeda.

4.2.5 Development Costs. Each Party will be solely responsible for all FTE Costs and Out-of-Pocket Costs such Party incurs in connection with the Development of Optioned Biologics and Optioned Products in any Collaboration Program after the Co-Funding End Date following Denali's exercise of the Denali Worldwide Royalty Option for such Collaboration Program, except as otherwise agreed by the Parties in writing.

4.3 Disclosure of Technology for Development Purposes.

4.3.1 Promptly after the Option Exercise Date for a particular Collaboration Program, Denali shall disclose and make available to Takeda the Regulatory Documentation, Denali Know-How, and Joint Program Know-How with respect to any Optioned Biologics or Optioned Products within the Collaboration Program, in each case that are Controlled by Denali and are necessary or reasonably useful for Takeda to Develop, Manufacture, or Commercialize such Optioned Biologics and Optioned Products within such Collaboration Program in the

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Territory in accordance with the terms of this Agreement. The JPT shall establish a process pursuant to which, after the Effective Date, but before Denali exercises the Denali Worldwide Royalty Option with respect to any Collaboration Program, the Parties shall disclose and make available to the other Party: Regulatory Documentation, Denali Know-How or Takeda Know-How (including, in each case, any Joint Program Know-How), and other Information claimed or covered by any Denali Patent, Takeda Patent, or Joint Program Patent or otherwise relating, directly or indirectly, to Optioned Biologics and Optioned Products within such Collaboration Program, in each case to the extent Controlled by such Party and that are necessary or reasonably useful for the other Party to Develop, Manufacture, or Commercialize such Optioned Biologics and Optioned Products within such Collaboration Program in the Territory in accordance with the terms of this Agreement, to the extent such items have not previously been provided to the other Party. The Parties shall cooperate and reasonably agree upon formats and procedures to facilitate the orderly and efficient exchanges of Regulatory Documentation, Information, or inventions contemplated under this Section 4.3.1.

4.3.2 After the Option Exercise Date for a particular Collaboration Program, each Party shall, to the extent requested by the other Party, provide such other Party with all reasonable assistance required in order to transfer to the other Party the Regulatory Documentation, Denali Know-How and Takeda Know-How (including, in each case, any Joint Program Know-How), and other Information required to be provided pursuant to Section 4.3.1, in each case in a timely manner, and shall assist the other Party with respect to the Exploitation of any Optioned Biologic and any Optioned Products within the relevant Collaboration Program in accordance with the terms of this Agreement; *provided* that such Party's requirement to provide the other Party any tangible items, including any documentation, shall be limited to those items then-existing and Controlled by such Party at the time of such request by the other Party; *provided*, *further*, that in the event Denali exercises the Denali Worldwide Royalty Option with respect to any Collaboration Program, Takeda shall not be required to make such Regulatory Documentation, Takeda Know-How (including any Joint Program Know-How), or other Information available to Denali. Without limiting the foregoing, prior to Denali's exercise of the Denali Worldwide Royalty Option, if visits of a Party's representatives to the other Party's facilities are reasonably requested by the other Party for purposes of transferring such Regulatory Documentation, Denali Know-How, Takeda Know-How, Joint Program Know-How, or other Information Controlled by a Party to the other Party or for purposes of the other Party acquiring expertise on the practical application of such Information or assisting on issues arising during such Exploitation, such Party shall use Commercially Reasonable Efforts to [***].

4.3.3 Any Out-of-Pocket Costs incurred by the Parties in performing disclosure and transfer activities pursuant to this Section 4.3, and if any supplies of Optioned Biologics or Optioned Product are transferred to the other Party in connection with such activities, the Manufacturing Cost of such materials shall be included as Development Costs; provided that following the Co-Funding End Date after Denali exercises the Denali Worldwide Royalty Option for a particular Collaboration Program, each Party will be solely responsible for all FTE Costs and Out-of-Pocket Costs it incurs to conduct such activities, except that Takeda shall reimburse the Manufacturing Cost of any materials supplied by Denali to Takeda. In addition, notwithstanding the above, neither Party shall be obligated to provide or make available to the other Party research tools, materials or Information generally applicable to Development of products for the treatment of diseases or conditions, to the extent such items are not reasonably necessary for the other Party to further Develop or Manufacture the applicable Optioned Biologics or Optioned Products in the Territory under this Agreement.

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4.4 Regulatory Matters.

4.4.1 Regulatory Lead. Effective from and after the Option Exercise Date for a given Optioned Product (and any Optioned Biologic therein) on an Indication-by-Indication and jurisdiction-by-jurisdiction basis: (a) Denali shall be the Regulatory Lead until the commencement of regulatory activities related to the Late Stage Development Activities with respect to such Optioned Product (or, if earlier, Denali's exercise of the Denali Worldwide Royalty Option with respect to the applicable Collaboration Program); (b) Takeda shall be the Regulatory Lead beginning on commencement of regulatory activities related to the Late Stage Development Activities for such Optioned Product [***]; and (c) on a jurisdiction-by-jurisdiction basis, the Commercial Lead shall be the Regulatory Lead [***].

4.4.2 Regulatory Activities. The following shall apply with respect regulatory activities relating to each Collaboration Program:

(a) Subject to Section 4.4.2(c) below, the then-Regulatory Lead shall have the lead role and responsibility with respect to the preparation, obtaining and maintenance of all Regulatory Documentation necessary to perform the applicable activities under the applicable Development Plan or Commercialization Plan. The Non-Regulatory Lead shall support the Regulatory Lead, as may be reasonably necessary, in the preparation, obtaining and maintenance of such Regulatory Documentation, and in the activities in support thereof, including providing necessary documents or other materials required by Applicable Law to obtain such Regulatory Approvals, in each case in accordance with the terms and conditions of this Agreement and the applicable Development Plan. Notwithstanding the foregoing, to the extent the Regulatory Lead is not the same Party as the Manufacturing Lead, the Manufacturing Lead shall prepare the CMC Module 3 of the Common Technical Document in English for the Optioned Product, and the Regulatory Lead will modify as appropriate, such module for use in Regulatory Approvals in the Territory. Notwithstanding anything to the contrary in this Section 4.4.2(a), during the period of time when (i) Denali is the Regulatory Lead pursuant to Section 4.4.1(a), Takeda shall, to the extent permissible under Applicable Law and notwithstanding Section 4.4.2(d), have the right to interact directly with the respective Regulatory Authority on an interaction directly related to the filing and preparation of Regulatory Documentation for the Late Stage Development Activities, subject to prior notification and coordination with Denali, and (ii) Takeda is the Regulatory Lead pursuant to Section 4.4.1(b), if Denali is to be the Commercial Lead in the United States with respect to a Collaboration Program, (A) Denali shall, to the extent permissible under Applicable Law, have the right to interact directly with the FDA on the Product Labeling for each Optioned Product in such Collaboration Program, subject to prior notification and coordination with Takeda, (B) Takeda shall not conduct any scheduled discussions, meetings, and conferences with the FDA on Product Labelling for Optioned Products included in such Collaboration Program without prior notification and coordination with Denali, and (C) notwithstanding Section 4.4.2(d), Denali shall have the right to have [***], or more if determined by the JPT, participate in all scheduled discussions, meetings, and conferences with the FDA on Product Labelling for each Optioned Product in such Collaboration Program for which Denali is to be the Commercial Lead in the United States pursuant to Section 4.4.2(d).

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(b) All Regulatory Documentation to the extent relating to an Optioned Biologic or Optioned Product with respect to an Indication within such Collaboration Program shall be owned by, and shall be the sole property and held in the name of the then-Regulatory Lead for such Indication. All Regulatory Documentation relating to the Optioned Biologics or Optioned Products that is not specific to any particular Indication shall be owned by, and shall be the sole property and held in the name of the then-Regulatory Lead for first Indication for which the applicable Optioned Biologics or Optioned Product received Regulatory Approval, or if no such Regulatory Approval has been obtained, the most advanced Indication with respect to the applicable Optioned Biologic or Optioned Product. In the event one Party replaces the other Party as the Regulatory Lead, the Parties shall, in manner consistent with the Transition Plan: (i) transition to such Regulatory Lead all applicable INDs for an Optioned Product; (ii) hereby assign to such Regulatory Lead all of such other Party's right, title and interest in and to all Regulatory Documentation (to the extent consistent with the above provisions of this Section 4.4.2(b) regarding ownership of such Regulatory Documentation) in the Territory and Controlled by such other Party during the Term; and (iii) duly execute and deliver, or cause to be duly executed and delivered, such instruments and shall do and cause to be done such acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary under, or as such Regulatory Lead may reasonably request to carry out more effectively the purpose of this Section 4.4.2(b).

(c) The Regulatory Lead in a Major Market for the applicable Optioned Biologics and Optioned Products shall provide the Non-Regulatory Lead with an opportunity to review and comment on all INDs, pre-meeting submissions, Drug Approval Applications, Product Labeling, material labeling supplements, Regulatory Authority meeting requests, core data sheets and other material regulatory submissions, in each case, in the Major Markets (collectively, "**Major Regulatory Filings**"). The Regulatory Lead shall consider in good faith the Non-Regulatory Lead's comments and use reasonable efforts to implement such comments. The Regulatory Lead shall provide access to interim drafts of such Major Regulatory Filings to the Non-Regulatory Lead via the access methods (such as secure databases) established by the JPT, and the Non-Regulatory Lead shall provide its comments on the final drafts of such Major Regulatory Filings or of proposed material actions within [***] Business Days (or [***] Business Days in the case of Drug Approval Applications), or such other period of time mutually agreed to by the Parties. In the event that a Regulatory Authority in the Territory establishes a response deadline for any such Major Regulatory Filing (or material action with respect thereto) shorter than such [***]-Business Day period (or [***]-Business Day period in the case of Drug Approval Applications), the Parties shall work cooperatively to ensure the Non-Regulatory Lead has a reasonable opportunity for review and comment within such deadlines. The Regulatory Lead shall consider in good faith any such comments of the Non-Regulatory Lead. Without limiting the foregoing, if Denali has elected to be the Commercial Lead in the United States for a particular Collaboration Program, all Drug Approval Applications to be filed in the United States for Optioned Products included in such Collaboration Program shall be drafted and prepared in close consultation with Denali.

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(d) The Regulatory Lead shall provide the Non-Regulatory Lead with prior written notice, to the extent the Regulatory Lead has advance knowledge, of any scheduled substantive meeting, conference, or discussion (including any advisory committee meeting) with a Regulatory Authority in the Major Markets relating to an Optioned Product within such Collaboration Program, within [***] Business Days after the Regulatory Lead first receives notice of the scheduling of such substantive meeting, conference, or discussion (or within such shorter period as may be necessary in order to give the Non-Regulatory Lead a reasonable opportunity to attend such meeting, conference, or discussion). Subject to Section 4.4.2(a), the Non-Regulatory Lead shall have the right to have [***] or more of its employees attend as an observer(s) (but not participate in) all such substantive meetings, conferences, and discussions.

(e) All costs incurred after the Option Exercise Date with respect to regulatory activities for to a particular Collaboration Program shall be a Development Cost or Allowable Expense, as appropriate; provided that from and after the Co-Funding End Date following Denali's exercise of the Denali Worldwide Royalty Option with respect to such Collaboration Program, each Party shall be solely responsible for all such costs incurred by such Party.

(f) The preceding sub-sections (c) and (d) will not apply to any Collaboration Program after Denali's exercise of the Denali Worldwide Royalty Option with respect to such Collaboration Program.

4.4.3 Regulatory Data. To the extent not provided pursuant to Section 4.3.1, the JPT shall establish a process pursuant to which each Party shall promptly provide to the other Party copies of or access to non-clinical data and Clinical Data, and other Information, results, and analyses with respect to any Development activities for a Collaboration Program and its Additional Development Activities (collectively, "**Regulatory Data**").

4.5 Records. Each Party shall maintain records in accordance with its standard practices, which in cases shall be consistent with standard practices in the pharmaceutical industry and in compliance with Applicable Law. Such records shall be retained by such Party for at least [***] years after the Calendar Year to which such records relate, or for such longer period as may be required by Applicable Law. Upon request, such Party shall provide copies of the records it has maintained pursuant to this Section 4.5 to the other Party.

4.6 Clinical Trial Register and Data Transparency. The JPT will cooperate to establish timelines and procedures for reviewing any public disclosure of Clinical Data. The Development Lead will, in accordance with Applicable Law and its internal data transparency policies, publish the results or summaries of Clinical Studies relating to an Optioned Biologic or Optioned Product on a clinical trial register maintained by it and the protocols of clinical trials relating to such Optioned Biologic or Optioned Product on www.ClinicalTrials.gov (or an equivalent register, or as otherwise required by Applicable Law or such Party's policies). In the event that the data transparency policies of the other Party (regardless if such policy is based upon Applicable Law or other internal guidelines) are materially different to the data transparency policies of the Development Lead, the JPT shall meet in good faith to resolve such material differences, *provided* that neither Party shall be permitted to prevent the disclosure of data by the other Party as required by such other Party's data transparency policies.

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4.7 Patient Samples. All patient samples collected and retained in connection with Clinical Studies involving an Optioned Biologic or Optioned Product that are performed under a Development Plan or for which costs are shared as Development Costs (together with compilations of Information comprising annotations regarding patient histories or correlating patient outcomes, with respect to such samples, "**Patient Samples**") shall be a shared resource of the Parties. Unless otherwise agreed by the Parties or otherwise set forth in this Section 4.7, all Patient Samples shall be maintained and stored at the facilities of a Third Party reasonably agreed by the Parties for the purposes of the conduct of Collaboration Program activities, and the fees paid to such Third Party in connection with such maintenance and storage shall be a Development Cost. Each Party's use of Patient Samples shall be in accordance with Applicable Law, including any informed consent and institutional review board regulations and all applicable requirements relating to the protection of human subjects. [***].

ARTICLE 5
MANUFACTURING

5.1 Manufacturing Activities. The Manufacturing Lead shall be responsible for Manufacturing or having Manufactured (using a reputable Third Party Provider) each Research Biologic, Optioned Biologic and Optioned Product, as applicable. The Manufacturing Lead shall use Commercially Reasonable Efforts to [***]. The Manufacturing Lead shall obtain supply of the required quantities of Optioned Biologics, Optioned Product and placebo used in Clinical Studies, or otherwise to support the Development activities to be conducted under a Development Plan, either by performing Manufacturing by itself or through its Affiliates, or from a reputable Third Party Provider of manufacturing services, in each case until [***]. Following [***], the Manufacturing Lead will have the sole right to determine which of its or a Third Party Provider's manufacturing sites will be used to manufacture the Optioned Product or component of the Optioned Product and may transfer the Manufacturing from one site to another, so long as such transfer would not reasonably be likely to have a material adverse effect on continued supply or, unless Denali has exercised the Denali Worldwide Royalty Option with respect to the Optioned Product, [***] increase in costs incurred in connection with or as a result of such transfer. Notwithstanding the foregoing, prior to any such transfer, the Manufacturing Lead will notify the Non-Manufacturing Lead of its intention to transfer Manufacturing from one site to another and shall permit the Non-Manufacturing Lead to carry out an audit of the proposed new site before such transfer takes place. In the event that the Manufacturing Lead [***] then, at the request of the Non-Manufacturing Lead, [***].

5.2 Manufacturing Lead. Denali shall be the Manufacturing Lead for each Research Program and Collaboration Program until the completion of the transfer of Manufacturing responsibilities to Takeda in accordance with this Section 5.2 and Section 5.6. If (a) Denali exercises the Denali Worldwide Royalty Option for such Collaboration Program or (b) Denali proposes to the JPT and the JPT agrees [***] that Denali should transfer Manufacturing Lead responsibilities to Takeda for such Collaboration Program following Takeda's exercise of the Option, provided that no such JPT agreement or [***] shall be required where such Manufacturing is performed by one or more Third Party Providers, then in each case the JPT will

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prepare, for the Parties' approval, a plan for the Manufacturing Technology Transfer consistent with Section 5.6 (the "**Manufacturing Transfer Plan**") to transfer Manufacturing responsibilities for such Collaboration Program to Takeda, after which Takeda shall become the Manufacturing Lead with respect to such Collaboration Program. Without limiting the foregoing, Takeda shall not become the Manufacturing Lead with respect to any Collaboration Program until the completion of the applicable Manufacturing Transfer Plan.

5.3 Manufacturing Costs. Subject to Section 1.52.2, Denali shall be solely responsible for all Manufacturing Costs incurred in furtherance of the applicable Research Plan. All Manufacturing Costs incurred in furtherance of a Development Plan or Commercialization Plan for a Collaboration Program shall be a Development Cost or Allowable Expense, as appropriate; *provided* that if Denali exercises the Denali Worldwide Royalty Option for a particular Collaboration Program, Takeda shall, following the Co-Funding End Date, bear all Manufacturing Costs and, to the extent that Denali is the Manufacturing Lead, shall reimburse Denali for its FTE Costs and Out-of-Pocket Costs incurred in connection with the Manufacture of Optioned Biologics and Optioned Products. The Manufacturing Lead will promptly inform the JPT of any circumstance which could reasonably be expected to result in a [***] or greater increase in the Manufacturing Costs for any Optioned Biologic or Optioned Product during the Calendar Years covered by any then-current applicable budgets. The JPT will discuss any reasonable recommendations that either Party may have to mitigate against such increase to the Manufacturing Costs.

5.4 Supply Agreements. If, in a given country or region, the Development Lead or the Commercial Lead are a different Party than the Manufacturing Lead for clinical supply of Phase III Trials or Commercialization use, then, upon either Party's request, the Parties shall enter into separate supply and associated quality agreements (each, a "**Supply and Quality Agreement**") covering the terms of supply to the Non-Manufacturing Lead for such Development or Commercialization activities. The Supply and Quality Agreement will contain terms and conditions that are reasonable and customary for agreements of such nature, including a right of the Non-Manufacturing Lead to include its Manufacturing Costs as Development Costs or Allowable Expenses, as applicable. If the Parties are unable to reach agreement on such provisions within [***] days of a request by either Party to enter into a Supply and Quality Agreement (which [***]-day period may be extended upon the mutual agreement of the Parties), upon request by either Party, the same shall be determined pursuant to Section 16.6.4. The terms of any such Supply and Quality Agreement, including the Manufacturing Lead's rights and the Non-Manufacturing Lead's obligations under such Supply and Quality Agreement, shall be consistent with rights of the Manufacturing Lead under the applicable CMO Supply Agreements. To the extent there is any conflict between the terms and conditions of such Supply and Quality Agreements and this Agreement with respect to the matters expressly covered by such Supply and Quality Agreements, then such Supply and Quality Agreements shall control.

5.5 Third Party Providers. If a Manufacturing Lead utilizes one or more Third Party Providers to supply Optioned Product to the Non-Manufacturing Lead, then with respect to activities covered by any CMO Supply Agreement entered into prior to the Effective Date or, if entered into after the Effective Date, in accordance with the penultimate sentence of this Section 5.5, and so long as the Manufacturing Lead uses Commercially Reasonable Efforts to [***]. If, after the Effective Date, the Manufacturing Lead enters into any agreements with Third

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Party Providers for Manufacturing services for clinical or Commercial supply of Optioned Biologics or Optioned Products under this Agreement, (a) the Manufacturing Lead shall [***] and (b) the Manufacturing Lead shall [***]. For clarity, the Manufacturing Lead is not required to [***].

5.6 Manufacturing Transfer.

5.6.1 Initial Transfer. In the event Takeda is to be the Manufacturing Lead with respect to any Collaboration Program, the Parties shall design the Manufacturing Transfer Plan such that the Takeda will become the Manufacturing Lead for such Collaboration Program as soon as possible after Takeda is appointed to become the Manufacturing Lead, *provided* that if such Manufacturing Technology Transfer solely involves the transfer of responsibility for manufacturing activities being conducted by a Third Party Provider under a CMO Supply Agreement from one Party to the other without changing the manufacturing facility, such Manufacturing Transfer Plan shall be completed within [***] or shall otherwise be completed within the time period specified in the applicable Manufacturing Transfer Plan. No Manufacturing Transfer Plan shall require Takeda to assume any CMO Supply Agreements between Denali and its Third Party Provider for Manufacturing activities for the relevant Collaboration Program unless Takeda consents to do so. In such instance, Denali shall, in accordance with the applicable Manufacturing Transfer Plan, [***]. In the event any such CMO Supply Agreement cannot [***], Denali shall use Commercially Reasonable Efforts to [***]. In the event the assignment of any such CMO Supply Agreement is conditioned (other than for notice), the Parties shall discuss such conditions in good faith and, if the Parties, mutually agree to satisfy such conditions for the assignment of the applicable CMO Supply Agreement, the Manufacturing Transfer Plan shall address such matter. As further provided in the Manufacturing Transfer Plan, Denali shall cooperate with Takeda with respect to such other steps as may be reasonably required to effect a full transfer to Takeda or Takeda's Third Party Provider of all Denali Know-How (including any Joint Program Know-How) that are necessary or reasonably useful for Takeda to implement the then-current process for the Manufacture of such Optioned Product and Optioned Biologic (the "**Manufacturing Process**") (together with the assignment of CMO Supply Agreements and enablement and assistance to enter into a new agreement with such Third Party Provider, the "**Manufacturing Technology Transfer**"). As a part of the Manufacturing Technology Transfer, Denali shall cause all appropriate employees and representatives of Denali and its Affiliates, and appropriate analytical and quality control employees and representatives of its Third Party Providers, at mutually convenient times, to meet with, employees or representatives of Takeda or its designated Third Party Provider at the applicable manufacturing facility: (a) to assist with the working up and use of the Manufacturing Process and with any training to the extent reasonably necessary to enable the use and practice the Manufacturing Process; and (b) to make available all necessary equipment Controlled by Denali, to support and execute the transfer of all applicable analytical methods and the validation thereof (including, all applicable Denali Know-How, Joint Program Know-How, methods, validation documents, manufacturing and release enabling reports, and other documentation, materials and sufficient supplies of all primary and other reference standards).

5.6.2 Subsequent Transfers. Without limiting the foregoing, after completion of the Manufacturing Transfer Plan, Denali shall, and shall use Commercially Reasonable Efforts to [***], provided that Denali shall use Commercially Reasonable Efforts to

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obtain such rights) to take the following actions, in each case, as reasonably requested by Takeda:

(a) make available, to Takeda or its designated Third Party Provider from time to time, all Manufacturing-related Denali Know-How, Joint Program Know-How, Information and materials relating to the Manufacturing Process Controlled by Denali and not transferred to Takeda or such Third Party Provider during the initial transfer, and all documentation constituting material support, performance advice, shop practice, standard operating procedures, specifications as to materials to be used and control methods, that are Controlled by Denali and reasonably necessary to enable Takeda or its designated Third Party Provider to use and practice the Manufacturing Process; and

(b) provide such other assistance as Takeda, or designated its Third Party Provider, as applicable, may reasonably request to enable Takeda or its designated Third Party Provider to use and practice the Manufacturing Process and otherwise to Manufacture the applicable Optioned Biologics and Optioned Products.

5.6.3 Transfer Costs. All FTE Costs and Out-of-Pocket Costs incurred by either Party in performing activities pursuant to this Section 5.6, including Manufacturing Technology Transfer activities and activities under Section 5.6.2, shall be included as Development Costs or Allowable Expenses, as applicable.

5.6.4 Third Party Agreements. Notwithstanding anything to the contrary in this Agreement, each Manufacturing Transfer Plan and any Manufacturing Technology Transfer shall be subject to the terms and conditions of the agreements between the Manufacturing Lead and its applicable Third Party Providers of manufacturing services and technology (each agreement, a "**CMO Supply Agreement**"). A list of CMO Supply Agreements existing as of the Execution Date are set forth on Schedule 5.6.4.

ARTICLE 6
COMMERCIALIZATION

6.1 General. Subject to the terms of this Agreement, following Takeda's exercise of its Option with respect to a particular Collaboration Program, the JPT (and the JSC, as applicable) shall oversee and, to the extent applicable, coordinate, the Commercialization of all Optioned Products within such Collaboration Program in the Field in the Territory.

6.2 Commercialization Activities.

6.2.1 Efforts. With respect to each Collaboration Program, for each jurisdiction in which Regulatory Approval is obtained, each Party shall use Commercially Reasonable Efforts to [***]. Each Commercialization Plan for a Collaboration Program shall reflect Commercially Reasonable Efforts to [***].Each Party shall perform any and all of its Commercialization activities with respect to each Collaboration Program, in good scientific manner and in compliance with all Applicable Law.

6.2.2 Allocation of Activities and Costs. For each Collaboration Program, each Party shall be responsible for day-to-day implementation of the Commercialization

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activities with respect to the Optioned Products within such Collaboration Program allocated to such Party under the applicable Commercialization Plan. Unless otherwise agreed by the Parties, the Commercial Lead shall have the responsibilities set forth in Sections 6.2.3 and 6.2.4. The Parties shall share all FTE Costs and Out-of-Pocket Costs incurred in connection with Commercialization activities to the extent included in Allowable Expenses; provided that following the Co-Funding End Date after Denali exercises the Denali Worldwide Royalty Option for a particular Collaboration Program, each Party will be solely responsible for all FTE Costs and Out-of-Pocket Costs it incurs to conduct Commercialization activities for such Collaboration Program, except as otherwise agreed by the Parties in writing.

6.2.3 Commercial Lead. Takeda shall be the Commercial Lead for each Collaboration Program in the Territory; *provided however*, that if Denali has not exercised the Denali Worldwide Royalty Option with respect to at least [***], Denali shall have the option to be designated as the Commercial Lead in the United States for the [***] for which Denali does not exercise the Denali Worldwide Royalty Option through the Development program. For clarity, Denali shall not be the Commercial Lead for the first commercial Collaboration Program. Denali may exercise such option by notifying Takeda and the JPT in writing of its election prior to [***]. If Denali issues a notice of its election to be the Commercial Lead in accordance with this Section 6.2.3 and a [***]. For clarity, if Denali does not timely issue its notice of election to be the Commercial Lead in the United States with respect to any Collaboration Program, Takeda shall be the Commercial Lead worldwide with respect to such Collaboration Program.

6.2.4 Co-Commercialization in the Co-Commercialization Territory. The Non-Commercial Lead in each country of the Co-Commercialization Territory for any Collaboration Program shall have the option to co-Commercialize the Optioned Products under such Collaboration Program in each country of the Co-Commercialization Territory by providing the Commercial Lead with written notification of its exercise of such option at least [***] months prior to the anticipated date of the first Regulatory Approval for the first Optioned Product under such Collaboration Program; *provided* that Denali shall not have the right to exercise such co-commercialization option with respect to any Collaboration Program for which Denali has exercised the Denali Worldwide Royalty Option. The Non-Commercial Lead may conduct Details with respect to Optioned Products, Phase IV Studies, and certain other marketing, promotional, and medical affairs activities with respect to Optioned Products, in each case, in a manner consistent with the Co-Commercialization Plan; *provided* that the Non-Commercial Lead shall not conduct greater than [***] of any such activities. The Commercial Lead shall consider in good faith the Non-Commercial Lead's views on pricing of the Optioned Products included in such Collaboration Program through the JPT, for each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option. For clarity, the Non-Commercial Lead shall not be allocated responsibilities with respect to regulatory and compliance matters, warehousing or distribution, sales, booking sales or reimbursement for the applicable Optioned Product, unless requested by the Commercial Lead and agreed to by such Non-Commercial Lead.

6.2.5 Commercialization Reports. For each Collaboration Program, each Party shall report on the Commercialization activities such Party has performed (or caused to be performed) under such Collaboration Program in accordance with the procedures established by the JPT. The JPT shall evaluate the work performed in relation to the goals of the applicable Commercialization Plan. Each Party shall provide such other Information as reasonably requested by the JPT.

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6.2.6 Supply Forecast. The Commercial Lead shall prepare quarterly, non-binding forecasts for the quantities of Optioned Product necessary pursuant to the applicable Commercialization Plan and shall provide such forecast to the applicable JPT for review at each JPT meeting.

6.3 Commercialization Plans.

6.3.1 Global Commercialization Plan. Reasonably in advance of the first Regulatory Approval for the first Optioned Product within a Collaboration Program, the Commercial Lead shall prepare for the JPT's discussion, review and finalization a Global Commercialization Plan for such Collaboration Program in reasonable scope, as well as a corresponding Commercialization Budget for such Global Commercialization Plan that complies with the requirements of this Agreement. The JPT shall present such plan to the JSC for approval. The JPT shall agree upon the appropriate level of detail to be included in the respective Global Commercialization Plan; *provided* that if Denali has exercised the Denali Worldwide Royalty Option with respect to such Collaboration Program, the Global Commercialization Plan shall be limited to material Commercialization activities in Major Markets with a high-level budget for such activities.

6.3.2 Exclusive Market Commercialization Plan. For each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option, the Commercial Lead shall also prepare, for the JPT's approval, an Exclusive Market Commercialization Plan, which shall be consistent with the Global Commercialization Plan for such Collaboration Program. The JPT shall agree upon the appropriate level of detail to be included in the respective Exclusive Market Commercialization Plan, taking into consideration the relative size and commercial potential of the applicable Major Market.

6.3.3 Co-Commercialization Plan. For each Collaboration Program for which Denali has not exercised the Denali Worldwide Royalty Option and for each country which the Non-Commercial Lead has exercised the co-commercialization option under Section 6.2.4, the Commercial Lead shall prepare, in consultation with the Non-Commercial Lead in each country and for the JPT's discussion, review and finalization, a Co-Commercialization Plan for such Collaboration Program. The JPT shall present such plan to the JSC for approval. Each Co-Commercialization Plan shall be consistent with the Global Commercialization Plan for the applicable Collaboration Program and shall include a corresponding Commercialization Budget for the activities covered by such Co-Commercialization Plan. Each Co-Commercialization Plan shall allocate such Commercialization activities between the Parties, taking into consideration the Parties' respective actual or reasonably anticipated capabilities, infrastructure and resources in each of the United States and China, as the case may be, relevant to the applicable Optioned Product at the time of expected First Commercial Sale in accordance with the terms of this Agreement.

6.3.4 Amendments and Updates. The JPT shall review the Commercialization Plans (including, if applicable, the associated Commercialization Budgets)

on a regular basis, and in no event less frequently than once each Calendar Year (as provided below), or more frequently as needed to take into account completion, commencement or cessation of Commercialization activities contemplated in the then-current applicable Commercialization Plan for, as well as any newly available Information related to, such Collaboration Program. Either Party, through its representatives on the JPT, may propose amendments to a Commercialization Plan (and/or, if applicable, the associated Commercialization Budget) for a given Collaboration Program from time to time. Any and all amendments to the Global Commercialization Plan or the Co-Commercialization Plan shall be subject to approval in accordance with Section 2.3.6. Any and all amendments to an Exclusive Market Commercialization Plan shall be approved by the JPT. In any event, an updated Commercialization Plan, including the associated Commercialization Budget (if applicable), shall be provided by the JPT (and approved by the JSC as required) no later than November 1 of each Calendar Year. If such revised Commercialization Plan (and associated Commercialization Budget (if applicable)) is not approved by the JSC by December 1 of a Calendar Year, then, until such time as such a revised Commercialization Plan (and associated Commercialization Budget (if applicable)) is approved in accordance with Section 2.3.6: (a) the then-current Commercialization Plan (and associated Commercialization Budget (if applicable)) for the relevant territory shall continue to govern the Parties' commercialization activities under this Agreement with respect to the applicable Collaboration Program; and (b) each Party shall be permitted to conduct the activities allocated to such Party in such then-current Commercialization Plan and to incur costs consistent with such associated Commercialization Budget, which costs shall be shared by the Parties as Allowable Expenses in accordance with Section 8.6.

6.4 Sales Representatives.

6.4.1 Denali and Takeda shall each ensure that its sales representatives do not make any representation, statement, warranty or guaranty with respect to an Optioned Product that is not consistent with the applicable, current package insert of prescribing information or other documentation accompanying or describing such Optioned Product, including mutually approved limited warranty and disclaimers, if any. Denali and Takeda shall each ensure that its sales representatives do not make any statements, claims or undertakings to any person with whom they discuss or promote Optioned Products that are not consistent with, nor provide or use any labeling, literature or other materials other than, those Promotional Materials currently approved for use by the JPT in the Co-Commercialization Territory. If at any time the Commercial Lead no longer approves the use of specified Promotional Materials in any country of the Co-Commercialization Territory, each Party shall take appropriate action to remove the Promotional Materials from use destroy such Promotional Materials or otherwise modify such Promotional Materials for an approved use.

6.4.2 Notwithstanding the foregoing, in the event the Non-Commercial Lead is co-Commercializing the Optioned Products in any country within the Co-Commercialization Territory, the Non-Commercial Lead shall have the right to review and comment on the training materials and programs to be used in such markets prior to the implementation of such training materials and programs, in accordance with the process established by the JPT, and the Commercial Lead shall give good faith consideration to the Non-Commercial Lead's comments regarding the training materials and programs, including any comments related to the training materials and programs compliance with Applicable Law.

6.4.3 Denali and Takeda shall each cause its sales representatives to comply with Applicable Law and industry guidelines related to the performance of its obligations hereunder.

6.4.4 Each Party shall maintain records of its sales representatives' activities in the Territory and each Party shall allow representatives of the other Party to inspect such records upon request during normal business hours and upon reasonable prior notice; *provided* that Denali shall no longer have such right with respect to a particular Collaboration Program after it exercises the Denali Worldwide Royalty Option with respect to such Collaboration Program.

6.4.5 If Denali is the Non-Commercial Lead and exercises its co-Commercialization rights in any country of the Co-Commercialization Territory in accordance with Section 6.2.3, the applicable Co-Commercialization Plan shall provide for sales representatives of each Party to be deployed to major metropolitan areas.

6.4.6 Calculation of Sales Force Costs. For the purposes of calculating the FTE Costs of each Party's sales representatives performing activities under the applicable Co-Commercialization Plan, the FTE Rate shall be deemed to be [***] of the applicable mutually agreed FTE Rate for such sales representative on a full-time basis; *provided* that for each sales representative who also engages in promotion activities for a product other than an Optioned Product during the relevant Calendar Quarter, the cost of such sales representative (for purposes of calculating Allowable Expenses), shall be reduced proportionately based on the Detail position of such other product(s) during such sales activities and a reasonable apportionment of the value of such Detail position(s) for such other product(s). For such purposes: (i) in a two-product Detail, the first position Detail shall be deemed [***] and the second position shall be deemed [***] of the value of the product Detail; (ii) in a three-product Detail, the first position Detail shall be deemed [***], the second position shall be deemed [***] and the third position shall be deemed [***] of the value of the product Detail; and (iii) the value of other similar multi-product promotions shall be allocated in a similar way. For example, if a sales representative is promoting only an Optioned Product and no other products in a Calendar Quarter, [***] of the FTE Rate for such sales representative shall be included for purposes of calculating the Allowable Expenses for such Calendar Quarter, and if such sales representative is promoting one other product and such other product is in the second Detail position, only [***] of the FTE Rate for such sales representative shall be included in calculating the Allowable Expenses for such Calendar Quarter.

6.5 Advertising and Promotional Materials. The Commercial Lead for a particular Collaboration Program and territory shall develop relevant sales, promotion, market access and advertising materials relating to the Optioned Products within such Collaboration Program and territory (collectively, "**Promotional Materials**") in each case consistent with Applicable Law, the applicable Commercialization Plans and any determinations made by the JPT with respect to such matters pursuant to Section 2.2.2(c)(ix). The Commercial Lead shall be responsible for the medical, regulatory and legal review of Promotional Materials and for the interpretation and

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adherence to the Applicable Law governing the preparation and use of such Promotional Materials, including any advance review of the Promotional Materials required by the applicable Regulatory Authority. Notwithstanding the foregoing, in the event the Non-Commercial Lead is co-Commercializing the Optioned Products in any country within the Co-Commercialization Territory, the Non-Commercial Lead shall have the right to review and comment on the Promotional Materials to be used in such markets prior to the implementation of such Promotional Materials, in accordance with the process established by the JPT, and the Commercial Lead shall give good faith consideration to the Non-Commercial Lead's comments regarding the Promotional Materials, including any comments related to the Promotional Materials' compliance with Applicable Law. The Commercial Lead for each market will own all right, title and interest in and to any and all Promotional Materials for an Optioned Product for use in such market (except with respect to any Corporate Names of the other Party included in any Promotional Materials). The Non-Commercial Lead will execute all documents and take all actions as are reasonably requested by the Commercial Lead to vest title to such Promotional Materials in the Commercial Lead.

6.6 Medical Inquiries. The Commercial Lead shall handle all medical questions or inquiries from members of the medical profession in any country within the Co-Commercialization Territory regarding the Optioned Products. In the event the Non-Commercial Lead is co-Commercializing the Optioned Products a country within the Co-Commercialization Territory, the Non-Commercial Lead shall, and shall cause its sales representatives or medical science liaisons (as applicable depending on the nature of the question or inquiry) to, refer to the Commercial Lead all such questions and inquiries within [***] hours of receipt, unless earlier notification is required pursuant to the Pharmacovigilance Agreement or Applicable Law. The Commercial Lead shall respond appropriately to all such inquires in a timely manner. The Parties' costs and expenses incurred in responding to medical questions and inquiries in accordance with this Section 6.6 shall be included in Allowable Expenses, unless Denali has exercised the Denali Worldwide Royalty Option for the relevant Collaboration Program.

6.7 Optioned Product Packaging. The Commercial Lead shall develop and approve packaging and Product Labeling for each Optioned Product, which in all cases shall be consistent with the applicable Commercialization Plan and in accordance with Applicable Law. The Parties' costs and expenses incurred in conducting such activities shall be included in Allowable Expenses, unless Denali has exercised the Denali Worldwide Royalty Option for the relevant Collaboration Program.

6.8 Sales and Distribution.

6.8.1 Booking Sales. The Commercial Lead in any jurisdiction or region for a particular Collaboration Program shall (a) book all sales of Optioned Products and (b) be responsible for warehousing and distributing the Optioned Products in such jurisdiction or region. If the Non-Commercial Lead in a country or region for a particular Collaboration Program receives any orders for an Optioned Product, it shall refer such orders to the Commercial Lead for such Collaboration Program in the applicable country or region.

6.8.2 Branding. The Commercial Lead for each jurisdiction or region shall be responsible for determining positioning, messaging, and branding for each Optioned Product in

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such jurisdiction or region; provided, that positioning, messaging, and branding for each Optioned Product shall be consistent with the applicable Commercialization Plans, and Applicable Law. The Parties' costs and expenses incurred in conducting such activities shall be included in Allowable Expenses, unless Denali has exercised the Denali Worldwide Royalty Option for the relevant Collaboration Program.

6.9 Shipping and Returns. The Commercial Lead with for each jurisdiction or region shall be responsible for handling all returns of the Optioned Products in such jurisdiction or region. If an Optioned Product sold in a jurisdiction or region is returned to the Non-Commercial Lead, the Non-Commercial Lead shall promptly ship such Optioned Product to a facility designated by the Commercial Lead. The Commercial Lead for each jurisdiction or region shall also be responsible for handling all aspects of such Optioned Product order processing, invoicing and collection, distribution, inventory, and receivables for each jurisdiction or region. The Parties' costs and expenses incurred in conducting such activities shall be included in Allowable Expenses, unless Denali has exercised the Denali Worldwide Royalty Option for the relevant Collaboration Program.

6.10 Recalls, Market Withdrawals or Corrective Actions. In the event that any Regulatory Authority issues or requests a recall or takes a similar action in connection with an Optioned Product, or in the event either Party determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal, in each case, in any jurisdiction or region, the Party notified of such recall or similar action, or the Party that desires such recall or similar action, shall within [***] hours, advise the other Party thereof by orally or in writing Unless Denali has exercised the Denali Worldwide Royalty Option, the Commercial Lead, in consultation with the Non-Commercial Lead, shall decide whether to conduct a recall in such jurisdiction or region (except in the case of a government mandated recall, when the Commercial Lead may act without such advance notice or consultation but, shall notify the Non-Commercial Lead as soon as possible) and the manner in which any such recall shall be conducted. Each Party shall make available to the other Party, upon request, all of such Party's pertinent records that such other Party may reasonably request to assist such other Party in effecting any recall. The costs and expenses of any recall in the Territory shall be included in calculating Allowable Expenses, unless Denali has exercised the Denali Worldwide Royalty Option for the relevant Collaboration Program.

6.11 Product Trademarks. Subject to Section 6.12, Takeda shall have the sole right to determine and own the Product Trademarks to be used with respect to the Exploitation of the Optioned Products on a worldwide basis. Subject to any pre-existing Trademarks a Party may have, neither Party shall, directly or indirectly: (a) use in their respective businesses, any Trademark that is confusingly similar to, misleading or deceptive with respect to or that dilutes any Product Trademark; and (b) do any act which endangers, destroys, or similarly affects, in any material respect, the value of the goodwill pertaining to the Product Trademarks. Each Party agrees to conform to the customary industry standards for the protection of Product Trademarks for products and such guidelines of Takeda with respect to manner of use (in the case of Denali, as provided in writing by Takeda) of the Product Trademarks. Without limiting any pre-existing Trademarks a Party may have, neither Party shall, directly or indirectly, attack, dispute, or contest the validity of or ownership of such Product Trademark anywhere in the Territory or any registrations issued or issuing with respect thereto.

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6.12 Markings. To the extent required by Applicable Law in a country or other jurisdiction in the Territory, the Promotional Materials, packaging, and Product Labeling for the Optioned Products used in connection with the Optioned Products in such country or other jurisdiction shall contain the Corporate Name of both the Commercial Lead and the Non-Commercial Lead.

ARTICLE 7
LICENSE GRANTS; EXCLUSIVITY

7.1 License Grants to Takeda.

7.1.1 Subject to the terms and conditions of this Agreement (including Section 7.1.4), with respect to each Designated Target, Denali hereby grants to Takeda a co-exclusive (with Denali) non-sublicensable (except in accordance with Section 7.3.1) license under the Denali Technology (including Denali's interest in the Joint Program Know-How and Joint Program Patents) solely to the extent necessary for Takeda to perform its obligations under the Research Plan for such Designated Target.

7.1.2 Subject to the terms and conditions of this Agreement (including Section 7.1.4), and effective automatically on the Option Exercise Date with respect to a Collaboration Program, Denali shall grant and hereby grants to Takeda, with respect to the Designated Target of such Collaboration Program (referred to as the Optioned Target below):

(a) a co-exclusive (with Denali) license, with the right to grant sublicenses in accordance with Section 7.3.2, under the Denali Technology (including Denali's interest in the Joint Program Know-How and Joint Program Patents), to Exploit Optioned Biologics and Optioned Products Directed to such Optioned Target in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans;

(b) a co-exclusive (with Denali) license and right of reference, with the right to grant sublicenses and further rights of reference in accordance with Section 7.3.2, under the Regulatory Approvals and any other Regulatory Documentation that Denali may Control with respect to the Optioned Biologics or Optioned Products Directed to such Optioned Target to Exploit such Optioned Biologics and Optioned Products in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans; and

(c) a co-exclusive (with Denali) license, with the right to grant sublicenses in accordance with Section 7.3.2, to use Denali's Corporate Names solely as required by Applicable Law to Exploit Optioned Biologics or Optioned Products Directed to such Optioned Target in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans.

7.1.3 Subject to the terms and conditions of this Agreement (including Section 7.1.4 and Section 7.8), Denali hereby grants to Takeda a non-exclusive, worldwide, perpetual, irrevocable, fully-paid, royalty-free license, with the right to grant sublicenses in

accordance with Section 7.3.3, under any [***] to Exploit [***]. For clarity, the foregoing shall not include the grant by Denali to Takeda of a license under any [***] to the extent Denali does not have the right to grant such license [***].

7.1.4 Certain Restrictions. Notwithstanding any other provision of this Agreement, the rights and licenses granted to Takeda under this Agreement shall not include, or be deemed to include, [***], except as expressly set forth in the Research Plan or as otherwise expressly agreed in writing in advance by the Parties. In no event shall Takeda use (or authorize the use of) any Denali Technology (other than Joint Program Know-How and Joint Program Patents) except for the purposes of [***]. For clarity, notwithstanding Denali's co-exclusive rights with Takeda under this Agreement as set forth in Section 7.1 and Section 7.2, during the Term with respect to each Collaboration Program, Denali shall not have [***]. For the avoidance of doubt, the co-exclusive rights granted by Denali to Takeda under this Agreement shall not prohibit Denali from Exploiting, and Denali shall retain all rights to Exploit, the [***] and [***] or [***], or [***] (other than any such [***]), for any purpose, subject to [***].

7.2 License Grants to Denali.

7.2.1 Subject to the terms and conditions of this Agreement, with respect to each Designated Target, Takeda hereby grants to Denali a co-exclusive (with Takeda), non-sublicensable (except in accordance with Section 7.3.4) license under the Takeda Technology (including Takeda's interest in the Joint Program Know-How and Joint Program Patents) solely to the extent necessary for Denali to perform its obligations under the Research Plan for such Designated Target.

7.2.2 Subject to the terms and conditions of this Agreement, and effective automatically on the Option Exercise Date with respect to a particular Collaboration Program, Takeda shall grant and hereby grants to Denali, with respect to the Designated Target of such Collaboration Program (referred to as the Optioned Target below):

(a) a co-exclusive (with Takeda) license, with the right to grant sublicenses in accordance with Section 7.3.5, under the Takeda Technology (including Takeda's interest in the Joint Program Know-How and Joint Program Patents), to Exploit Optioned Biologics and Optioned Products Directed to such Optioned Target in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans;

(b) a co-exclusive (with Takeda) license and right of reference, with the right to grant sublicenses and further rights of reference in accordance with Section 7.3.5, under the Regulatory Approvals and any other Regulatory Documentation that Takeda may Control with respect to the Optioned Biologics or Optioned Products Directed to such Optioned Target to Exploit such Optioned Biologics and Optioned Products in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans; and

(c) a co-exclusive (with Takeda) license, with the right to grant sublicenses in accordance with Section 7.3.5, to use Takeda's Product Trademarks and Takeda's

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Corporate Names solely as required by Applicable Law to Exploit Optioned Biologics or Optioned Products Directed to such Optioned Target in the Field in the Territory in a manner consistent with the applicable Development Plan and the applicable Commercialization Plans.

7.2.3 Without limiting Denali's rights under Section 9.1, subject to the terms and conditions of this Agreement (including Section 7.8 below), Takeda hereby grants to Denali a non-exclusive, worldwide, perpetual, irrevocable, fully-paid, royalty-free (subject to Section 7.5.2(d)) license, [***], under Takeda's and/or any of its Affiliate's interest in any [***] to [***].

7.2.4 **Certain Restrictions**. In no event shall Denali use (or authorize the use of) any Takeda Technology (other than Joint Program Know-How and Joint Program Patents) except for the purposes of [***]. For clarity, notwithstanding Takeda's co-exclusive rights with Denali under this Agreement as set forth in Section 7.1 and Section 7.2, Takeda shall not have the right to [***].

7.3 Sublicenses.

7.3.1 Takeda shall have the right to grant sublicenses under the licenses granted to Takeda under Section 7.1.1, to its Affiliates (through multiple tiers) and Third Party Providers (without the right to grant further sublicenses) solely in accordance with Section 7.4; *provided* that any such sublicenses shall be materially consistent with the terms and conditions of this Agreement.

7.3.2 Takeda shall have the right to grant sublicenses (or further rights of reference), through multiple tiers of sublicensees, under the licenses and rights of reference granted in Section 7.1.2, to its Affiliates and other Persons; *provided* that [***]. Notwithstanding the foregoing, Takeda shall not, without Denali's prior written consent, grant to a Sublicensee any such sublicense or rights of reference with respect to [***] (a) [***], (b) [***], or (c) unless such Sublicensee is a Significant Biopharmaceutical Company, [***]. For such purposes, a "**Significant Biopharmaceutical Company**" means [***].

7.3.3 Subject to Section 7.8 below, Takeda shall have the right to grant sublicenses, through multiple tiers of sublicensees, under the licenses granted to Takeda under Section 7.1.3, to its Affiliates and other Persons; *provided* that [***] and any such Person to whom Takeda grants such rights has agreed [***].

7.3.4 Denali shall have the right to grant sublicenses under the licenses granted to Denali under Section 7.2.1, to its Affiliates (through multiple tiers) and Third Party Providers (without the right to grant further sublicenses) solely in accordance with Section 7.4; *provided* that [***].

7.3.5 Denali shall have the right to grant sublicenses (or further rights of reference) under the licenses and rights of reference granted to Denali under Section 7.2.2 to its Affiliates and other Persons: (a) [***]; (b) [***]; or (c) otherwise solely in connection with the engagement of a subcontractor in accordance with Section 7.4 for the performance of the activities that Denali has the right to conduct in connection with a Collaboration Program under this Agreement.

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7.3.6 Subject to Section 7.8 below, Denali shall have the right to grant sublicenses, through multiple tiers of sublicensees, under the licenses granted to Denali under Section 7.2.3, to [***] and [***]; *provided* that [***] and [***].

7.3.7 Each sublicensing Party (or Party whose Affiliate grants a sublicense) shall [***] and shall [***].

7.4 Subcontracting. Each Party and its Affiliates may subcontract the performance of any of its research activities, Development activities and Commercialization activities in the Territory with respect to each Collaboration Program undertaken in accordance with this Agreement to one or more Third Party Providers pursuant to a Subcontract Agreement which shall be consistent with the terms of this Agreement; *provided*, that: (a) each Party shall [***] and shall [***]; and (b) the Subcontract Agreement shall (i) contain [***] and (ii) provide such subcontracting Party [***]. Notwithstanding the foregoing, the subcontracting Party shall [***] and shall [***].

7.5 Third Party Intellectual Property.

7.5.1 Denali's In-License Agreement.

(a) **Existing In-Licenses**. It is understood that Denali's In-License Agreements existing as of the Execution Date (collectively, the "**Existing In-License Agreements**") may require that particular provisions be incorporated into a sublicense granted thereunder. The text of any such provisions in the Existing In-License Agreements are set out on Schedule 7.5.1 attached hereto and shall be deemed incorporated by reference into this Agreement. Takeda agrees to be bound by the provisions set out on Schedule 7.5.1 to the extent applicable to Takeda in its capacity as a sublicensee under each such Existing In-License Agreement for so long as the applicable Existing In-License Agreement is in full force and effect and thereafter with respect to any surviving [***] obligations, and, to the extent required by any such Existing In-License Agreement as of the Execution Date, the relevant Third Party licensor shall be deemed to be a third party beneficiary of this Agreement solely for the purposes of enforcing any of such Third Party licensor's rights against Takeda in its capacity as a sublicensee under such Existing In-License Agreement.

(b) **Denali New Technology**. If, after the Effective Date, Denali acquires from any Third Party subject matter within the Denali Technology to be applied to a Biologic(s) or Product(s) being Developed or Commercialized under this Agreement ("**Denali New Technology**"), the following shall apply: Denali shall [***] and provide [***]. In the event [***], then such Denali New Technology shall [***]. In the event [***], then such Denali New Technology shall [***].

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(c) **Payment Obligations for Denali's Product In-License Agreements**. If any Denali Technology or Denali New Technology is subject to payment to a Third Party under a Product In-License Agreement, the following shall also apply:

(i) Prior to the Option Exercise Date for a Collaboration Program and after the Option Exercise Date, except as set forth in clause (ii) below, Denali shall be responsible for any payments due to a Third Party under any Product In-License Agreement.

(ii) Following the Option Exercise Date for a particular Collaboration Program all amounts that become owing to such Third Party as a result of a Party's exercise of any such Denali Technology or Denali New Technology in performance of activities under this Agreement shall be included as Allowable Expenses, *provided* that [***], *provided further* that if Denali has exercised the Denali Worldwide Royalty Option, such amounts shall be paid by Takeda but subject to Takeda's right to offset any such payment under Section 8.7.5(e) against royalty payments by Takeda to Denali.

(d) [***].

(e) **Payment Obligations for Denali's Platform In-License Agreements**. If any Denali Technology or Denali New Technology is subject to payment to a Third Party under a Platform In-License Agreement [***], the following shall apply:

(i) Prior to the Option Exercise Date for a Collaboration Program and after the Option Exercise Date, except as set forth in clause (ii) below, [***].

(ii) Following the Option Exercise Date for a particular Collaboration Program, [***].

(iii) Notwithstanding the foregoing in clauses (i) and (ii) above, if any subject matter included within a Platform In-License Agreement pertains to [***], then the JSC shall [***].

7.5.2 Takeda's In-License Agreements. If, after the Effective Date, Takeda wishes to acquire or actually acquires from any Third Party subject matter within the Takeda Technology to be applied to a Biologic(s) or Product(s) being Developed or Commercialized under this Agreement, or incorporate any Third Party subject matter already acquired by Takeda into any Biologic(s) or Product(s) being Developed or Commercialized under this Agreement (any such acquired subject matter, "**Takeda New Technology**"), the following shall apply:

(a) **Takeda New Technology that is** [***]. For any subject matter that is [***]. In such event, Denali shall [***]. In the event that [***]. For clarity, such Takeda New Technology shall be [***].

(b) **Other Takeda New Technology**. For any other subject matter, Takeda shall so notify the JSC and provide the JSC with a summary of the terms of any license or agreement under which Takeda acquired such Takeda New Technology that would be applicable to such a Biologic(s) or Product(s). In the event the JSC agrees in writing to apply such Takeda New Technology to Biologic(s) or Product(s) under this Agreement, then such Takeda New Technology shall be included in Takeda Technology and subject to the terms and conditions of this Agreement. In the event the JSC does not agree in writing to apply such Takeda New Technology to Biologic(s) or Product(s), then such Takeda New Technology shall thereafter be deemed excluded from the Takeda Technology hereunder. [***].

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(c) **Payment Obligations for Takeda New Technology Allocated to Optioned Biologics, Optioned Products and Collaboration Programs**. Any royalties or other amounts that become owing to such Third Party with respect to such Takeda New Technology to the extent allocable to the Development, Manufacture or Commercialization of an Optioned Biologic or Optioned Product or the Collaboration Programs hereunder and incurred after the applicable Option Exercise Date, shall be included in calculating Allowable Expenses, as applicable, *provided* that [***], *provided* further that if Denali has exercised the Denali Worldwide Royalty Option with respect to the applicable Collaboration Program, any such royalties or other amounts shall be paid by Takeda, subject to Takeda's right to offset such payments under Section 8.7.5(e).

(d) **Payment Obligations for Takeda New Technology that is** [***]. Any royalties or other amounts that become owing to such Third Party with respect to [***] to the extent allocable to [***] shall be the sole responsibility of [***].

7.5.3 Coordination with Third Party Agreements. The obligations of each Party and the rights of the other Party under this Agreement, including with respect to Prosecution and Maintenance and enforcement of Patents, shall be subject to, and limited by, any agreements pursuant to which such Party acquired or licensed any particular Patents or Information or other subject matter.

7.6 Retention of Rights.

7.6.1 Except as expressly provided herein, Denali grants no other right or license, including any rights or licenses to the Denali Technology, the Regulatory Documentation, Denali's Corporate Names, or any other Patent or intellectual property rights not otherwise expressly granted herein.

7.6.2 Except as expressly provided herein, Takeda grants no other right or license, including any rights or licenses to the Takeda Technology, the Regulatory Documentation, Takeda's Corporate Names, or any other Patent or intellectual property rights not otherwise expressly granted herein.

7.7 Confirmatory Patent License. Each Party shall if requested to do so by the other Party promptly enter into confirmatory license agreements in the form or substantially the form reasonably requested by such other Party for purposes of recording the licenses granted under this Agreement with the applicable patent offices as such other Party considers appropriate. Until the execution of any such confirmatory licenses, so far as may be legally possible, Denali and Takeda shall have the same rights in respect of the Denali Technology and Takeda Technology, as the case may be, and be under the same obligations to each other in all respects as if the said confirmatory licenses had been executed.

7.8 Exclusivity.

7.8.1 On a Designated Target-by-Designated Target basis during the applicable Exclusivity Period, except as permitted under this Agreement, each Party agrees for itself and its Affiliates not to: (a) [***] (each a "**Competing Product**"), nor (b) authorize or assist any Third Party to do any of the foregoing; *provided* that if a [***], then a [***].

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7.8.2 Notwithstanding the provisions of Section 7.8.1, if, during the Exclusivity Period, (i) a Party or any of its Affiliates acquires rights to a Competing Product through an Acquisition, such Acquisition, and the commercialization of such Competing Product thereafter, shall not constitute a breach of Section 7.8.1 if such Party or such Affiliate, as applicable, (x) [***] and (y) prior to [***]; or (ii) a Party [***]; *provided*, that, such [***].

ARTICLE 8
PAYMENTS

8.1 Upfront Payments.

8.1.1 Initial Equity Investment. No later than [***] Business Days following the Effective Date, Takeda shall purchase Four Million Two Hundred Fourteen Thousand Five Hundred Fifty-Nine (4,214,559) shares of Denali common stock for One Hundred Ten Million Dollars ($110,000,000) (the "**Aggregate Stock Purchase Price**") pursuant to the terms of the Stock Purchase Agreement. For the avoidance of doubt, the Aggregate Stock Purchase Price represents a price per share of approximately Twenty-Six Dollars and Ten Cents ($26.10), which represents [***], plus a premium as partial consideration paid in return for those rights granted to Takeda under the Agreement.

8.1.2 Additional Upfront Consideration. On or promptly after the Effective Date, Denali shall submit an invoice to Takeda for the Additional Upfront Consideration. Within [***] Business Days following the date of such invoice, in partial consideration paid in return for those rights granted to Takeda under this Agreement, Takeda shall pay to Denali a one-time payment in the amount of Forty Million Dollars ($40,000,000) (the "**Additional Upfront Consideration**"). The Additional Upfront Consideration shall not be refundable or creditable against any future payments by Takeda to Denali under this Agreement.

8.2 Research Program Payments.

8.2.1 Research Milestone Payments.

(a) With respect to each Designated Target and subject to Section 3.2.3(f), Takeda shall pay to Denali, in accordance with Sections 8.4 and 8.8, the milestone payments set forth below following the first achievement of each corresponding research milestone event set forth below (each, a "**Research Milestone**") with respect to the [***] to achieve the applicable stage of development:

Research Milestone Event	Milestone Payment
[***]	[***]
[***]	[***]
[***]	[***]

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(b) With respect to [***] and the achievement of Research Milestone 1, [***] shall be payable upon the [***] and [***] shall be payable upon [***].

(c) With respect to the Research Milestones for each Designated Target, if Research Milestone 2 or 3 is achieved before a milestone payment has been made with respect to a lower-numbered Research Milestone, or if a Development Milestone is achieved by an Optioned Biologic or Optioned Product directed to such Designated Target before a milestone payment has been made with respect to one or more Research Milestone for such Designated Target, then all milestone payments corresponding to such lower-numbered Research Milestones for such Designated Target shall be deemed achieved upon achievement of the subsequent Research Milestone or Development Milestone, as applicable. Notwithstanding the foregoing, with respect to a particular Research Program, if [***], then [***].

(d) For the avoidance of doubt, a Research Milestone may be achieved after the Option Exercise Date with respect to the applicable Collaboration Program.

(e) Each Research Milestone is payable [***] with respect to each Designated Target, regardless of how many Research Biologics meet such milestone event, and no Research Milestone payment shall be made more than [***] times under this Agreement. The total amount payable by Takeda to Denali under this Section 8.2.1 shall not exceed (i) Twenty-Five Million Dollars ($25,000,000) with respect to each Designated Target and (ii) Seventy-Five Million Dollars ($75,000,000) in the aggregate. In the event the Parties replace any Designated Target with a Replacement Designated Target, then Takeda shall not be required to make any Research Milestone Payment with respect to such Replacement Designated Target to the extent such Research Milestone Payment has already been made by Takeda for the original Designated Target. Notwithstanding the foregoing, if [***] and, at the time of such replacement, only [***] of the milestone payment corresponding to Research Milestone 1 has been paid pursuant to Section 8.2.1(b), then a milestone payment of [***] shall be due upon achievement of Research Milestone 1 with respect to the applicable Replacement Designated Target (which achievement may occur prior to such replacement and the milestone shall be paid in accordance with the terms of Section 8.4); provided that if such Replacement Designated Target is [***] will be due upon [***].

8.2.2 Option Exercise Fee. On a Collaboration Program-by-Collaboration Program basis, if Takeda submits the Option Exercise Notice to Denali, Denali shall submit to Takeda an invoice for the one-time payment in the amount of Five Million Dollars ($5,000,000) (the "**Option Exercise Fee**"). Takeda shall pay such Option Exercise Fee by the later of [***] Days after: (i) receipt of such invoice or (ii) the Parties have received all required approvals from all applicable governmental authorities pursuant to Section 3.2.4(c).

8.3 Development Milestones.

8.3.1 With respect to each Collaboration Program for which Takeda exercises its Option and each corresponding Optioned Target, Takeda shall pay to Denali, in accordance with Sections 8.4 and 8.8, the milestone payments set forth below following the first

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achievement of each of the following development and regulatory milestones (each, a "**Development Milestone**") for the [***] to achieve the applicable stage of development:

Development Milestone Event	Milestone Payment
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

8.3.2 For purposes of this Section 8.3:

(a) The [***] for the purposes of Development Milestones 1, 2 and 3 in the table above may, but need not, be the same [***].

(b) With respect to a given Optioned Target, if a [***] is [***], and a [***] was not previously conducted for [***], then a [***] will be deemed [***] and [***] solely for purposes of determining payments under this Section 8.3. Similarly, if [***], and a [***] and/or [***] was not [***], then such [***] will be deemed [***] solely for purposes of determining payments under this Section 8.3. Any such event deemed to have been achieved, if it would have triggered a payment under Section 8.3, will trigger a payment at the time it is deemed to have occurred. For example, consider the following scenario: [***].

8.3.3 Upon [***], Takeda shall pay to Denali, in accordance with Sections 8.4 and 8.8, an additional milestone payment equal to [***], *provided* that such milestone payment shall instead be [***] (such payment, as applicable, the "**Additional Event Payment**") if [***]. If at the time of [***], the Additional Event Payment has not been paid or become payable, then upon [***], such Additional Event Payment (with the amount thereof determined pursuant to this Section 8.3.3 at the time of [***]) shall also become due and payable to Denali. For clarity, the Additional Event Payment will be due one time only for all Collaboration Programs.

8.3.4 Each Development Milestone shall be due [***] with respect to each Collaboration Program, regardless of how many Optioned Biologics and/or Optioned Products meet such milestone event, and no Development Milestone payment shall be made more than [***] under this Agreement. The Additional Event Payment payable pursuant to Section 8.3.3 shall be due only once under this Agreement. The total amount payable by Takeda to Denali

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under this Section 8.3 shall not exceed: (i) [***] with respect to each Collaboration Program, except for the Collaboration Program in connection with which the Additional Event Payment is triggered, in which case the total amount payable by Takeda to Denali under this Section 8.3 for such Collaboration Program only shall not exceed [***]; and (ii) Seven Hundred Seven Million Five Hundred Thousand Dollars ($707,500,000) in the aggregate.

8.4 Reports and Payments for Research Milestones and Development Milestones. With respect to each Research Milestone set out in Section 8.2.1 and each Development Milestone set out in Section 8.3, the Party who achieves such Research Milestone or Development Milestone, as applicable, (or under whose authority such Research Milestone or Development Milestone, as applicable, is achieved) shall notify the other Party in writing within [***] Business Days after the achievement thereof. If Denali notifies Takeda of such milestone event, Denali shall include an invoice for the corresponding milestone payment with such notice. If Takeda notifies Denali of such milestone event, Denali shall promptly after receipt of such notice submit an invoice to Takeda for the corresponding milestone amount. Takeda shall pay to Denali the corresponding milestone payment set out in Section 8.2.1 or Section 8.3, as applicable, no later than [***] days after receipt of the applicable invoice. If any Research Milestone is achieved with respect to any Research Biologic Directed to an Initial Designated Target prior to the Effective Date, then Denali shall notify Takeda of the achievement of such milestone on or promptly after the Effective Date and shall submit an invoice to Takeda for the corresponding milestone payment (or include such amount in the invoice to be submitted to Takeda by Denali pursuant to Section 8.1.2), which invoice shall become due and payable within [***] Business Days after receipt. If any Research Milestone is achieved with respect to any Research Biologic Directed to a Replacement Designated Target prior to the approval of the initial Research Plan by the JSC for such Replacement Designated Target, then Denali shall notify Takeda of the achievement of such milestone and, promptly after such approval and notice, Denali shall submit an invoice to Takeda for the corresponding milestone payment, which invoice shall become due and payable within [***] days after receipt. For example, if [***] occur prior to the Effective Date or prior to the applicable approval of the initial Research Plan by the JSC, then Denali shall notify Takeda and Takeda shall pay such corresponding milestone payment in accordance with the foregoing provisions. For the avoidance of doubt, each milestone payment set forth in Section 8.2.1 and Section 8.3 shall not be refundable and shall not be creditable against future milestone payments or other amounts paid or payable by Takeda to Denali under this Agreement.

8.5 Commercial Milestones. With respect to each Optioned Product Directed to a particular Optioned Target, Takeda shall pay to Denali, in accordance with Section 8.8, a one-time milestone payment (each, a "**Sales Milestone**") in the amount of Seventy-Five Million Dollars ($75,000,000) the first time Annual Net Sales for such Optioned Product equal or exceed [***]. Promptly after the achievement of such Sales Milestone, Denali shall submit an invoice to Takeda for the corresponding milestone payment. Each such Sales Milestone shall be due no later than [***] days after receipt of the applicable invoice. Each milestone payment made under this Section 8.5 shall not be refundable or creditable against any future payments by Takeda to Denali under this Agreement.

8.6 Cost-Profit Sharing. On a Collaboration Program-by-Collaboration Program basis, beginning on the Option Exercise Date and until the Co-Funding End Date if Denali

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exercises the Denali Worldwide Royalty Option with respect to such Collaboration Program, Denali and Takeda shall share equally: (a) Development Costs, (b) Allowable Expense and (c) Net Revenues as follows.

8.6.1 Costs.

(a) **General**. Within [***] Business Days, unless such timing is adjusted by approval of the JSC, after the end of each calendar month, each Party will provide the other Party with a good faith estimate of the Development Costs and Allowable Expenses it incurred for each applicable Collaboration Program in such calendar month. The Finance Working Group will establish the level of detail necessary in such estimate for each Party to satisfy its internal reporting requirements. No later than [***] Business Days prior to the end of each Calendar Quarter, unless such timing is adjusted by approval of the JSC, each Party will provide the other Party with a reasonably detailed estimate of the Development Costs and Allowable Expenses it incurred for such Collaboration Program in such Calendar Quarter, which will include the actual costs for the first two calendar months and good faith estimate for the last month of such quarter. Within [***] Business Days after the end of each Calendar Quarter, unless such timing is adjusted by approval of the JSC, each Party will provide other Party with a report of actual Development Costs and Allowable Expenses for such Collaboration Program for such Calendar Quarter, which report will contain a detailed and itemized calculation of such costs for each Optioned Product. Notwithstanding the foregoing, the JSC may agree to have different reporting requirements for Development Costs and Allowable Expenses for any Collaboration Program. In addition to the annual approval of the relevant budgets for each Collaboration Program, prior to the end of each Calendar Year, each Party will provide the Finance Working Group with a non-binding estimate of its Development Costs and Allowable Expenses for each Collaboration Program for the [***] year period (detailed on a Calendar Year basis) following the first Calendar Year covered by such approved budget; *provided*, that the Parties will review and discuss such estimated costs at the Finance Working Group and/or the JPT for the relevant Collaboration Program.

(b) **Expense Review**. Each Party shall have the right to review and submit any reasonable objection to the Development Costs or Allowable Expenses set forth in the other Party's report within [***]. Any dispute as to respect to a Development Cost or Allowable Expense shall be resolved by the Finance Working Group in accordance with Section 8.6.6.

8.6.2 Net Sales and Net Revenues. In order to satisfy each Party's internal reporting requirements, within [***] Business Days, unless such timing is adjusted by approval of the JSC, after the end of each calendar month, each Party will provide the other Party with a good faith estimate of Net Sales and Net Revenues for each applicable Collaboration Program for such calendar month in the countries for which it is the Commercial Lead. The Finance Working Group will establish the level of detail necessary in such estimate for each Party to satisfy its internal reporting requirements and reporting requirements pursuant to its applicable Accounting Standards. Within [***] Business Days prior to the end of each Calendar Quarter, unless such timing is adjusted by approval of the JSC, each Party will provide the other Party with a reasonably detailed estimate of Net Sales and Net Revenues for such Calendar Quarter in the countries for which it is the selling Party, which will include the actual Net Sales and Net

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Revenues for the first [***] calendar months and a good faith estimate for the last calendar month of such Calendar Quarter. Within [***] days after the end of each Calendar Quarter, unless such timing is adjusted by approval of the JSC, each Party will provide the other Party with a report of Net Sales and Net Revenue for such Calendar Quarter in the countries for which it is the Commercial Lead, which report will contain a detailed and itemized calculation of Net Sales and Net Revenues for each Optioned Product in such countries during such Calendar Quarter.

8.6.3 Reporting, Reconciliation and True-Up. Within [***] days after the end of each Calendar Quarter, Takeda will calculate and provide to each Party and the Finance Working Group a report of the amount each Party is responsible for with respect to all Collaboration Programs such that the Parties share equally all Development Costs and Allowable Expenses, subject to Section 8.6.1, and all Net Revenues, for each Collaboration Program for such Calendar Quarter (excluding any Collaboration Program for which Denali has exercised the Denali Worldwide Royalty Option after the Co-Funding End Date for such Collaboration Program). The Parties will make a balancing payment between the Parties in order to effect the net revenue and cost allocation set forth in this Section 8.6 within [***] days after delivery of such report. Notwithstanding the foregoing, to the extent a Party incurs Development Costs or Allowable Expenses prior to the Option Exercise Date for a particular Collaboration Program (collectively "**Pre-Option Expenses**"), such Pre-Option Expenses shall be reconciled and trued-up between the Parties as a part of the reconciliation with respect to such Collaboration Program for the first Calendar Quarter after the Option Exercise Date for such Collaboration Program (but only if Takeda exercises the Option for the applicable Collaboration Program).

8.6.4 Certain Other Matters Relating to Cost Calculations.

(a) On a Calendar Year basis, if the Development Costs and Allowable Expenses incurred by a Party are in excess of the applicable Development Budget and/or Commercialization Budget, such excess amounts may be included in calculating the amount of Development Costs and Allowable Expenses incurred in such Calendar Year and to be shared by the Parties only to the extent that such amounts do not exceed [***] of the total amounts to be incurred by such Party in such Calendar Year under all Development Budgets and Commercialization Budgets, in the aggregate for such Calendar Year; *provided however* that [***].

(b) **Allocation of FTE Costs and Out-of-Pocket Costs**. It is understood that Development Costs and Allowable Expenses shall (A) [***], and (B) [***]. To the extent that any activity is conducted (or an Out-of-Pocket Cost or FTE Cost is incurred) in support of both an Optioned Product and other products, services or efforts of a Party, or in support of more than one Collaboration Program, and to the extent any Out-of-Pocket Costs or FTE Costs incurred are otherwise not solely attributable to a particular Collaboration Program in the Territory, then such Out-of-Pocket Costs and FTE Costs for the applicable activity shall be included in Development Costs and Allowable Expenses only to the extent fairly and reasonably allocated between the relevant Collaboration Program and such other products, services or efforts or other Collaboration Programs, respectively, in each case in accordance with Accounting Standards. [***].

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(c) **Treatment of Overhead; Other Matters**. The Parties acknowledge and agree that Development Costs and Allowable Expenses shall not include any allocation of overhead except [***]. Except to the extent already included in FTE Costs, Development Costs and Allowable Expenses shall not include either Party's costs to the extent pertaining to legal, accounting, finance or alliance management activities associated with overseeing execution of and compliance with this Agreement, unless otherwise agreed by the Parties under this Agreement or otherwise in writing. Development Costs and Allowable Expenses shall also exclude any costs attributable to a breach of this Agreement by either Party.

8.6.5 Financial Reporting Activities; Finance Working Group. With respect to the financial reporting activities between the Parties, unless Denali has exercised the Denali Worldwide Royalty Option for all Collaboration Programs, the JSC shall establish a finance working group ("**Finance Working Group**") to coordinate the activities and reporting by the Parties as set forth in Section 8.6.1 and to assist the JSC in its responsibilities with respect to the review and resolution of financial matters. In particular, the Finance Working Group shall:

(a) facilitate the creation of Development Budgets and Commercialization Budgets, including the annual updates thereto;

(b) reconcile financial and accounting matters between the Parties;

(c) initiate and execute an effective and efficient revenue and cost sharing process (cross-charges);

(d) cooperate to ensure that any Development Budget or Commercialization Budget agreed to for a Calendar Year (or any other given period) can be interpreted for the purposes of both Parties' internal financial and audit reporting requirements, including each Party's fiscal year reporting;

(e) monitor the budget, expense and revenue reporting requirements between the Parties related to the Collaboration Programs to ensure that each Party is able to comply with its respective internal financial and audit reporting requirements and, as appropriate, recommending to the JSC for approval, changes to the reporting requirements under this Agreement; and

(f) undertake such other tasks with respect to the implementation and reporting for the Parties' sharing of Development Costs, Allowable Expenses and Net Revenues as the Parties mutually agree.

8.6.6 Cost-Profit Sharing Disputes. [***].

8.7 Denali Worldwide Royalty Option.

8.7.1 Exercise by Denali. On a Collaboration Program-by-Collaboration Program basis, after the Option Exercise Date, Denali may, upon prior written notice to Takeda as specified in this Section 8.7.1, opt out of sharing future Development Costs, Allowable Expenses and Net Revenues with respect to all Optioned Products within the applicable Collaboration Program in the Territory and instead receive a royalty on sales of such Optioned

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Products in the Territory (a "**Denali Worldwide Royalty Option**"). Denali shall provide (a) [***] prior written notice if Denali exercises such right [***], and (b) [***] prior written notice if Denali exercises such right [***]. The date on which the applicable notice period expires is referred to in this Agreement as the "**Co-Funding End Date**".

8.7.2 Co-Funding Termination. Notwithstanding anything to the contrary in this Agreement, on a Collaboration Program-by-Collaboration Program basis, if [***] (a "**Co-Funding Termination**"), [***].

8.7.3 Applicability to the Agreement. Except as expressly set forth otherwise in this Agreement, a Co-Funding Termination [***] pursuant to Section 8.7.2 shall for all purposes have the same effect as Denali having exercised the Denali Worldwide Royalty Option.

8.7.4 Effect of Denali Worldwide Royalty Option. Following the exercise of the Denali Worldwide Royalty Option with respect to a Collaboration Program, without limiting the other terms and conditions of this Agreement applicable to such Denali Worldwide Royalty Option, and effective from and after the Co-Funding End Date or the effective date of the Co-Funding Termination pursuant to Section 8.7.2, as the case may be: (a) Denali shall not be obligated or allowed to share in Development Costs, Allowable Expenses and Net Revenues accrued after such Co-Funding End Date or effective date of the Co-Funding Termination, as applicable; (ii) Takeda shall make the applicable royalty payments to Denali as set forth in Section 8.7.5; and (iii) Takeda shall be the Development Lead, Regulatory Lead, Manufacturing Lead (subject to Section 5.2) and Commercial Lead for Optioned Products included in the applicable Collaboration Program in the entire Territory, and Denali's right with respect to the co-commercialization of such Optioned Products under Section 6.2.4 included in the applicable Collaboration Program shall expire; provided that Denali may conduct certain Development activities as the Parties mutually agree in writing. Once exercised with respect to a particular Collaboration Program and the Optioned Products Directed to the Optioned Target of such Collaboration Program, such Denali Worldwide Royalty Option shall be irrevocable.

8.7.5 Royalties. If Denali exercises the Denali Worldwide Royalty Option for a Collaboration Program, Takeda shall make the following royalty payments to Denali for sales of the relevant Optioned Products in the Territory:

(a) **Base Case Denali Worldwide Royalty Option Royalties**. In the event Denali exercises the Denali Worldwide Royalty Option pursuant to Section 8.7.1 (or a Co-Funding Termination occurs) before Denali has co-funded Development Costs and Allowable Expenses for such Collaboration Program that [***], Takeda shall pay to Denali royalties at the applicable royalty rates specified in the table below on the Net Sales of the Optioned Products included in such Collaboration Program in the Territory.

Collaboration Program Annual Net Sales	Royalty Rate
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

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(b) **Denali** [***] **Royalties** In the event Denali exercises the Denali Worldwide Royalty Option pursuant to Section 8.7.1 (or a Co-Funding Termination occurs) after Denali has co-funded Development Costs and Allowable Expenses for such Collaboration Program that [***] in aggregate, in lieu of the royalties specified in Section 8.7.5(a), Takeda shall pay to Denali royalties at the applicable royalty rates specified in the table below on the Net Sales of the Optioned Products included in such Collaboration Program in the Territory.

Collaboration Program Annual Net Sales	Royalty Rate
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

(c) **Royalty Term**. Royalties under Section 8.7 shall be payable on Net Sales on a country-by-country basis beginning upon the First Commercial Sale of an Optioned Product in a country in the Territory until the expiration of the Royalty Term in such country (at which time sales in such country shall be excluded from all calculations of aggregate Net Sales hereunder). "**Royalty Term**" means, with respect to a country and Optioned Product, the period commencing on the First Commercial Sale of such Optioned Product in such country and ending upon the later of [***].

(d) **Reduction For Biosimilar Entry In A Country**. On an Optioned Product-by-Optioned Product basis, the royalty rates set forth in Section 8.7.5 for Net Sales of such Optioned Product in a country of the Territory shall be reduced by [***] during which the Biosimilar Competition Percentage in such country with respect to the applicable Optioned Product is [***] and shall be reduced to [***] during which the Biosimilar Competition Percentage in such country with respect to such Optioned Product is [***].

(e) **In-License Agreements**. The Parties shall each be responsible for [***] of any royalties related to the sale of an Optioned Product or other payments with respect to Optioned Products due under any In-License Agreement to the extent provided in Sections 7.5.1, 7.5.2, or 9.4, as applicable. At Denali's request, Takeda shall credit Denali's portion of any such amount owed pursuant to this Section 8.7.5(e), and which is paid by Takeda, against any royalties payable to Denali pursuant to this Section 8.7.5. Takeda shall take such credit during any Calendar Quarter for which royalties are payable hereunder; *provided*, that in no event will such credit reduce such royalties for such Calendar Quarter and a Collaboration Program by more than [***]. Any share of Denali's portion that remains uncredited due to the application of such floor may be carried forward to subsequent Calendar Quarters.

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(f) **Manner of Royalty Payment**. Within [***] days following the end of each Calendar Quarter after the First Commercial Sale of an Optioned Product in the Territory (or if later the first Calendar Quarter in which royalties are payable by Takeda to Denali in accordance with this Section 8.7.5), Takeda shall provide Denali with a report containing the following information for the applicable Calendar Quarter and on an Optioned Product-by-Optioned Product basis (to the extent applicable): [***]. Takeda shall pay all amounts due to Denali under this Section 8.7, including with respect to Net Sales by Takeda, its Affiliates and their respective Sublicensees, for such Calendar Quarter at the time of the submission of such quarterly report.

8.8 Mode of Payment. All payments to either Party under this Agreement shall be made from a U.S. or Japanese entity (through a banking institution located in the United States or Japan) by deposit of Dollars in the requisite amount to such bank account as the receiving Party may from time to time designate by notice to the paying Party. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to, this Agreement (including the calculation of Net Sales expressed in currencies other than Dollars), a Party shall convert any amount expressed in a foreign currency into Dollar equivalents using an exchange rate equal to the daily average of the rates of exchange for the currency of the country from which the amounts are payable as reported by Bloomberg or an equivalent resource as agreed by the Parties, during the Calendar Quarter for which a payment is due.

8.9 Withholding Taxes.

8.9.1 The amounts payable pursuant to this Agreement ("**Payments**") shall not be reduced on account of any Taxes unless required by Applicable Law. A payor shall deduct and withhold from the Payments any Taxes that it is required by Applicable Law to deduct or withhold. Notwithstanding the foregoing, the Parties shall use commercially reasonable efforts to take all such acts and to sign all such documents as will enable them to take advantage of any applicable double taxation agreement or treaty, and if a recipient is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, or recovery of, applicable withholding tax, it may deliver to the payor or the appropriate governmental authority the prescribed forms necessary to reduce the applicable rate of withholding or to relieve the payor of its obligation to withhold tax. In such case, the payor shall apply the reduced rate of withholding, or not withhold, as the case may be, *provided* that the payor is in receipt of evidence (e.g., the recipient's delivery of all applicable documentation), in a form reasonably satisfactory to the payor, at least [***] week prior to the time that the Payments are due. If, in accordance with the foregoing, the payor withholds any amount, it shall pay to the recipient the balance when due, make timely payment to the proper taxing authority of the withheld amount, and send the recipient proof of such payment within [***] days following that payment.

8.9.2 If a Party that owes a payment under this Agreement assigns its rights and obligations to any person as permitted in accordance with Section 16.3 and if, solely as a result of such assignment, the withholding or deduction of taxes required by Applicable Law with respect to payments owed by such assignee under this Agreement is increased, then any amount payable under this Agreement shall be increased to take into account such withheld or deducted taxes as may be necessary so that, after making all required tax withholdings and deductions (including tax withholdings and deductions on amounts payable under this Section 8.9), the payee receives an amount equal to the sum it would have received absent such assignment.

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8.10 Indirect Taxes. All payments are exclusive of value added taxes, sales taxes, consumption taxes and other similar taxes (the "**Indirect Taxes**"). If any Indirect Taxes are chargeable in respect of any payments, the paying Party shall pay such Indirect Taxes at the applicable rate in respect of such payments following receipt, where applicable, of an Indirect Taxes invoice in the appropriate form issued by the receiving Party in respect of those payments. The Parties shall issue invoices for all amounts payable under this Agreement consistent with Indirect Tax requirements and irrespective of whether the sums may be netted for settlement purposes. If the Indirect Taxes originally paid or otherwise borne by the paying Party are in whole or in part subsequently determined not to have been chargeable, all reasonably necessary steps requested by the paying Party will be taken by the receiving Party to receive a refund of these undue Indirect Taxes from the applicable governmental authority or other fiscal authority and any amount of undue Indirect Taxes repaid by such authority to the receiving Party (net of any amounts incurred with respect to the receipt of such amounts) will be transferred to the paying Party within [***] days of receipt.

8.11 Interest on Late Payments. If any payment or portion thereof due to either Party under this Agreement is not paid when due, then such paying Party shall pay interest thereon at a rate equal to [***], plus [***] or, if lower, the maximum rate permitted by Applicable Law, calculated on the number of days such payment is delinquent, compounded annually and computed on the basis of a three hundred sixty-five (365) day year.

8.12 Financial Records. Each Party shall keep complete and accurate books and records pertaining to Development Costs, Allowable Expenses and Net Revenues with respect to the Optioned Products, and Development of the Optioned Biologics or Optioned Products, including books and records of actual expenditures with respect to the budgets set forth in each Development Plan and each Commercialization Plan, in sufficient detail to calculate all amounts payable hereunder and to verify compliance with its obligations under this Agreement. Such books and records shall be retained by such Party until the later of (a) [***] years after the end of the period to which such books and records pertain, and (b) the expiration of the applicable tax statute of limitations (including any extensions thereof), or for such longer period as may be required by Applicable Law.

8.13 Audit. At the request of the other Party, each Party shall permit an independent public accounting firm of nationally recognized standing designated by the other Party and reasonably acceptable to the audited Party, at reasonable times during normal business hours and upon reasonable notice, to audit the books and records maintained pursuant to Section 8.12 to ensure the accuracy of all reports and payments made hereunder. Such examinations may not (a) be conducted for any Calendar Quarter more than [***] years after the end of such quarter, (b) be conducted more than once in any [***] period (unless a previous audit during such [***] period revealed an underpayment with respect to such period) or (c) be repeated for any Calendar Quarter; except in each case, for cause. The accounting firm shall disclose to the auditing Party whether the reports are correct or not, and the details concerning any discrepancies sufficient for the auditing Party to understand any such discrepancies. Absent manifest error by such independent accounting firm, the determination of such independent accounting firm shall be

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binding on the Parties. Except as provided below, the cost of this audit shall be borne by the auditing Party, unless the audit reveals a variance of more than the greater of [***] or [***] from the reported amounts for the inspected period, in which case the audited Party shall bear the cost of the audit. If such audit concludes that (i) additional amounts were owed by the audited Party, the audited Party shall pay the additional amounts, with interest from the date originally due as provided in Section 8.11, or (ii) excess payments were made by the audited Party, the auditing Party shall, at its election, reimburse such excess payments or elect that such excess payments shall be offset against future payments due to the auditing Party under this Agreement, in either case ((i) or (ii)), within [***] days after the date on which such audit is completed by the auditing Party.

8.14 Confidentiality. The receiving Party shall treat all information subject to review under this Article 8 in accordance with the confidentiality provisions of Article 11 and the Parties shall enter into a reasonably acceptable confidentiality agreement with the independent accountant obligating such accountant to retain all such financial information in confidence pursuant to such confidentiality agreement.

8.15 No Other Compensation. Each Party hereby agrees that the terms of this Agreement fully define all consideration, compensation and benefits, monetary or otherwise, to be paid, granted or delivered by one (1) Party to the other Party in connection with the transactions contemplated herein. Neither Party previously has paid or entered into any other commitment to pay, whether orally or in writing, any of the other Party's employees, directly or indirectly, any consideration, compensation or benefits, monetary or otherwise, in connection with the transaction contemplated herein.

ARTICLE 9
INTELLECTUAL PROPERTY

9.1 Ownership of Intellectual Property.

9.1.1 Ownership of Patents and Know-How Generated under this Agreement. Each Party shall solely own all rights, title and interest in and to all Information and inventions that are conceived, discovered, developed or otherwise made by or on behalf of such Party or its Affiliates and Sublicensees, in conducting activities with respect to a Research Biologic, Optioned Biologic, Optioned Product or a Designated Target under this Agreement, together with all intellectual property rights therein, provided that Denali shall own [***] (the "**Covered ATV Platform Technology**") and any claim of a Patent Covering such Information and invention shall be deemed an [***]. Takeda hereby assigns, and agrees to assign, to Denali all right, title and interest in and to all Covered ATV Platform Technology and the same shall be deemed to be Denali's Confidential Information for all purposes under this Agreement, notwithstanding Sections 1.38, 11.1.2 and 11.1.5. Other than any Covered ATV Platform Technology, the Parties shall each own an equal, undivided interest in any and all rights, title and interest in and to all Information and inventions that are conceived, discovered, developed or otherwise made by or on behalf of both Parties or their respective Affiliates and sublicensees jointly, in conducting activities with respect to a Research Biologic, Optioned Biologic, Optioned Product or a Designated Target under this Agreement, together with all intellectual property rights therein (such Information, the "**Joint Program Know-How**" and the Patents

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claiming Joint Program Know-How, the "**Joint Program Patents**"). [***]. Notwithstanding the foregoing, the Parties acknowledge that, [***] under this Agreement (the "**Required Assigned Technology**"). Without limiting the foregoing, Takeda hereby assigns, and agrees to assign, to Denali such Required Assigned Technology and the same shall be deemed to be Denali's Confidential Information for all purposes under this Agreement, notwithstanding Sections 1.38, 11.1.2 and 11.1.5.

9.1.2 Assignment and Disclosure Obligation. Each Party shall cause all employees who perform activities for such Party under this Agreement to be under an obligation to assign their rights in any Information and inventions resulting therefrom to such Party. For clarity, the requirements of Sections 7.4 and 16.15 shall apply to each Party's use of Third Party Providers, Affiliates and/or Sublicensees, to perform activities for such Party under this Agreement.

9.1.3 Ownership of Corporate Names. Each Party shall retain all right, title and interest in and to its Corporate Names.

9.2 Maintenance and Prosecution of Patents. As between the Parties, with respect to Denali Patents, Takeda Patents, ATV Platform Patents, Product Patents and Joint Program Patents:

9.2.1 Assignment of Controlling Party.

(a) **Product Patents**. Denali shall be the Controlling Party with respect to any Product Patents worldwide. Unless agreed to by the Parties, Denali shall file the Product Patents in at least the countries and jurisdictions set forth in Schedule 9.2.1(c) and use Commercially Reasonable Efforts to [***]. Notwithstanding Section 9.2.3, [***].

(b) **ATV Platform Patents and Other Denali Patents**. Denali shall be Controlling Party with respect to the (i) ATV Platform Patents and (ii) other Denali Patents that are not Product Patents or Joint Program Patents, in each case, worldwide and at Denali's sole cost and expense. Notwithstanding Sections 9.2.2 and 9.2.3, Denali's obligations under Sections 9.2.2 and 9.2.3 with respect to ATV Platform Patents and such Denali Patents shall be [***]. For avoidance of doubt, [***].

(c) **Takeda Patents; and Joint Program Patents that are not ATV Platform Patents**. Takeda shall be the Controlling Party with respect to (i) [***] (collectively, such Patents described in (i) and (ii), "**Takeda Prosecuted Patents**"), worldwide and at Takeda's sole cost and expense. [***].

9.2.2 Controlling Party. Responsibility for the Prosecution and Maintenance of the Denali Patents, Takeda Patents and Joint Program Patents shall be allocated as set out above in Section 9.2.1. The Controlling Party with respect to a Patent shall have the right, but not the obligation, through the use of outside counsel reasonably acceptable to the Non-Controlling Party, to Prosecute and Maintain such Patent worldwide, subject to the terms of this Section 9.2. The Controlling Party shall keep the Non-Controlling Party fully informed of all steps with regard to the Prosecution and Maintenance of such Patent, including by providing the Non-

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Controlling Party with a copy of material communications to and from any patent authority regarding such Patents, and by providing the Non-Controlling Party drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow for a reasonable opportunity for the Non-Controlling Party to review and comment thereon. The Controlling Party shall consider in good faith the requests and suggestions of the Non-Controlling Party with respect to such drafts and with respect to strategies for Prosecution and Maintenance of such Patent, and implement, as appropriate, such requests and suggestions of the Non-Controlling Party. To the extent the Controlling Party does not agree with any such comments from the Non-Controlling Party, such disagreement shall be referred promptly to the Patent Working Group for resolution. If the Patent Working Group cannot reach agreement on such matter [***], then [***]. Notwithstanding the foregoing, the Controlling Party shall promptly inform the Non-Controlling Party of any adversarial patent office proceeding, including a request for, or filing or declaration of, any interference, or Post-Grant Proceeding relating to such a Patent. Subject to Section 9.3.2, the Parties shall thereafter consult and cooperate to determine a course of action with respect to any such proceeding and the Controlling Party shall consider in good faith all comments, requests and suggestions provided by the Non-Controlling Party.

9.2.3 Step In Rights. In the event that the Controlling Party decides not to Prosecute and Maintain a [***], or any claim thereof in a country or other jurisdiction, the Controlling Party shall provide reasonable prior written notice to the Non-Controlling Party of such intention (which notice shall, in any event, be given no later than [***] days prior to the next deadline for any action that may be taken with respect to such Patent in such country or other jurisdiction), the Non-Controlling Party shall thereupon have the option, in its sole discretion, to assume the control and direction of the Prosecution and Maintenance of such Patent at its expense in such country or other jurisdiction. Upon the Non-Controlling Party's written acceptance of such option, the Controlling Party shall reasonably cooperate with the Non-Controlling Party in such country or other jurisdiction as provided under Section 9.2.2.

9.2.4 Patent Working Group. The Parties shall establish a patent working group ("**Patent Working Group**") to the extent useful to facilitate cooperation with respect to Prosecution and Maintenance activities contemplated by this Section 9.2 and coordination between the Parties with respect to such matters.

9.2.5 Patent Term Extension and Supplementary Protection Certificate. The Controlling Party shall be responsible for making decisions regarding patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, wherever applicable. The Controlling Party shall have the responsibility of applying for any extension or supplementary protection certificate with respect to such Patents. The Controlling Party shall keep the Non-Controlling Party fully informed of its efforts to obtain such extension or supplementary protection certificate. The Non-Controlling Party shall provide prompt and reasonable assistance, as requested by the Controlling Party, including by taking such action as patent holder as is required under any Applicable Law to obtain such patent extension or supplementary protection certificate. The Controlling Party shall pay all expenses in regard to obtaining the extension or supplementary protection certificate (except to the extent any such expense constitutes an Allowable Expense).

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9.2.6 Patent Listings. The Commercial Lead for a particular Optioned Product in a particular country of the Territory shall have the sole right to make all patent listings of Denali Patents and Takeda Patents (including Joint Program Patents, in each case) with Regulatory Authorities for such Optioned Product in such country, provided that [***]. Subject to the foregoing proviso, the other Party shall cooperate with the Commercial Lead's reasonable requests in connection therewith, including meeting any submission deadlines, to the extent required or permitted by Applicable Law.

9.2.7 Prosecution and Maintenance Costs. Except as otherwise expressly provided in this Section 9.2, Out-of-Pocket Costs incurred by a Party in connection with the Prosecution and Maintenance activities undertaken by a Party pursuant to this Section 9.2 shall be included in the Allowable Expense; *provided* that if Denali has exercised the Denali Worldwide Royalty Option with respect to any Collaboration Program, such Out-of-Pocket Costs related to such Collaboration Program shall be shared equally between the Parties.

9.3 Enforcement of Patents.

9.3.1 Notice. Each Party shall promptly notify the other Party in writing of any alleged or threatened infringement of the ATV Platform Patents, Product Patents, or other Joint Program Patents, Denali Patents or Takeda Patents by a Third Party of which such Party becomes aware based on the development, commercialization, or an application to market a product containing a Research Biologic, Optioned Biologic or any Optioned Product (each, a "**Product Infringement**").

9.3.2 Prosecuted Infringements.

(a) **First Right**. Prior to the exercise of the Option with respect to a Collaboration Program, Denali shall have the sole right to prosecute any Product Infringement or Post-Grant Proceeding arising in connection with the prosecution of any Product Infringement. Following exercise of the Option with respect to a Collaboration Program, the Enforcing Party shall have the first right, but not the obligation, to prosecute any Product Infringement or Post-Grant Proceeding arising in connection with the prosecution of such Product Infringement, including the defense of the validity and enforceability of any such Patent that is the subject of such Product Infringement (the "**Prosecuted Infringements**"). For any particular Collaboration Program in any particular territory subject to the first sentence of this Section 9.3.2(b), the Party that is the Commercial Lead for such Collaboration Program in such territory shall have the first right to be the Enforcing Party with respect to prosecution of all Product Infringement with respect to (i) [***] and (ii) [***], in each case, pertaining to an Optioned Biologic or Option Product within such Collaboration Program in such territory. Subject to Section 9.3.2(c), Takeda shall have the sole right to be the Enforcing Party with respect to the prosecution of all Product Infringement with respect to [***]. Denali shall have the sole right to be the Enforcing Party with respect to the prosecution of all Product Infringement with respect to [***], unless such [***] is (x) a [***] or (y) [***].

(b) **Backup Enforcement Rights for Product Patents**. Subject to the last two sentences of Section 9.3.2(a) above, if the Party having the first enforcement right (but not the sole right) under Section 9.3.2(a) does not take commercially reasonable steps to

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prosecute a Product Infringement (i) within [***] days following [***], or (ii) provided such date occurs after the first such notice of the Product Infringement is provided, [***] Business Days before [***], whichever comes first, then the other Party may be the Enforcing Party and prosecute such Prosecuted Infringement at its own expense.

(c) **Coordination of Enforcement Rights and Non-Enforcing Party Participation Rights**. In the event the Enforcing Party prosecutes any Prosecuted Infringement, the Non-Enforcing Party, where necessary, shall furnish a power of attorney solely for such purpose or shall join in, or be named as a necessary party to, such action. The Non-Enforcing Party shall have the right to join as a party to such claim, suit, or proceeding and participate with its own counsel at its own expense; *provided* that the Enforcing Party shall retain control of the prosecution of such claim, suit, or proceeding. During the conduct of any Prosecuted Infringement by an Enforcing Party with respect to the alleged or threatened infringement of Product Patents or Joint Program Patents by an infringer, the Non-Enforcing Party agrees not to conduct a Prosecuted Infringement with respect to the same infringer other than as a necessary party to or joined in such Prosecuted Infringement prosecuted by the Enforcing Party or with the prior written consent of the Enforcing Party.

9.3.3 Conduct of Patent Litigation Under the Biologics Price Competition and Innovation Act. If either Party receives a copy of an application submitted to the FDA under Subsection (k) of Section 351 of the PHSA or equivalent in any other jurisdiction (a "**Biosimilar Application**") naming an Optioned Product as a reference product or otherwise becomes aware that such a Biosimilar Application has been filed (such as in an instance described in Section 351(l)(9)(C) of the PHSA), either Party shall, within [***] Business Days, notify the other Party so that the other Party may seek permission to view the application and related confidential information from the filer of the Biosimilar Application under Section 351(l)(1)(B)(iii) of the PHSA or equivalent in any other jurisdiction. If either Party receives any equivalent or similar certification or notice in any other jurisdiction, either Party shall, within [***] Business Days, notify and provide the other Party with copies of such communication. Regardless of the Party that is the "reference product sponsor" for purposes of such Biosimilar Application, the Commercial Lead in a particular country in the Territory with respect to the applicable Collaboration Program shall be the Enforcing Party and the Enforcing Party shall have the sole right, but not the obligation, to initiate litigation against the filer of the Biosimilar Application, including whether or not to utilize, in whole or in part, the procedures provided in Section 351 of the PHSA or equivalent in any other jurisdiction, provided that Denali shall be the Enforcing Party with respect to any [***] and [***] or [***] and Takeda shall be the Enforcing Party with respect to any [***]. If an Enforcing Party institutes any such litigation, then the other Party shall join as a party to such claim, suit or proceeding in any country requiring it as a party.

9.3.4 Cooperation; Settlement. The Parties agree to cooperate fully in any infringement action pursuant to this Section 9.3 and consult with the other as to the strategy for the defense of the Denali Patents, Takeda Patents, and Joint Program Patents. During any such claim, suit, or proceeding, the Enforcing Party shall: (a) provide the Non-Enforcing Party with drafts of all pleadings and other material documents filed with the court or tribunal prior to their submission, in sufficient time to allow the Non-Enforcing Party to review, consider and substantively comment thereon; (b) reasonably consider taking action to incorporate the Non-Enforcing Party's comments on all such all pleadings and other material documents; and (c) not settle any such claim, suit, or proceeding in a manner that: (i) [***]; or (ii) [***].

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9.3.5 Expenses. Except as otherwise expressly provided in this Section 9.3, Out-of-Pocket Costs incurred by a Party in connection with a Prosecuted Infringement or otherwise in performing activities pursuant to this Section 9.3 shall be (i) included as Allowable Expenses; or (ii) otherwise born by the Party who is the Enforcing Party if and after Denali exercises the Denali Worldwide Royalty Option.

9.3.6 Recovery. Except as otherwise provided in this Section 9.3.6, any recovery obtained as a result of litigation described in Section 9.3.1 or 9.3.3 (whether by way of settlement or otherwise) shall be, after first reimbursing each Party's Out-of-Pocket Costs, included in Net Sales. If Denali exercises the Denali Worldwide Royalty Option, such recoveries received with respect to the applicable Collaboration Program and any period after Denali exercised such Denali Worldwide Royalty Option shall be first applied to reimburse each Party's Out-Of-Pocket Costs and the remainder shall be shared at a rate of [***] to Takeda and [***] to Denali.

9.4 Infringement Claims by Third Parties. If the manufacture, sale, or use of an Optioned Biologic or Optioned Product in the Territory pursuant to this Agreement results in, or may result in, any claim, suit, or proceeding by a Third Party alleging patent infringement by a Party (or its Affiliates or Sublicensees), such Party shall promptly notify the other Party thereof in writing. Unless the Parties otherwise agree in writing, each Party shall have the right to defend itself against any such claim, suit, or proceeding that names such Party as a defendant; *provided* that the other Party may participate in any such claim, suit, or proceeding with counsel of its choice. Without limitation of the foregoing, if a Party finds it necessary or desirable to join the other Party as a party to any such action, such other Party shall execute all papers and perform such acts as shall be reasonably required. Each Party shall keep the other Party reasonably informed of all material developments in connection with any such claim, suit, or proceeding. Each Party agrees to provide the other Party with copies of all pleadings filed in such action and to allow the other Party reasonable opportunity to participate in the defense of the claims. The Party who is subject to an infringement action agrees not to settle such action, or make any material admissions or assert any position in such action, in a manner that [***]. Except as otherwise agreed by the Parties, Out-of-Pocket Costs incurred by a Party in performing activities pursuant to this Section 9.4 shall be included in Allowable Expenses, or if Denali has exercised the Denali Worldwide Royalty Option with respect to the relevant Collaboration Program, borne by Takeda subject to Takeda's right to offset [***] of such costs against its royalty obligations to Denali.

9.5 Invalidity or Unenforceability Defenses or Actions.

9.5.1 Notice. Each Party shall promptly notify the other Party in writing of any alleged or threatened assertion of invalidity or unenforceability of any of the Denali Patents, Takeda Patents or Joint Program Patents by a Third Party, in each case of which such Party becomes aware.

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9.5.2 Product Patents and Joint Program Patents Not in Connection with a Prosecuted Infringement. The Controlling Party with respect to the Prosecution and Maintenance of a Product Patent or Joint Program Patent (other than a Joint Program Patent that is a Takeda Prosecuted Patent), as determined in accordance with Section 9.2.1, shall have the right, but not the obligation, to defend and control the defense of the validity and enforceability of such Product Patent or Joint Program Patent that does not arise in connection with any Prosecuted Infringement. The Non-Controlling Party may participate in any such claim, suit, or proceeding with counsel of its choice at its own expense; *provided* that the Controlling Party shall retain control of the defense in such claim, suit, or proceeding. If the Controlling Party elects not to defend or control the defense of such Patents, or otherwise fails to initiate and maintain the defense of any such claim, suit or proceeding, then the Non-Controlling Party may conduct and control the defense of any such claim, suit or proceeding at its own expense.

9.5.3 [***] **Patents and** [***] **Patents**. As between the Parties, [***] shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the (i) [***] Patents and (ii) other [***] Patents that are not [***] Patents or [***] Patents, in each case, at its own expense.

9.5.4 [***] **Patents**. [***] shall have the sole right, but not the obligation, to defend and control the defense of the validity and enforceability of the [***] Patents at its own expense.

9.5.5 Cooperation. Each Party shall assist and cooperate with the other Party as such other Party may reasonably request from time to time in connection with its activities set forth in this Section 9.5, including by being joined as a party plaintiff in such action or proceeding, providing access to relevant documents and other evidence, and making its employees available at reasonable business hours, and consult with the other as to the strategy for the defense of the Denali Patents, Takeda Patents, and Joint Program Patents. In connection with any such defense or claim or counterclaim, the controlling Party shall not settle any such claim, suit, or proceeding in a manner that: (i) [***]; or (ii) [***]. Except as otherwise expressly provided in this Section 9.5, Out-of-Pocket Costs incurred by a Party in performing activities pursuant to this Section 9.5 shall be (a) included in as Allowable Expenses, or (b) otherwise borne by the Party who is the controlling Party if and after Denali exercises the Denali Worldwide Royalty Option, to the extent not otherwise reimbursed.

9.5.6 Notwithstanding anything to the contrary in this Section 9.5, in the event any invalidity and/or unenforceability action is a counterclaim to or part of a declaratory judgment action in anticipation of an enforcement action, then the terms and conditions of Section 9.3 shall apply, and not Sections 9.5.2 through 9.5.4.

9.6 Product Trademarks.

9.6.1 Ownership and Prosecution of Product Trademarks. Takeda shall own all right, title, and interest to the Product Trademarks in the Territory, and shall be responsible for the registration, prosecution, and maintenance thereof. Denali shall provide all assistance and documents reasonably requested by Takeda in support of its prosecution, registration, and maintenance of the Product Trademarks.

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9.6.2 Enforcement of Product Trademarks. Takeda shall have the sole right and responsibility for taking such action as Takeda, after consultation with Denali, deems necessary against a Third Party based on any alleged, threatened, or actual infringement, dilution, misappropriation, or other violation of, or unfair trade practices or any other like offense relating to, the Product Trademarks by a Third Party in the Territory.

9.6.3 Third Party Claims. Takeda shall have the sole right and responsibility for defending against any alleged, threatened, or actual claim by a Third Party that the use or registration of the Product Trademarks in the Territory infringes, dilutes, misappropriates, or otherwise violates any Trademark or other right of that Third Party or constitutes unfair trade practices or any other like offense, or any other claims as may be brought by a Third Party against a Party in connection with the use of the Product Trademarks with respect to an Optioned Product in the Territory.

9.6.4 Notice and Cooperation. Each Party shall provide to the other Party prompt written notice of any actual or threatened infringement of the Product Trademarks in the Territory and of any actual or threatened claim that the use of the Product Trademarks in the Territory violates the rights of any Third Party. Each Party agrees to cooperate fully with the other Party with respect to any enforcement action or defense commenced pursuant to this Section 9.6.

9.6.5 Out of Pocket Costs. All Out-of-Pocket Costs incurred by a Party in performing activities pursuant to this Section 9.6 shall be an Allowable Expense; provided that from and after the Co-Funding End Date following Denali's exercise of the Denali Worldwide Royalty Option with respect to a Collaboration Program, each Party shall be solely responsible for all Out-of-Pocket costs it incurs pursuant to this Section 9.6.

9.7 Inventor's Remuneration. Each Party shall be solely responsible for any remuneration that may be due such Party's inventors under any applicable inventor remuneration laws.

ARTICLE 10
PHARMACOVIGILANCE AND SAFETY

10.1 Pharmacovigilance. Within [***] days after the Option Exercise Date for the first Collaboration Program, the Parties shall enter into an agreement to initiate a process for the exchange of safety data (including post-marketing spontaneous reports received by each Party and its Affiliates) in a mutually agreed format in order to monitor the safety of the Optioned Biologics or Optioned Products and to meet reporting requirements with any applicable Regulatory Authority (the "**Pharmacovigilance Agreement**"). Notwithstanding the foregoing, after the Option Exercise Date, in no case shall exchange of adverse events ("**AEs**") occur later than [***] days for fatal or life threatening AEs, [***] days for other related serious AEs, and [***] days for non-serious AEs.

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10.2 Global Safety Database.

10.2.1 Denali shall initially set up, hold, and maintain the global safety database for Optioned Biologics and Optioned Products with respect to safety data obtained in connection with each Research Program and the Early Stage Development Activities for each Collaboration Program.

10.2.2 In connection with the commencement of Late Stage Development Activities by Takeda for a Collaboration Program and in accordance with the Transition Plan, Denali shall transfer to Takeda, in the electronic format agreed upon by the Parties at the JPT, the complete contents of the safety database maintained by Denali pursuant to Section 10.2.1 for the Optioned Biologics and Optioned Products corresponding to such Collaboration Program. Thereafter Takeda shall maintain the global safety database for such Optioned Biologics and Optioned Products. Each Party's and its Affiliates' costs incurred in connection with receiving, recording, reviewing, communicating, reporting, and responding to adverse events with respect to such Optioned Biologics and Optioned Product and in establishing and maintaining a global safety database for such Optioned Biologics and Optioned Products shall be included in the calculation of Allowable Expenses; provided that from and after the Co-Funding End Date following Denali's exercise of the Denali Worldwide Royalty Option with respect to a Collaboration Program, each Party shall be solely responsible for all such costs it incurs.

ARTICLE 11
CONFIDENTIALITY AND NON-DISCLOSURE

11.1 Confidentiality Obligations. At all times during the Term and for a period of [***] following termination or expiration of this Agreement in its entirety, each Party shall, and shall cause its officers, directors, employees and agents to, keep confidential and not publish or otherwise disclose to a Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or indirectly, by the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement or is reasonably necessary or useful for the performance of such Party's obligations, or the exercise of rights expressly granted to such Party under, this Agreement. Notwithstanding the foregoing, to the extent the receiving Party can demonstrate by documentation or other competent proof, the confidentiality and non-use obligations under this Section 11.1 with respect to any Confidential Information shall not include any information that:

11.1.1 has been published by a Third Party or otherwise is or becomes part of the public domain by public use, publication, general knowledge or the like through no wrongful act, fault or negligence on the part of the receiving Party;

11.1.2 is in the receiving Party's possession prior to disclosure by the disclosing Party, to the extent the receiving Party has the right to use and disclose such information;

11.1.3 is subsequently lawfully received by the receiving Party from a Third Party, to the extent the receiving Party has the right to use and disclose such information without breach of any agreement between such Third Party and the disclosing Party;

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11.1.4 is published or otherwise generally made available to Third Parties by the disclosing Party without restriction on disclosure; or

11.1.5 is independently developed by or for the receiving Party without reference to, or use or disclosure of, the disclosing Party's Confidential Information.

Specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination is in the public domain or in the possession of the receiving Party.

11.2 Permitted Disclosures. Each Party may disclose Confidential Information to the extent that such disclosure is:

11.2.1 in the reasonable opinion of the receiving Party's legal counsel, required to be disclosed pursuant to law, regulation or a valid order of a court of competent jurisdiction or other supra-national, federal, national, regional, state, provincial and local governmental body of competent jurisdiction, (including by reason of filing with securities regulators, but subject to Section 11.4); *provided*, that the receiving Party shall, unless otherwise prohibited, first have given advanced written notice (and to the extent possible, at least [***] Business Days' notice) to the disclosing Party and (other than with regard to disclosures to securities regulators or to comply with applicable securities law, which disclosures are covered in Section 11.4) give the disclosing Party a reasonable opportunity to take whatever action it deems necessary to protect its Confidential Information. In the event that no such protective order or other remedy is obtained, or the disclosing Party waives compliance with the terms of this Agreement, the receiving Party shall furnish only that portion of Confidential Information which the receiving Party is advised by counsel is legally required to be disclosed;

11.2.2 made by or on behalf of the receiving Party to the Regulatory Authorities in connection with any filing, application or request for Regulatory Approval in accordance with the terms of this Agreement; *provided*, that reasonable measures shall be taken to assure confidential treatment of such Confidential Information to the extent practicable and consistent with Applicable Law;

11.2.3 made by or on behalf of the receiving Party to a patent authority as may be reasonably necessary or useful for purposes of preparing, obtaining, defending or enforcing a Patent in accordance with the terms of this Agreement; *provided*, that reasonable measures shall be taken to assure confidential treatment of such Confidential Information, to the extent such protection is available;

11.2.4 made to its or its Affiliates' financial and legal advisors who have a need to know such disclosing Party's Confidential Information and are either under professional codes of conduct giving rise to expectations of confidentiality and non-use or under written agreements of confidentiality and non-use, in each case, substantially similar to the obligations of confidentiality and non-use of the receiving Party pursuant to this Article 11;

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11.2.5 made by the receiving Party or its Affiliates to potential or actual investors or acquirers as may be necessary in connection with their evaluation of such potential or actual investment or acquisition; *provided*, that such Persons shall be subject to obligations of confidentiality and non-use with respect to such Confidential Information substantially similar to the obligations of confidentiality and non-use of the receiving Party pursuant to this Article 11;

11.2.6 made by a Party or its Affiliates or Sublicensees to its or their advisors, consultants, clinicians, vendors, service providers, contractors, existing or prospective collaboration partners, existing or prospective licensees, existing or prospective sublicensees, or other Third Parties, in each case, to the extent necessary or useful in connection with the Development of Research Biologics, Optioned Biologics or Optioned Products, the Exploitation of the Optioned Biologics, the Optioned Products, or otherwise in connection with the performance of its obligations or exercise of its rights as contemplated by this Agreement; *provided*, that such Persons shall be subject to obligations of confidentiality and non-use with respect to such Confidential Information of the other Party substantially similar to the obligations of confidentiality and non-use in this Article 11; or

11.2.7 a disclosure of the terms of this Agreement, which is made only on a need-to-know basis, to Persons who are subject to obligations of confidentiality and non-use substantially similar to the obligations of confidentiality and non-use in this Article 11.

For any disclosures made by the receiving Party pursuant to Sections 11.2.4–11.2.7 shall remain responsible for any failure of the relevant Person to treat such Confidential Information as required under this Article 11. For clarity, in any case where the foregoing disclosure must be subject to obligations of confidentiality and non-use substantially similar to those under this Article 11, it is understood that [***].

11.3 Use of Name. Except as expressly provided in this Agreement, neither Party shall mention or otherwise use the name, logo, or Trademark of the other Party or any of its Affiliates (or any abbreviation or adaptation thereof) in any publication, press release, marketing and promotional material, website, or other form of publicity, without the prior written approval of such other Party. Notwithstanding the foregoing, the restrictions imposed by this Section 11.3 shall not prohibit either Party from making any disclosure identifying the other Party that, in the opinion of the disclosing Party's counsel, is required by Applicable Law (including stock exchange rules); *provided*, that such Party shall submit the proposed disclosure identifying the other Party in writing to the other Party as far in advance as reasonably practicable (and in no event less than [***] Business Days prior to the anticipated date of disclosure unless such proposed disclosure is required under Applicable Law, or the rules of an applicable securities exchange, in each case to be made in [***] Business Days or less) so as to provide a reasonable opportunity to comment thereon.

11.4 Public Announcements. The Parties have agreed upon the content of a joint press release to announce the collaboration which shall be issued substantially in the form attached hereto as Schedule 11.4 upon execution of this Agreement. Neither Party shall issue any

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other public announcement, press release, or other public disclosure regarding this Agreement or the Parties' activities hereunder without the other Party's prior written consent (which shall not be unreasonably withheld, delayed, or conditioned), except for any such disclosure regarding [***], or any such disclosure that is, in the opinion of the disclosing Party's counsel, required by Applicable Law or the rules of a stock exchange on which the securities of the disclosing Party are listed, or is otherwise expressly permitted in accordance with this Article 11. In the event a Party desires to make a public announcement regarding the exercise of any Option or payment of any milestone or that is, in the opinion of its counsel, required by Applicable Law or the rules of a stock exchange on which its securities are listed to make such a public disclosure, such Party shall submit the proposed disclosure in writing to the other Party as far in advance as reasonably practicable (and in no event less than [***] Business Days prior to the anticipated date of disclosure, unless such proposed disclosure is required under Applicable Law, or the rules of an applicable securities exchange, in each case to be made in [***] Business Days or less) so as to provide a reasonable opportunity to comment thereon. Specifically and notwithstanding the foregoing, the Parties acknowledge that [***]. As used in this Section 11.4, [***]. After release of any such press release, public announcement, public disclosure or presentation by a Party in accordance with this Section 11.4, such Party may further disclose the information contained such press release, public announcement, public disclosure or presentation without the need for further notice to or review by the other Party under this Section 11.4 or otherwise.

11.5 Publications.

11.5.1 Neither Party shall publish, publicly present, or otherwise publicly disclose any materials that [***] or pertain to [***], except in accordance with Section 11.5.2, without the prior written consent of the other Party, not to be unreasonably withheld, delayed, or conditioned. Each Party shall submit any such proposed publication or presentation to the other Party in accordance with Section 11.5.2.

11.5.2 Each Party shall have the right to review any paper proposed for publication by the other Party, including any oral presentation or abstract, that contains [***] or pertains to [***] or that includes [***]. Before any such paper is submitted for publication or an oral presentation is made, the publishing or presenting Party shall deliver a then-current copy of the paper or materials for oral presentation to the other Party at least [***] days prior to submitting the paper to a publisher or making such other presentation or disclosure. The other Party shall review any such paper and give its comments to the publishing Party within [***] days of the delivery of such paper to the other Party. With respect to oral presentation materials, abstracts and the like, the other Party shall make reasonable efforts to expedite review of such materials and abstracts, and shall return such items as soon as practicable to the publishing or presenting Party with appropriate comments, if any. Notwithstanding the foregoing, the publishing or presenting Party shall comply with the other Party's request to delete references to such other Party's Confidential Information in any such paper and will withhold publication of any such paper or any presentation of same for an additional [***] days in order to permit the Parties to obtain Patent protection if either Party reasonably deems it necessary. Any publication shall include recognition of the contributions of the other Party according to standard practice for assigning scientific credit, either through authorship or acknowledgement, as may be appropriate. Notwithstanding the foregoing, prior to the Option Exercise Date for a Collaboration Program, Denali shall have the sole right to [***], provided that Takeda shall have [***]. Notwithstanding

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the foregoing it is understood that the requirements of this Section 11.5.2 are subject to and limited by the provisions of Sections 11.2.1 and 11.4 (*i.e.*, with respect to disclosures required by Applicable Law), and [***]. Notwithstanding the foregoing, following a Denali Worldwide Royalty Option exercise with respect to a Collaboration Program, Takeda will have the [***] right to publish or present [***] or results of [***], *provided* that Denali shall have the right to review and comment on any such publication or public presentation as provided in this Section 11.5.2. After release of any publication or presentation by a Party in accordance with this Section 11.5.2, such Party may further disclose the information contained in such publication or presentation without the need for further notice to or review by the other Party under this Section 11.5.2 or otherwise.

11.6 Prior Confidentiality. Any Information disclosed by a Party or its Affiliate to the other Party or its Affiliate prior to the Execution Date under that certain Confidentiality Agreement between the Parties or their respective Affiliates dated [***] shall be deemed to have been disclosed under this Agreement, and covered by the provisions of this Article 11.

11.7 Survival. All Confidential Information shall continue to be subject to the terms of this Agreement for the period set forth in Section 11.1.

ARTICLE 12
REPRESENTATIONS, WARRANTIES AND COVENANTS

12.1 Mutual Representations and Warranties. Denali and Takeda each represents and warrants to the other, as of the Execution Date, as follows:

12.1.1 Organization. It is duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform its obligations under this Agreement.

12.1.2 Authorization. The execution and delivery of this Agreement and the performance by it of its obligations hereunder have been duly authorized by all necessary corporate action, and do not violate (a) such Party's charter documents, bylaws, or other organizational documents, (b) in any material respect, any agreement, instrument, or contractual obligation to which such Party is bound, (c) any requirement of any Applicable Law existing as of the Execution Date and applicable to such Party, or (d) any order, writ, judgment, injunction, decree, determination, or award of any court or governmental agency in effect as of the Execution Date and applicable to such Party.

12.1.3 Binding Agreement. This Agreement is a legal, valid, and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity).

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12.1.4 No Inconsistent Obligation. It is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement.

12.2 Additional Representations and Warranties of Denali. Denali further represents and warrants to Takeda, as of the Execution Date (and [***], and covenants, as follows:

12.2.1 All issued patents and patent applications owned by or exclusively licensed to Denali or any of its Affiliates that meet the description of (i) or (ii) of the Denali Patents definition are Controlled by Denali or such Affiliate(s). Such patents and patent applications that Denali owns, or licensed exclusively to Denali or any of its Affiliates, and to Denali's knowledge that are licensed non-exclusively to Denali or any of its Affiliates under any Existing In-Licensed Agreements, in each case that exist as of the Execution Date, are listed on Schedule 12.2.1 (the "**Existing Patents**").

12.2.2 There are no claims, judgments, or settlements that have been brought or obtained against Denali or any of its Affiliates relating to the Existing Regulatory Documentation, the Existing Patents, or the Denali Know-How. No claim or litigation has been brought or to Denali's knowledge threatened in writing by any Person alleging, that (a) the Existing Patents are invalid or unenforceable, or (b) the Existing Regulatory Documentation, the Existing Patents, or the Denali Know-How, or the disclosing, copying, making, assigning, or licensing of the Existing Regulatory Documentation, the Existing Patents, or the Denali Know-How, or the Development or Commercialization of the Research Biologics as contemplated herein, does or will violate, infringe, misappropriate or otherwise conflict or interfere with, any Patent or other intellectual property or proprietary right of any Person.

12.2.3 Denali has not granted to any Third Party any rights under the Patents and/or Information owned or in-licensed by Denali or any of its Affiliates for use in connection with the Designated Targets, and is entitled to grant the licenses to Takeda expressly provided herein.

12.2.4 (a) To Denali's knowledge, Denali has the right to use all Information and Patents necessary to conduct the activities under the Research Programs for the Initial Designated Targets, and (b) the Development or Commercialization of the Research Biologics Directed to the Initial Designated Targets as contemplated herein will not conflict with any other license or agreement to which Denali or any of its Affiliates is a party.

12.2.5 Neither Denali nor, to Denali's knowledge, any counter party is in material breach of any Product In-License Agreement or Platform In-License Agreement. Denali has not threatened to terminate, nor alleged any material breach under, any such Product In-License Agreement or Platform In-License Agreement. Denali has not received any written notice from any counter party to any Product In-License Agreement or Platform In-License Agreement threatening to terminate an In License Agreement or Platform In-License Agreement or alleging that Denali is in material breach of a Product In-License Agreement or Platform In-License Agreement. To Denali's knowledge, each Product In-License Agreement and Platform In-License Agreement is in full force and effect. Schedules 1.118 and 1.123 list all Product In-License

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Agreements and all Platform In-License Agreements in existence as of the Execution Date, and Denali has provided or made available to Takeda a true and complete copy of each such agreement to Takeda prior to the Execution Date.

12.2.6 To Denali's knowledge, the Existing Patents are being prosecuted in the respective patent offices in the Territory in accordance with Applicable Law. To Denali's knowledge, the Existing Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

12.2.7 To Denali's knowledge, no Person is infringing or threatening to infringe or misappropriating or threatening to misappropriate the Existing Patents, the Denali Know-How, or the Regulatory Documentation.

12.2.8 No written claim has been filed, or to Denali's knowledge, threatened in writing, against Denali or any of its Affiliates by any Third Party alleging that the conception, development, or reduction to practice of the Regulatory Documentation, the Existing Patents, or Denali Know-How constitute or involved the misappropriation of trade secrets or other rights or property of any Person.

12.2.9 Denali has conducted, and to Denali's knowledge, its contractors and consultants have conducted, all Development of the Research Biologics prior to the Execution Date in accordance with Applicable Law. Denali and its Affiliates have employed (and, with respect to such tests and studies that Denali will perform, will employ) Persons with appropriate education, knowledge and experience to conduct and to oversee the conduct of the pre-clinical and Clinical Studies with respect to the Research Biologics.

12.2.10 Neither Denali nor any of its employees nor to its knowledge, any of the agents performing hereunder, has ever been, is currently, or is the subject of a proceeding that could lead to it or such employees or agents becoming, as applicable, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual. For purposes of this provision, the following definitions shall apply:

(i) A "**Debarred Individual**" is an individual who has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from providing services in any capacity to a Person that has an approved or pending drug or biological product application.

(ii) A "**Debarred Entity**" is a corporation, partnership or association that has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from submitting or assisting in the submission of any abbreviated drug application, or a subsidiary or affiliate of a Debarred Entity.

(iii) An "**Excluded Individual**" or "**Excluded Entity**" is (A) an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal health care programs such as Medicare or Medicaid by the Office of the Inspector General (OIG/HHS) of the U.S. Department of Health and Human Services, or (B) is an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal procurement and non-procurement programs, including those produced by the U.S. General Services Administration (GSA).

(iv) A "**Convicted Individual**" or "**Convicted Entity**" is an individual or entity, as applicable, who has been convicted of a criminal offense that falls within the ambit of 21 U.S.C. §335a (a) or 42 U.S.C. §1320a - 7(a), but has not yet been excluded, debarred, suspended or otherwise declared ineligible.

12.3 Additional Covenants of Denali. Denali covenants to Takeda as follows:

12.3.1 [***], Denali shall: (a) [***], (b) [***], (c) [***], (d) [***], or (e) [***].

12.3.2 During the Term, Denali shall (a) [***], and (b) [***].

12.3.3 Denali will not [***].

12.3.4 If, during the Term, [***].

12.3.5 Denali shall be responsible for [***].

12.4 Additional Covenants of Takeda. Takeda covenants to Denali as follows:

12.4.1 During the Term, Takeda shall (a) [***], and (b) [***].

12.4.2 Neither Takeda nor any of its Affiliates will [***].

12.4.3 If, during the Term, [***].

12.4.4 Takeda shall be responsible for [***].

12.5 DISCLAIMER OF WARRANTIES. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATIONS OR GRANTS ANY WARRANTIES, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, WHETHER WRITTEN OR ORAL, OR EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF QUALITY, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR USE OR PURPOSE OR ANY WARRANTY AS TO THE VALIDITY OF ANY PATENTS OR THE NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

ARTICLE 13
INDEMNITY

13.1 Indemnification of Denali. Takeda shall indemnify Denali, its Affiliates and its and their respective directors, officers, employees, and agents (the "**Denali Indemnitees**") and defend and save each of them harmless, from and against any and all losses, damages, liabilities, penalties, costs, and expenses (including reasonable attorneys' fees and expenses) (collectively, "**Indemnified Losses**") in connection with any and all suits, investigations, claims, or demands

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of Third Parties (collectively, "**Third Party Claims**") incurred by or rendered against the Denali Indemnitees arising from or occurring as a result of:

(a) the Development of Research Biologics by or under the authority of Takeda;

(b) the Development, Manufacture, Commercialization or other Exploitation of Optioned Biologics and Optioned Products by or under the authority of Takeda, including any Additional Development Activities conducted by or under the authority of Takeda; or

(c) the negligence, reckless conduct or willful misconduct on the part of Takeda or its Affiliates or their respective directors, officers, employees, and agents in performing its or their obligations under this Agreement;

(d) a breach by Takeda of this Agreement, including any breach of a representation, warranty or covenant by Takeda made under Article 12;

except in the case of clauses (a) through (d), for those Indemnified Losses for which Denali, in whole or in part, has an obligation to indemnify Takeda pursuant to Section 13.2 hereof, as to which Indemnified Losses each Party shall indemnify the other to the extent of their respective liability for such Indemnified Losses.

13.2 Indemnification of Takeda. Denali shall indemnify Takeda, its Affiliates and its and their respective directors, officers, employees, and agents (the "**Takeda Indemnitees**"), and defend and save each of them harmless, from and against any and all Indemnified Losses in connection with any and all Third Party Claims incurred by or rendered against the Takeda Indemnitees arising from or occurring as a result of:

(a) the Development of Research Biologics by or under the authority of Denali;

(b) the Development, Manufacture, Commercialization, or other Exploitation of the Optioned Biologics and Optioned Products, and any Research Biologics for which Takeda does not exercise the Option, by or under the authority of Denali either during the Term or after the termination of this Agreement (with respect to a Terminated Biologic or Terminated Product), including any Additional Development Activities conducted by or under the authority of Denali;

(c) the negligence, reckless conduct or willful misconduct on the part of Denali or its Affiliates or its or their respective directors, officers, employees, and agents in performing its obligations under this Agreement;

(d) a breach by Denali of this Agreement, including any breach of a representation, warranty or covenant by Denali made under Article 12.

except, in the case of clauses (a) through (d) above for those Indemnified Losses for which Takeda, in whole or in part, has an obligation to indemnify Denali pursuant to Section 13.1 hereof, as to which Indemnified Losses each Party shall indemnify the other to the extent of their respective liability for the Indemnified Losses.

13.3 Certain Indemnified Losses. Any Indemnified Losses and all Out-of-Pocket Costs incurred by a Party to conduct its indemnification obligations under Section 13.1 or 13.2, (other than those Indemnified Losses and Out-of-Pocket Costs that result from [***], in connection with any Third Party Claim brought against either Party resulting directly or indirectly from (a) [***]; (b) [***], or (c) [***], shall be included as an Allowable Expense, except in each case (b) and (c) with respect to any Collaboration Program for which Denali has exercised the Denali Worldwide Royalty Option. If either Party learns of any Third Party Claim with respect to Indemnified Losses covered by this Section 13.3, such Party shall provide the other Party with prompt written notice thereof. The Parties shall confer with respect to how to respond to such Third Party Claim and how to handle such Third Party Claim in an efficient manner. In the absence of such an agreement, each Party shall have the right to take such action as it deems appropriate.

13.4 Notice of Claim. All indemnification claims in respect of a Party, its Affiliates, or their respective directors, officers, employees and agents shall be made solely by such Party to this Agreement (the "**Indemnified Party**"). The Indemnified Party shall give the indemnifying Party prompt written notice (an "**Indemnification Claim Notice**") of any Indemnified Losses or discovery of fact upon which such Indemnified Party intends to base a request for indemnification under this Article 13, but in no event shall the indemnifying Party be liable for any Indemnified Losses to the extent such Indemnified Losses arise from any delay in providing such notice. Each Indemnification Claim Notice must contain a description of the claim and the nature and amount of such Indemnified Loss (to the extent that the nature and amount of such Indemnified Loss is known at such time). The Indemnified Party shall furnish promptly to the indemnifying Party copies of all papers and official documents received in respect of any Indemnified Losses and Third Party Claims.

13.5 Control of Defense.

13.5.1 In General. Subject to the provisions of Sections 9.4, 9.5, and 9.6, at its option, the indemnifying Party may assume the defense of any Third Party Claim by giving written notice to the Indemnified Party within [***] days after the indemnifying Party's receipt of an Indemnification Claim Notice. The assumption of the defense of a Third Party Claim by the indemnifying Party shall not be construed as an acknowledgment that the indemnifying Party is liable to indemnify the Indemnified Party in respect of the Third Party Claim, nor shall it constitute a waiver by the indemnifying Party of any defenses it may assert against the Indemnified Party's claim for indemnification. Upon assuming the defense of a Third Party Claim, the indemnifying Party may appoint as lead counsel in the defense of the Third Party Claim any legal counsel selected by the indemnifying Party which shall be reasonably acceptable to the Indemnified Party. In the event the indemnifying Party assumes the defense of a Third Party Claim, the Indemnified Party shall immediately deliver to the indemnifying Party all original notices and documents (including court papers) received by the Indemnified Party in connection with the Third Party Claim. Should the indemnifying Party assume the defense of a Third Party Claim, except as provided in Section 13.5.2, the indemnifying Party shall not be liable to the Indemnified Party for any legal expenses subsequently incurred by such Indemnified

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Party in connection with the analysis, defense or settlement of the Third Party Claim unless specifically requested in writing by the indemnifying Party. In the event that it is ultimately determined that the indemnifying Party is not obligated to indemnify, defend or hold harmless the Indemnified Party from and against the Third Party Claim, the Indemnified Party shall reimburse the indemnifying Party for any Indemnified Losses incurred by the indemnifying Party in its defense of the Third Party Claim.

13.5.2 Right to Participate in Defense. Without limiting Section 13.5.1, any Indemnified Party shall be entitled to participate in, but not control, the defense of such Third Party Claim and to employ counsel of its choice for such purpose; *provided*, that such employment shall be at the Indemnified Party's own expense unless (a) the employment thereof, and the assumption by the indemnifying Party of such expense, has been specifically authorized by the indemnifying Party in writing, (b) the indemnifying Party has failed to assume the defense and employ counsel in accordance with Section 13.5.1 (in which case the Indemnified Party shall control the defense), or (c) the interests of the Indemnified Party and the indemnifying Party with respect to such Third Party Claim are sufficiently adverse to prohibit the representation by the same counsel of both Parties under Applicable Law, ethical rules or equitable principles.

13.5.3 Settlement. With respect to any Indemnified Losses relating solely to the payment of money damages in connection with a Third Party Claim and that shall not result in the Indemnified Party's becoming subject to injunctive or other relief or otherwise adversely affect the business of the Indemnified Party in any manner, and as to which the indemnifying Party shall have acknowledged in writing the obligation to indemnify the Indemnified Party hereunder, the indemnifying Party shall have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Indemnified Loss, on such terms as the indemnifying Party, in its sole discretion, shall deem appropriate. With respect to all other Indemnified Losses in connection with Third Party Claims, where the indemnifying Party has assumed the defense of the Third Party Claim in accordance with Section 13.5.1, the indemnifying Party shall have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Indemnified Loss; *provided*, that it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld, delayed, or conditioned). If the indemnifying Party does not assume and conduct the defense of a Third Party Claim as provided above, the Indemnified Party may defend against such Third Party Claim. Regardless of whether the indemnifying Party chooses to defend or prosecute any Third Party Claim, no Indemnified Party shall admit any liability with respect to, or settle, compromise or dispose of, any Third Party Claim in a manner that would have a material adverse effect on the Indemnified Party or admit wrongdoing on behalf of the Indemnified Party, without the prior written consent of the indemnifying Party. The indemnifying Party shall not be liable for any settlement, compromise or other disposition of an Indemnified Loss by an Indemnified Party that is reached without the written consent of the indemnifying Party.

13.5.4 Cooperation. Regardless of whether the indemnifying Party chooses to defend or prosecute any Third Party Claim, the Indemnified Party shall, and shall cause each indemnitee to, cooperate in the defense or prosecution thereof and shall furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith. Such cooperation shall include access during normal business hours afforded to the

indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Third Party Claim, and making Indemnified Parties and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder, and the indemnifying Party shall reimburse the Indemnified Party for all its reasonable out-of-pocket expenses in connection therewith.

13.5.5 Expenses. Except as provided above, the reasonable and verifiable costs and expenses, including fees and disbursements of counsel, incurred by the Indemnified Party in connection with any Third Party Claim shall be reimbursed on a Calendar Quarter basis in arrears by the indemnifying Party, without prejudice to the indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to refund in the event the indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

13.6 Special, Indirect, and Other Losses. EXCEPT (A) [***], (B) FOR A PARTY'S BREACH OF ITS OBLIGATIONS UNDER [***], AND (C) TO THE EXTENT ANY SUCH DAMAGES ARE REQUIRED TO BE PAID TO A THIRD PARTY AS PART OF A CLAIM FOR WHICH A PARTY PROVIDES INDEMNIFICATION UNDER THIS ARTICLE 13, NEITHER PARTY NOR ANY OF ITS AFFILIATES SHALL BE LIABLE FOR INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR CONSEQUENTIAL DAMAGES, INCLUDING LOSS OF PROFITS OR BUSINESS INTERRUPTION (TO THE EXTENT THE SAME ARE CONSEQUENTIAL DAMAGES), HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE IN CONNECTION WITH OR ARISING IN ANY WAY OUT OF THE TERMS OF THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THE USE OF AN OPTIONED BIOLOGIC OR OPTIONED PRODUCT, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGE.

13.7 Insurance. Each Party shall obtain and carry in full force and effect the minimum insurance requirements set forth herein. Such insurance (a) shall be primary insurance with respect to each Party's own participation under this Agreement, (b) shall be issued by a recognized insurer rated by A.M. Best "A-VII" (or its equivalent) or better, or an insurer pre-approved in writing by the other Party, (c) shall list the other Party as an additional named insured thereunder, and (d) shall require [***] days' written notice to be given to the other Party prior to any cancellation or non-renewal thereof.

13.7.1 Types and Minimum Limits. The types of insurance and minimum limits shall be:

(a) Worker's Compensation with statutory limits in compliance with the worker's compensation laws of the state or states in which the Party has employees in the United States (excluding Puerto Rico).

(b) Employer's Liability coverage with a minimum limit of [***] per occurrence; *provided*, that a Party has employees in the United States (excluding Puerto Rico).

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(c) General Liability Insurance with a minimum limit of [***] per occurrence and [***] in the aggregate. Beginning at least [***] days prior to the initiation of a Clinical Study, General Liability Insurance shall include Clinical Trial Insurance. Beginning at least [***] days prior to First Commercial Sale of an Optioned Product, General Liability Insurance shall also include product liability insurance of [***].

13.7.2 Certificates of Insurance. Upon request by a Party, the other Party shall provide Certificates of Insurance evidencing compliance with this Section 13.7.2. The insurance policies shall be under an occurrence form, but if only a claims-made form is available to a Party, then such Party shall continue to maintain such insurance after the expiration or termination of this Agreement for the longer of (a) a period of [***] years following termination or expiration of this Agreement in its entirety, or (b) with respect to a particular Party, last sale of an Optioned Product (or but for expiration or termination, would be considered an Optioned Product) sold under this Agreement by a Party.

13.7.3 Self-Insurance. Notwithstanding the foregoing, (a) Takeda may self-insure, in whole or in part, the insurance requirements described above and (b) Denali may self-insure, in whole or in part, the insurance requirements described above [***].

ARTICLE 14
TERM AND TERMINATION

14.1 Term. This Agreement shall commence on the Execution Date (subject to Section 15.1) and, unless earlier terminated as set forth below, shall continue in force and effect until (a) the expiration of the last-to-expire Option Period if Takeda has not exercised any of its Options prior to such expiration or (b) if Takeda has exercised any of its Options prior to the expiration of the applicable Option Period, for so long as an Optioned Biologic or Optioned Product Directed to an Optioned Target is being Developed or Commercialized pursuant to this Agreement (such period, the "**Term**").

14.2 Termination for Material Breach. If either Party (the "**Non-Breaching Party**") believes that the other Party (the "**Breaching Party**") has materially breached any of its material obligations under this Agreement, then the Non-Breaching Party may deliver notice of such material breach to the Breaching Party (a "**Default Notice**"). If the Breaching Party does not dispute that it has committed a material breach of any of its material obligations under this Agreement and the Breaching Party fails to cure such breach within [***] after receipt of the Default Notice, the Non-Breaching Party may terminate this Agreement upon written notice to the Breaching Party; *provided* that if such material breach is with respect to only a Collaboration Program (and not this Agreement in its entirety), such termination shall be limited to such Collaboration Program. If the Breaching Party disputes the Default Notice within the [***] cure-period, the dispute shall be resolved pursuant to Section 16.6.4. If, as a result of the application of such dispute resolution procedures, the Breaching Party is determined to be in material breach of any of its material obligations under this Agreement (an "**Adverse Ruling**") and the Breaching Party fails to complete the actions specified by the Adverse Ruling to cure such material breach within any of the remaining [***] cure period after such ruling is issued, then the Non-Breaching Party may terminate this Agreement upon written notice to the Breaching Party; *provided* that if such material breach is with respect to only a Collaboration Program (and not this Agreement in its entirety), such termination shall be limited to such Collaboration Program. Notwithstanding anything to the contrary, in the event [***].

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14.3 For Convenience. Beginning [***] after the Effective Date, Takeda may terminate this Agreement: (a) in its entirety; or (b) with respect to a particular Designated Target(s) (and the associated Collaboration Program(s)), for any or no reason, upon [***] days prior written notice to Denali. Without limiting Takeda's obligations under [***], beginning after the completion of Denali's Early Stage Development Activities with respect to an Optioned Product within a Collaboration Program, if at any time Takeda has not, for a period of [***], either directly or through an Affiliate or Third Party, engaged in [***] activities in support of [***] of any Optioned Product within such Collaboration Program in or for a Major Market then except to the extent (i) [***] or (ii) [***] was (1) [***], or (2) [***], Denali may, at its sole discretion, provide written notice to Takeda of its intent to terminate this Agreement with respect to such Collaboration Program and, if Takeda does not commence and sustain [***] activities in support of [***] of any Optioned Product within such Collaboration Program within [***] after such notice from Denali, Denali may terminate this Agreement with respect to such Collaboration Program immediately upon written notice to Takeda. For clarity, the determination of whether the activities being undertaken by or on behalf of Takeda are [***] for the purposes of this Section 14.3 shall be based on those activities taken as a whole, in light of then-current facts and circumstances related to such Collaboration Program, and such determination shall be subject to the dispute resolution procedures in Section 16.6.4.

14.4 Termination for Insolvency. Either Party may terminate this Agreement in its entirety at any time during the Term by giving written notice to the other Party if the other Party files in any court or agency pursuant to any statute or regulation of any state or country a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee for the other Party or its assets, or if the other Party is served with an involuntary petition against it, filed in any insolvency proceeding, and such petition shall not be dismissed with [***] days after the filing thereof, or if the other Party makes a general assignment for the benefit of creditors.

14.5 Termination for Patent Challenge. Either Party may terminate this Agreement upon notice to the other Party in the event that such other Party, or any of its Affiliates or Sublicensees, or any Third Party designated by such other Party, takes any action, directly or indirectly, or knowingly provides financial or other assistance, including legal or technical advice, directly or indirectly, to any Third Party to challenge the validity, enforceability, scope, inventorship or ownership of any of such Party's Patents that are licensed to the other Party under this Agreement in any court or tribunal or any patent office in a jurisdiction, or in any arbitration proceeding, including in connection with an opposition proceeding, re-examination or post-grant proceeding, but excluding any counter-claim filed by such Party or any of its Affiliates or Sublicensees as a defense to a claim of patent infringement of the applicable Patent licensed under this Agreement, and within [***] days after written notice thereof by such Party, such other Party does not withdraw or cause to be withdrawn such action.

14.6 Termination for a Material Safety Event. With respect to any Collaboration Program for which Takeda has exercised the Option, Takeda may terminate this Agreement with respect to such Collaboration Program, upon [***] days prior written notice to Denali, if a

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Material Safety Event occurs with respect to such Collaboration Program; *provided* that the JSC unanimously agrees that a Material Safety Event has occurred as of the date of such written notice. For such purposes a "**Material Safety Event**" means an event that [***], is reasonably likely to [***] that (when considered in totality) is reasonably likely: (a) [***]; and/or (b) [***].

14.7 Effects of Termination and Option Expiration.

14.7.1 Licenses to Intellectual Property. In the event of any termination of this Agreement in its entirety or with respect to a Terminated Program, subject to Section 14.10 below:

(a) all rights and licenses granted by Denali under Article 7, and all obligations of Takeda with respect thereto, shall immediately terminate with respect to the Terminated Programs;

(b) all rights and licenses granted by Takeda under Article 7, and all obligations of Denali with respect thereto, shall immediately terminate with respect to the Terminated Programs;

(c) subject to the terms of this Section 14.7.1(c) and solely with respect to the Terminated Program(s):

(i) Takeda shall, and hereby does effective as of the effective date of termination, grant Denali a license, with the right to grant multiple tiers of sublicenses, under (1) Takeda Know-How reasonably necessary to Exploit the Biologics and Products Directed to the Terminated Target(s) for the Terminated Program in the forms that are being or have been Developed and/or Commercialized at the time of such termination and Takeda's interest in any Joint Program Know-How and (2) Takeda Patents reasonably necessary to Exploit (or that otherwise Cover) the Biologics and Products Directed to such Terminated Target(s) in the forms that are being or have been Developed and/or Commercialized at the time of such termination and Takeda's interest in any Joint Program Patents, in each case solely for the purposes of Exploiting Biologics and Products Directed to the Terminated Target(s) for such Terminated Program(s). For avoidance of doubt, [***].

(ii) Takeda shall assign to Denali or its designee all Regulatory Approvals, Regulatory Documentation and Product Trademarks for the Terminated Products Controlled by Takeda. In each case, unless otherwise required by Applicable Law or requested by Denali, the foregoing assignment (or availability) shall be made within [***] days after the effective date of any expiration or termination of this Agreement, and if such assignment cannot be made under Applicable Law within such period, as soon as practicable thereafter. Pending transfer of Takeda's Regulatory Approvals and Regulatory Documentation for the Terminated Products, Takeda hereby grants to Denali (or its designee) a right of reference to all such Regulatory Approvals and Regulatory Documentation for the Terminated Product for all uses in connection with the Terminated Product. Takeda shall provide the applicable Regulatory Authority a letter confirming this right of reference at any time within [***] days after Denali's request and shall take such other actions and execute such other documents as Denali may reasonably request to further confirm and give effect to this right of reference.

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Notwithstanding the definition of Confidential Information, all such Regulatory Documentation and Regulatory Approvals for the Terminated Products and all Joint Program Know-How that is [***] to the Terminated Products shall be deemed to be the Confidential Information of Denali and not Takeda.

(iii) Denali shall additionally have the right to immediately have Takeda commence the transfer of the Manufacturing Process to Denali or its designee, with such transfer to be carried out in accordance with the terms of Section 5.6 applied *mutatis mutandis*.

(iv) Takeda shall provide to Denali the Takeda Know-How (to the extent licensed under clause (i) above), Regulatory Documentation, Clinical Data and other Information pertaining to the Terminated Program (to the extent such items exist as of the date of such termination), and Denali shall have the right to use and disclose the same in connection with the Exploitation of the Terminated Program. Takeda shall have no obligation to translate any such Takeda Know-How, Regulatory Documentation, Clinical Data or other Information into English or any other language.

(d) Promptly following any such termination, at either Party's request, the Parties shall [***]: (i) whether [***]; (ii) if [***]; (iii) the [***], *provided*, that [***]; (iv) [***]; and (v) [***]. In the event the Parties [***]. It is understood that the Parties intend [***].

(e) Denali shall be responsible for (A) making any payments (including royalties, milestones and other amounts) payable by Takeda to Third Parties under any Third Party agreements with respect to the Patents or Information that are the subject of the licenses granted to Denali under the Takeda Know-How and/or Takeda Patents in Section 14.7.1(c) by making such payments directly to Takeda and, in each instance, Denali shall make the requisite payments to Takeda and provide the necessary reporting information to Takeda in sufficient time to enable Takeda to comply with its obligations under such Third Party agreements, and (B) complying with any other obligations included in any such Third Party agreements that are applicable to the grant to Denali of such license or to the exercise of such license by Denali or any of its Affiliates or sublicensees; and Takeda shall be responsible for paying or providing to any such Third Party any payments or reports made or provided by Denali under this Section 14.7.1(e). Upon request by Denali, Takeda shall disclose to Denali a true and complete written description of the applicable payment and other obligations under such Third Party agreements, and Denali's obligation to reimburse Takeda such amounts and comply with such obligations following such request shall be limited to those payment and other obligations as so disclosed by Takeda.

(f) Denali may terminate its license pursuant to Section 14.7.1(c) under any Patent or Information with respect to a Terminated Product by so notifying Takeda in writing, in which case the terminated Patent or Information, respectively, shall be excluded from such license and Denali shall have no obligation to pay royalties (if any are due with respect to such license) or reimburse any Third Party payments (or abide by other Third Party obligations) under Section 14.7.1 with respect to such Patent or Information to the extent so excluded. For clarity, Denali agrees to indemnify the Takeda Indemnitees and defend and save each of them

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harmless, from and against any and all Indemnified Losses in connection with any and all Third Party Claims incurred or rendered against the Takeda Indemnitees arising from or occurring as a result of the Development, Manufacture, Commercialization, or other Exploitation of any Terminated Biologic or Terminated Product in accordance with Section 13.2, and any such termination by Denali shall not limit Denali's obligation to indemnify Takeda for any such Third Party Claims made by such Third Party related to the Exploitation of the Terminated Biologic or Terminated Product after the effective date of termination.

(g) For clarity, upon any termination of this Agreement in its entirety or with respect to a Terminated Program: (i) the Designated Target for such Terminated Program (the "**Terminated Target**") shall thereafter cease to be a Designated Target, such program shall cease to be a Collaboration Program, any Biologic Directed to the Terminated Target shall cease to be a Research Biologic or Optioned Biologic, as applicable (each, a "**Terminated Biologic**"), and any product containing such Terminated Biologic (each, a **"Terminated Product**") shall cease to be a Optioned Product, as applicable, in each case for all purposes of this Agreement; and, in any case (ii) all rights of Takeda, and all obligations of Denali, under this Agreement with respect to such Terminated Target, Terminated Biologics and Terminated Products shall terminate, except for those rights and obligations expressly surviving under Sections 14.7, 14.8 and 14.10. For clarity: (A) Sections 11.4 and 11.5 shall not apply to public statements or publications by or under the authority of Denali to the extent the same pertain to the Terminated Program, Terminated Biologic, Terminated Product or Terminated Target; and (C) the Joint Committees shall have no further authority or oversight with respect to the Terminated Program.

14.8 Transition. In the event of termination of this Agreement, whether in its entirety or with respect to a Terminated Program, the following also shall apply.

14.8.1 Development. In the event Takeda is conducting (or is having conducted on its behalf) any (a) on-going Clinical Studies of Optioned Biologic or Optioned Product or (b) any ongoing non-clinical studies and/or manufacturing process development activities (including, formulation studies, stability studies, scale up tests, etc.) of Optioned Biologic or Optioned Product, in each case following the date a notice of termination has been issued by Denali or Takeda, as applicable, Takeda agrees, at Denali's request (except as provided below): (i) unless such termination was made in accordance with Section 14.6, to continue for a period of [***] after the effective date of termination ("**Development Wind-Down Period**") any such Clinical Studies, non-clinical studies or manufacturing process development activities, or any portion thereof; or (ii) to the extent so requested by Denali, (A) to promptly transition to Denali or its designee such Clinical Studies, non-clinical studies or manufacturing process development, or portions thereof as then being conducted in accordance with the Development Plan for such Terminated Program in effect immediately prior to the applicable termination date or (B) to terminate such Clinical Studies, non-clinical studies, manufacturing process development, or portions thereof (provided that such termination would not be inconsistent with Takeda's ethical obligations). Notwithstanding the foregoing, if the relevant termination is by Takeda pursuant to Section 14.2 or 14.4, Takeda shall have the right to elect whether to continue, transition to Denali (or its designee) or wind-down any such on-going Clinical Studies. [***].

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14.8.2 Commercialization. Except to the extent the applicable termination was made in accordance with Section 14.6, if this Agreement is terminated after the First Commercial Sale of a Terminated Product and Takeda is the Commercial Lead with respect to the applicable Terminated Product, Takeda, its Affiliates and its Sublicensees shall continue to distribute such Terminated Product, in accordance with the terms and conditions of this Agreement, in each country for which Regulatory Approval therefor has been obtained, until [***] after the effective date of termination (the "**Commercialization Wind-down Period**"); *provided* that Takeda, its Affiliates and its Sublicensees shall cease such activities, or any portion thereof, in a given country upon [***] days' notice by Denali requesting that such activities (or portion thereof) be ceased. Notwithstanding any other provision of this Agreement, during the Commercialization Wind-down Period, Takeda's and its Affiliates' and Sublicensees' rights with respect to Terminated Products shall be non-exclusive and, without limiting the foregoing, Denali shall have the right to engage one or more other distributor(s) and/or licensee(s) of the Terminated Product in all or part of the Territory. Any Terminated Product sold or disposed of by Takeda, its Affiliates or its Sublicensees in the Territory during the Commercialization Wind-down Period shall be subject to applicable payment obligations under Article 8. Unless [***], any Terminated Product sold or disposed of by Denali, its Affiliates or its Sublicensees (but not, for clarity any sales during such period by Takeda, its Affiliates, or Sublicensees) in the Territory during the Commercialization Wind-down Period shall be subject to applicable payment obligations to Takeda under Section 14.7.1. Within [***] days of expiration of the Commercialization Wind-down Period, Takeda shall notify Denali of any quantity of Terminated Product remaining in Takeda's inventory and Denali shall have the option, upon notice to Takeda, to repurchase any such quantities of the Terminated Product from Takeda at a price equal to [***] of such quantities (to the extent [***]).

14.8.3 Supply Obligations. Upon Denali's request, to the extent that Takeda is the Manufacturing Lead for the Terminated Program prior to the termination of this Agreement, Takeda shall either (a) assign to Denali Takeda's agreement(s) with its Third Party Provider for the Terminated Biologics, Terminated Products and placebo, or alternatively, use reasonable efforts to facilitate Denali's entering into a direct supply agreement with such Third Party Provider of the Terminated Biologics, Terminated Products and placebo on comparable terms to those between Takeda and such Third Party Provider (in each case assuming Takeda is then obtaining supply of Terminated Biologics, Terminated Products or placebo from a Third Party Provider) and (b) except to the extent the applicable termination was made in accordance with Section 14.6 (Termination for a Material Safety Event), to the extent Takeda or its Affiliate is producing its own supply of the Terminated Product, Terminated Biologic or placebo, use Commercially Reasonable Efforts to [***], until the date on which Denali notifies Takeda in writing that Denali has secured an alternative manufacturer for the Terminated Biologics and/or Terminated Products, but in no event more for than [***] after the effective date of any expiration or termination of this Agreement. In the case of (b), Denali shall pay to Takeda a transfer price for the materials supplied equal to [***] for Terminated Products delivered within the first [***] after the effective date of termination, and, as the case may be, [***] for Terminated Products delivered thereafter; *provided*, *however*, in the event the applicable termination was made for Denali's breach or insolvency, the transfer price for materials supplied shall equal [***] beginning on the effective date of the termination.

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14.8.4 Cooperation. Without limiting the foregoing, each Party shall use Commercially Reasonable Efforts to [***]. If Takeda has entered into contracts that solely pertain to a Terminated Program with Third Parties (including contract manufacturers or vendors) whose services are reasonably necessary for Denali to assume responsibility for the Terminated Program, then Takeda shall, to the extent reasonably possible and requested in writing by Denali, assign all of such Third Party contracts to Denali.

14.8.5 Grant of Rights. Without limiting the foregoing, Denali shall grant to Takeda, its Affiliates or its Sublicensees (as the case may be) any licenses or rights of reference to any Denali Technology, Regulatory Approvals and Regulatory Documentation, Clinical Data, Information, Product Trademarks and Denali's Corporate Name reasonably necessary for Takeda, its Affiliates or its Sublicensees to fulfill the obligations set forth in this Section 14.8.

14.9 Remedies. Except as otherwise expressly provided herein, termination of this Agreement (either in its entirety or with respect to a Terminated Program) in accordance with the provisions hereof shall not limit remedies that may otherwise be available in law or equity.

14.10 Accrued Rights; Surviving Obligations. Termination or expiration of this Agreement (either in its entirety or with respect to one (1) or more country(ies) or other jurisdiction(s)) for any reason shall be without prejudice to any rights that shall have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration shall not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. Without limiting the foregoing, Sections [***] of this Agreement shall survive the termination or expiration of this Agreement for any reason. If this Agreement is terminated with respect to a Terminated Program but not in its entirety, then following such termination, the foregoing provisions of this Agreement shall remain in effect with respect to the Terminated Program (to the extent such provisions would survive and apply in the event this Agreement expires or is terminated in its entirety), and all provisions not surviving in accordance with the foregoing shall terminate upon termination of this Agreement with respect to the Terminated Program and be of no further force and effect (and, for purposes of clarity, all provisions of this Agreement shall remain in effect with respect to any Collaboration Program that is not the Terminated Program).

14.11 Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement are intended to be, and shall otherwise be deemed to be, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code for purposes of Section 365(n) of the United States Bankruptcy Code (the "**Bankruptcy Code**") or any analogous provisions in any other country or jurisdiction. The Parties agree that the licensee of such intellectual property under this Agreement shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code, or any analogous provisions in any other country or jurisdiction. If a bankruptcy proceeding is commenced by or against either Party under the Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the non-debtor Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any intellectual property licensed hereunder, and embodiments of such intellectual property, which, if not already in the non-debtor Party's possession, shall be delivered to the non-debtor Party within [***] Business Days of such request; *provided*, that the debtor Party is excused from its obligation to deliver such intellectual property to the extent the debtor Party continues to perform all of its obligations under this Agreement and this Agreement has not been rejected pursuant to the Bankruptcy Code or any analogous provision in any other country or jurisdiction.

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ARTICLE 15
HSR COMPLIANCE

15.1 HSR Act Compliance. Notwithstanding anything to the contrary in this Agreement, this Agreement is binding upon the Parties as of the Execution Date to the extent permitted by the HSR Act, but the provisions of Article 2–Article 9 (other than Section 9.1) shall not take effect until the Effective Date. As used herein, the "**HSR Clearance Date**" means such time as: (a) the Parties shall have complied with all applicable requirements of the HSR Act; (b) the waiting period under the HSR Act shall have expired or been terminated early; (c) no judicial or administrative proceeding opposing consummation of all or any part of this Agreement shall be pending; (d) no injunction (whether temporary, preliminary or permanent) prohibiting consummation of the transactions contemplated by this Agreement or any material portion hereof shall be in effect; and (e) no requirements or conditions shall have been formally requested or imposed by the DOJ or FTC in connection therewith that are not reasonably and mutually satisfactory to the Parties (collectively, the "**HSR Conditions**"). In the event that the HSR Conditions are not met within [***], then either Party may terminate this Agreement upon notice, in which case, notwithstanding any provisions that are stated to survive under Section 14.10, all provisions of this Agreement shall terminate and be of no force or effect whatsoever, except only that any liability of either Party for failing to comply this Section 15.1 shall survive.

15.2 HSR Filing. Both Parties shall promptly file following the Execution Date (and in any event, within [***] Business Days after the Execution Date) their respective pre-merger notification and report forms with the United States Federal Trade Commission ("**FTC**") and the United States Department of Justice ("**DOJ**") pursuant to the HSR Act, which forms shall specifically request early termination of the initial HSR Act waiting period.

15.3 Cooperation.

15.3.1 The Parties shall use diligent efforts to promptly obtain clearance required under the HSR Act for the consummation of this Agreement and the transactions contemplated hereby and shall keep each other apprised of the status of any communications with, and any inquiries or requests for additional information from, the FTC and the DOJ and shall comply promptly with any such inquiry or request; *provided*, *however*, that neither Party shall be required to consent to the divestiture, sale, license or other disposition or holding separate of any of its or its Affiliates' assets or to consent to any other structural or conduct remedy, and each Party and its Affiliates shall have no obligation to contest, administratively or in court, any ruling, order or other action of the FTC or DOJ or any Third Party respecting the transactions contemplated by this Agreement.

15.3.2 The Parties shall instruct their respective counsel to cooperate with each other and use Commercially Reasonable Efforts to [***]. In the context of this Section 15.3.2, diligent efforts and cooperation include counsel's undertaking: (i) to keep each other appropriately informed of communications received from and submitted to personnel of the

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reviewing antitrust authority; and (ii) to confer with each other regarding appropriate contacts with and response to personnel of the FTC or DOJ. Takeda shall be responsible for the HSR Act filings fees and each Party shall be responsible for the costs and expenses of its own legal and other advice in relating to the HSR Act filing.

ARTICLE 16
MISCELLANEOUS

16.1 Force Majeure. Neither Party shall be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts, or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God or acts, omissions or delays in acting by any governmental authority (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement) (such event, a "**Force Majeure Event**"). The non-performing Party shall notify the other Party of such force majeure within [***] days after such occurrence by giving written notice to the other Party stating the nature of the event, its anticipated duration, and any action being taken to avoid or minimize its effect. The suspension of performance shall be of no greater scope and no longer duration than is necessary and the non-performing Party shall use diligent efforts to remedy its inability to perform.

16.2 Export Control. This Agreement is made subject to any restrictions concerning the export of products or technical information from the United States or other countries that may be imposed on the Parties from time to time. Each Party agrees that it will not export, directly or indirectly, any technical information acquired from the other Party under this Agreement or any products using such technical information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency or other governmental entity in accordance with Applicable Law.

16.3 Acquisition, Change in Control, Assignment.

16.3.1 Without the prior written consent of the other Party, neither Party shall sell, transfer, assign, delegate (except as expressly permitted under this Agreement), pledge, or otherwise dispose of, whether voluntarily, involuntarily, by operation of law or otherwise, this Agreement or any of its rights or duties hereunder; *provided*, that (a) either Party may make such an assignment without the other Party's consent to (i) [***], (ii) [***]; or (iii) [***] and (b) Denali may [***]. With respect to an assignment to [***], the assigning Party shall [***]. Any attempted assignment or delegation in violation of this Section 16.3 shall be void and of no effect. All validly assigned and delegated rights and obligations of the Parties hereunder shall be binding upon and inure to the benefit of and be enforceable by and against the successors and permitted assigns of Denali or Takeda, as the case may be. The permitted assignee or transferee shall assume all obligations of its assignor or transferor under this Agreement. Without limiting

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the foregoing, the grant of rights set forth in this Agreement shall be binding upon any successor or permitted assignee of a Party, and the obligations of the other Party, including the payment obligations, shall run in favor of any such successor or permitted assignee of such Party's benefits under this Agreement.

16.3.2 The rights to Information, materials and intellectual property: (a) Controlled by a Third Party permitted assignee of a Party, which Information, materials and intellectual property were Controlled by such assignee immediately prior to such assignment; or (b) Controlled by an Affiliate of a Party who becomes an Affiliate through any Change in Control of or Acquisition by such Party, in each case (a) and (b) prior to such assignment or transfer, as applicable, shall be automatically excluded from the rights licensed or granted to the other Party under this Agreement, so long as such Information, materials and intellectual property are not utilized by such Third Party or Affiliate in connection with the Development, Manufacture or Commercialization of a Research Biologic, Optioned Biologic or Optioned Product that incorporates any non-public Takeda Technology or Denali Technology.

16.4 Severability. If any provision of this Agreement is held to be illegal, invalid, or unenforceable under any present or future law, and if the rights or obligations of either Party under this Agreement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Agreement shall be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part hereof, (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid, or unenforceable provision or by its severance herefrom, and (d) in lieu of such illegal, invalid, or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid, and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the Parties. To the fullest extent permitted by Applicable Law, each Party hereby waives any provision of law that would render any provision hereof illegal, invalid, or unenforceable in any respect.

16.5 Governing Law, Jurisdiction and Service.

16.5.1 Governing Law. This Agreement or the performance, enforcement, breach or termination hereof shall be interpreted, governed by and construed in accordance with the laws of the State of [***], United States, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction; *provided*, that all questions concerning (a) determination of whether Information and inventions are conceived, discovered, developed, or otherwise made by a Party for the purpose of allocating proprietary rights (including Patent, copyright or other intellectual property rights) therein, shall, for purposes of this Agreement, be made in accordance with Applicable Law in the United States and (b) the construction or effect of Patents shall be determined in accordance with the laws of the country or other jurisdiction in which the particular Patent has been filed or granted, as the case may be. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

16.5.2 Service. Each Party further agrees that service of any process, summons, notice or document by registered mail to its address set forth in Section 16.7 shall be effective service of process for any action, suit, or proceeding brought against it under this Agreement in any such court.

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16.6 Dispute Resolution. Except for disputes resolved by the procedures set forth in Section 2.3.6 or 16.10 or for which either Party has final decision-making authority as provided in Section 2.3.6, if a dispute arises between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith (a "**Dispute**"), it shall be resolved pursuant to this Section 16.6.

16.6.1 General. Any Dispute shall first be referred to the senior executive officers of the Parties, who shall confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the senior executive officers shall be conclusive and binding on the Parties. If the senior executive officers are not able to agree on the resolution of any such issue within [***] days (or such other period of time as mutually agreed by the senior executive officers) after such issue was first referred to them, then, except as otherwise set forth in Section 16.6.2 or 16.6.4, either Party may, by written notice to the other Party, elect to initiate a proceeding pursuant to the procedures set forth in Section 16.6.4 for purposes of having the matter settled.

16.6.2 Intellectual Property Disputes. In the event that a Dispute arises with respect the validity, scope, enforceability, inventorship or ownership of any Patent, Trademark or other intellectual property rights, and such Dispute cannot be resolved in accordance with Section 16.6.1, unless otherwise agreed by the Parties in writing, such Dispute shall not be submitted to an ADR proceeding in accordance with Section 16.6.4 and instead, either Party may initiate litigation in a court of competent jurisdiction, notwithstanding Section 16.5, in any country or other jurisdiction in which such rights apply.

16.6.3 Jurisdiction. Each of the Parties hereby submits to the jurisdiction [***] in any proceeding arising out of or relating to this Agreement, agrees not to commence any suit, action or proceeding relating thereto except in such court, and waives, to the fullest extent permitted by law, the right to move to dismiss or transfer any action brought in such court on the basis of any objection to personal jurisdiction, venue or inconvenient jurisdiction. Any rights to trial by jury with respect to any suit, action, proceeding or claim (whether based upon contract, tort or otherwise), directly or indirectly, arising out of or relating to this Agreement hereunder are expressly and irrevocably waived by each of the Parties.

16.6.4 Expert Arbitration. Any dispute expressly stated in this Agreement to be resolved pursuant to this Section 16.6.4 shall take place pursuant to the procedures described in Schedule 16.6.4.

16.6.5 Interim Relief. Notwithstanding anything herein to the contrary, nothing in this Section 16.6 shall preclude either Party from seeking interim or provisional relief, including a temporary restraining order, preliminary injunction or other interim equitable relief concerning a Dispute, if necessary to protect the interests of such Party. This Section 16.6.5 shall be specifically enforceable.

*** Certain information in this agreement has been omitted and filed separately with the Securities and Exchange Commission. [***] indicates that text has been omitted and is the subject of a confidential treatment request.

16.7 Notices.

16.7.1 Notice Requirements. Any notice, request, demand, waiver, consent, approval, or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be deemed given only if (a) delivered by hand, (b) sent by facsimile transmission (with complete transmission confirmed), or (c) by internationally recognized overnight delivery service that maintains records of delivery, addressed to the Parties at their respective addresses specified in Section 16.7.2 or to such other address as the Party to whom notice is to be given may have provided to the other Party in accordance with this Section 16.7.1. Such notice shall be deemed to have been given as of the date delivered by hand or transmitted by facsimile or electronic mail (with complete transmission confirmed) or on the [***] Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. Any notice delivered by facsimile or electronic mail shall be confirmed by a hard copy delivered as soon as practicable thereafter. This Section 16.7.1 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

16.7.2 Address for Notice.

If to Takeda, to:

Takeda Pharmaceutical Company Limited
1-1, Doshomachi 4-chome
Chuo-ku, Osaka 540-8645
Japan
Attention: Legal Department
Facsimile:

with a copy to:

Takeda Pharmaceuticals
1 Takeda Parkway
Deerfield, IL 60015
Attention: General Counsel
Facsimile:

with a further copy (which shall not constitute notice) to:

Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304-1130
Attention:
E-mail:

If to Denali, to:

Denali Therapeutics, Inc.
151 Oyster Point Blvd
South San Francisco, CA 94080
Attention:
Email:

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with a copy (which shall not constitute notice) to:

Wilson Sonsini Goodrich and Rosati P.C.
12235 El Camino Real, Suite 200
San Diego, California 92130
Attention:
Facsimile:

16.8 Entire Agreement; Amendments. This Agreement, together with the Schedules attached hereto, and the Stock Purchase Agreement, sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and all prior agreements, understandings, promises, and representations, whether written or oral, with respect thereto are superseded hereby (including that certain Confidentiality Agreement between the Parties or their respective Affiliates dated [***]). Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement or the Stock Purchase Agreement. No amendment, modification, release, or discharge shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

16.9 English Language. This Agreement shall be written and executed in, and all other communications under or in connection with this Agreement shall be in, the English language. Any translation into any other language shall not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version shall control.

16.10 Equitable Relief. Each Party acknowledges and agrees that the restrictions set forth in Section 7.8, Article 9 and Article 11 are reasonable and necessary to protect the legitimate interests of the other Party and that such other Party would not have entered into this Agreement in the absence of such restrictions, and that any breach or threatened breach of any provision of such Section or Articles may result in irreparable injury to such other Party for which there may be no adequate remedy at law. In the event of a breach or threatened breach of any provision of such Section or Articles, the non-breaching Party shall be authorized and entitled to seek from any court of competent jurisdiction injunctive relief, whether preliminary or permanent and specific performance. Nothing in this Section 16.10 is intended, or should be construed, to limit either Party's right to equitable relief or any other remedy for a breach of any other provision of this Agreement.

16.11 Waiver and Non-Exclusion of Remedies. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

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16.12 No Benefit to Third Parties. Except as provided in Article 13, covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other Persons.

16.13 Further Assurance. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof, or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

16.14 Relationship of the Parties. It is expressly agreed that Denali, on the one hand, and Takeda, on the other hand, shall be independent contractors and that the relationship between the Parties shall not constitute a partnership, joint venture, or agency, including for all tax purposes; *provided, however,* [***] (and any disputes related thereto shall be resolved pursuant to Section 16.6.4 of this Agreement). Neither Denali, on the one hand, nor Takeda, on the other hand, shall have the authority to make any statements, representations, or commitments of any kind, or to take any action, which shall be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party.

16.15 Performance by Affiliates And Sublicensees. Each Party may use one (1) or more of its Affiliates and/or (sub)licensees to exercise its rights and/or perform its obligations and duties hereunder (including by licensing rights hereunder where such rights are held in the name of any such Affiliate). In such event: (a) [***]; (b) [***], and (d) [***].

16.16 Counterparts; Facsimile Execution. 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 (1) and the same instrument. This Agreement may be executed by facsimile or electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were original signatures.

16.17 References. Unless otherwise specified, (a) references in this Agreement to any Article, Section or Schedule shall mean references to such Article, Section or Schedule of this Agreement, (b) references in any Section to any clause are references to such clause of such Section, and (c) references to any agreement, instrument, or other document in this Agreement refer to such agreement, instrument, or other document as originally executed or, if subsequently amended, replaced, or supplemented from time to time, as so amended, replaced, or supplemented and in effect at the relevant time of reference thereto.

16.18 Construction. Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders and the word “or” is used in the inclusive sense (and/or). Whenever this Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The captions of this Agreement are for convenience of reference only and in no way

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define, describe, extend, or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The term “including,” “include,” or “includes” as used herein shall mean “including, but not limited to,” and shall not limit the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provisions.

[*SIGNATURE PAGE FOLLOWS.****]***

THIS AGREEMENT IS EXECUTED by the authorized representatives of the Parties as of the Execution Date.

Denali Therapeutics Inc.

By: /s/ Ryan J. Watts
Name: Ryan J. Watts
Title: CEO

Takeda Pharmaceutical Company Limited

By: /s/ Fumihiko Sato
Name: Fumihiko Sato
Title: Head of Portfolio Strategic Relations

Confidential

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Schedule 11.4

Press Release
[ATTACHED]

Confidential

Takeda and Denali Therapeutics Collaborate to Develop and Commercialize Therapies for Neurodegenerative Diseases

Collaboration includes three named programs for the treatment of Alzheimer's disease and other neurodegenerative diseases, utilizing Denali's Antibody Transport Vehicle (ATV) technology to enhance blood-brain barrier (BBB) penetration.

Osaka, Japan and South San Francisco, CA, January 5, 2018 – Takeda Pharmaceutical Company Limited (TSE: 4502) and Denali Therapeutics (NASDAQ: DNLI) today announced that they have entered into a strategic option and collaboration agreement to develop and commercialize up to three specified therapeutic product candidates for neurodegenerative diseases. Each program is directed to a genetically validated target for neurodegenerative disorders, including Alzheimer's disease and other indications, and incorporates Denali's ATV platform for increased exposure of biotherapeutic products in the brain.

"This partnership further exemplifies Takeda's continued commitment to developing genetically validated therapies for neurodegenerative diseases through an enhanced portfolio comprised of new modalities," said Emiliangelo Ratti, Head of the Neuroscience Therapy Area at Takeda. "We are excited to partner with the Denali team, whose innovative technology is uniquely poised to deliver the next generation of antibody therapeutics for patients."

"We are impressed with Takeda's commitment to developing treatments for difficult to treat neurodegenerative diseases and look forward to partnering with them to bring medicines to patients," said Denali CEO Ryan Watts, Ph.D. "Takeda has a great track record of partnering with biotech firms in addition to unique development expertise and a strong global commercial presence."

Terms of Collaboration

Under the terms of the agreement, Takeda will make an initial payment to Denali of $150 million through a combination of cash upfront payments and the purchase of Denali equity. In addition, Denali is eligible to receive development and commercial milestone payments, including $90 million in preclinical milestones and opt-in payments.

Denali will be responsible for all development activities and costs prior to IND filing for each of the three programs. Takeda has the option to co-develop and co-commercialize each of the three programs. If Takeda exercises the option, the parties will then jointly conduct clinical development and share all costs equally. Denali will lead early clinical development activities and Takeda will lead late stage clinical development activities. Takeda and Denali will jointly commercialize products in the United States and China, and Takeda will have exclusive commercialization rights in all other markets. The parties will share global profits equally. The agreement will become effective when the requirements of the Hart–Scott–Rodino Antitrust Improvements Act of 1976 have been satisfied.

About Takeda Pharmaceutical Company

Takeda Pharmaceutical Company Limited (TSE: 4502) is a global, research and development-driven pharmaceutical company committed to bringing better health and a brighter future to patients by translating science into life-changing medicines. Takeda focuses its R&D efforts on oncology, gastroenterology and neuroscience therapeutic areas plus vaccines. Takeda conducts R&D both internally and with partners to stay at the leading edge of innovation. New innovative products, especially in oncology and gastroenterology, as well as Takeda's presence in emerging markets, are currently fueling the growth of Takeda. Approximately 30,000 Takeda employees are committed to improving quality of life for patients, working with Takeda's partners in health care in more than 70 countries. For more information, visit https://www.takeda.com/newsroom/.

Additional information about Takeda is available through its corporate website, www.takeda.com, and additional information about Takeda Oncology, the brand for the global oncology business unit of Takeda Pharmaceutical Company Limited, is available through its website, www.takedaoncology.com.

About Denali Therapeutics

Denali is a biopharmaceutical company developing a broad portfolio of therapeutic candidates for neurodegenerative diseases. Denali is based in South San Francisco. For additional information, please visit www.denalitherapeutics.com.

Cautionary Note Regarding Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, but are not limited to, the potential benefits of the collaboration; plans to conduct clinical development activities and commercialize products; the expectation as to when the agreement will become effective; and other information relating to the transaction between Takeda and Denali. Actual results are subject to risks and uncertainties and may differ materially from those indicated by these forward-looking statements as a result of these risks and uncertainties, including but not limited to: the risk that the agreement may not become effective in a timely manner or at all; risks related to obtaining the requisite regulatory approvals; the risk of the occurrence of any event, change or other circumstance that could give rise to the termination of the agreement (including without limitation the failure to timely obtain requisite regulatory approvals); risks related to the effect of the announcement of the transaction on Denali's business relationships, operating results and business generally; and other risks, including those described in Denali's Prospectus filed with the SEC on December 8, 2017. The forward-looking statements in this press release are based on information available to Denali as of the date hereof. Denali and Takeda disclaim any obligation to update any forward-looking statements, except as required by law.

# # #

Takeda Contact:
Kelly Schlemm, +1-617-551-8865
kelly.schlemm@takeda.com

Denali Therapeutics Contact:
Morgan Warners, +1-202-295-0124
mwarners@gpg.com

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Exhibit 10.17

COMMON STOCK PURCHASE AGREEMENT

TABLE OF CONTENTS

EXHIBITS

COMMON STOCK PURCHASE AGREEMENT

THIS COMMON STOCK PURCHASE AGREEMENT (this "**Agreement**"), is made as of January 3, 2018 by and among Denali Therapeutics Inc., a Delaware corporation (the "**Company**"), and Takeda Pharmaceutical Company Limited, a corporation organized under the laws of Japan (the "**Investor**").

The parties hereby agree as follows:

1. Defined Terms Used in this Agreement. In addition to the terms defined above, the following terms used in this Agreement shall be construed to have the meanings set forth or referenced below.

(a) "**Accredited Investor**" means an "accredited investor" within the meaning of SEC Rule 501 of Regulation D, as presently in effect.

(b) "**Affiliate**" means, with respect to a Person, any other Person that, directly or indirectly, through one (1) or more intermediaries, controls, is controlled by or is under common control with such Person. For purposes of this definition, "control" and, with correlative meanings, the terms "controlled by" and "under common control with" means (a) the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract relating to voting rights or corporate governance, or otherwise; or (b) the ownership, directly or indirectly, of more than fifty percent (50%) of the voting securities or other ownership interest of a Person (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity). The parties acknowledge that in the case of certain entities organized under the laws of certain countries outside of the United States, the maximum percentage ownership permitted by law for a foreign investor may be less than fifty percent (50%), and that, in such case, such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management or policies of such entity.

(c) "**Board**" means the Board of Directors of the Company.

(d) "**Closing**" has the meaning set forth in Section 2.2(a).

(e) "**Code**" means the Internal Revenue Code of 1986, as amended.

(f) "**Common Stock**" has the meaning set forth in Section 3.2(a)(i).

(g) "**Company SEC Reports**" has the meaning set forth in Section 3.10(a).

(h) "**Exchange Act**" means the Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(i) "**Financial Statements**" has the meaning set forth in Section 3.10.

(j) "**GAAP**" means U.S. generally accepted accounting principles.

(k) "**Knowledge,**" including the phrase "to the Company's knowledge," shall mean the actual knowledge (after reasonable inquiry of their direct reports) of the President and Chief Executive Officer, Chief Operating Officer, Chief Financial Officer and Chief Medical Officer of the Company.

(l) "**Market Standoff Agreement**" means agreement dated as of even date herewith, in the form of Exhibit A attached to this Agreement.

(m) "**Material Adverse Effect**" means a material adverse effect on the business, assets (including intangible assets), liabilities, financial condition, property, or results of operations of the Company.

(n) "**Person**" means any individual, corporation, partnership, trust, limited liability company, association or other entity.

(o) "**Preferred Stock**" has the meaning set forth in Section 3.2(a)(ii).

(p) "**Purchase Price**" has the meaning set forth in Section 2.1.

(q) "**Restated Certificate**" means the current Amended and Restated Certificate of Incorporation of the Company.

(r) "**SEC**" means the U.S. Securities and Exchange Commission.

(s) "**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

(t) "**Shares**" has the meaning set forth in Section 2.1.

(u) "**Standstill and Stock Restriction Agreement**" means the agreement between the Company and the Investor in the form of Exhibit B attached to this Agreement.

(v) "**Transaction Agreements**" means this Agreement and the Standstill and Stock Restriction Agreement.

2. Purchase and Sale of Common Stock.

2.1 Sale and Issuance of Common Stock. Subject to the terms and conditions of this Agreement, Investor agrees to purchase at the Closing and the Company agrees to sell and issue to Investor at the Closing 4,214,559 shares of Common Stock (the "**Shares**") for an aggregate purchase price of $110,000,000 (the "**Purchase Price**"), payable by wire transfer to a bank account designated by the Company. This Agreement is being entered into pursuant to Article 8.1.1 of that certain Option and Collaboration Agreement, dated on the date hereof, between the Company and Investor (the "**Option and Collaboration Agreement**"), and Investor acknowledges and agrees that, by entering into this Agreement, the Company has satisfied in full its obligations under Article 8.1.1 of the Option and Collaboration Agreement.

2.2 Closing; Delivery; Adjustments.

(a) The purchase and sale of the Shares shall take place remotely via the exchange of documents and signatures on the tenth (10th) Business Day (as such term is defined in the Option and Collaboration Agreement) following the "**Effective Date**" (as such term is defined in the Option and Collaboration Agreement) or at such other time and place as the Company and the Investor mutually agree upon, orally or in writing (which time and place are designated as the "**Closing**"). At the Closing, the Company shall sell, and the Investor shall purchase the Shares.

(b) At the Closing, the Company shall instruct its transfer agent to deliver confirmation of book-entry issuance of the Shares being purchased by Investor at such Closing against payment of the Purchase Price therefor.

(c) All numbers of shares and dollar amounts set forth in this Agreement are subject to appropriate adjustment in the event of any stock dividend, stock split, combination or similar recapitalization affecting such shares.

3. Representations and Warranties of the Company. The Company hereby represents and warrants to the Investor that the following representations are true and correct as of the date hereof except as otherwise indicated.

3.1 Organization, Good Standing, Corporate Power and Qualification. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to carry on its business as presently conducted and as proposed to be conducted. The Company is duly qualified to transact business and is in good standing in each jurisdiction in which the failure to so qualify would have a Material Adverse Effect.

3.2 Company Capitalization.

(a) The authorized and issued capital of the Company consists, as of the date hereof, of:

(i) 400,000,000 shares of Common Stock, $0.01 par value per share (the "**Common Stock**"), 90,157,709 shares of which are issued and outstanding. All of the outstanding shares of Common Stock have been duly authorized, are fully paid and nonassessable and were issued in compliance with all applicable federal and state securities laws.

(ii) 40,000,000 shares of Preferred Stock, $0.01 par value per share (the "**Preferred Stock**"), none of which are issued and outstanding.

3.3 Subsidiaries. The Company does not currently own or control, directly or indirectly, any interest in any other corporation, partnership, trust, joint venture, limited liability company, association, or other business entity. The Company is not a participant in any joint venture, partnership or similar arrangement.

3.4 Authorization. All corporate action required to be taken by the Company's Board and stockholders in order to authorize the Company to enter into the Transaction Agreements, and to issue the Shares at the Closing, has been taken or will be taken prior to the Closing. All action on the part of the officers of the Company necessary for the execution and delivery of the Transaction Agreements, the performance of all obligations of the Company under the Transaction Agreements to be performed as of the Closing, and the issuance and delivery of the Shares has been taken or will be taken prior to the Closing. The Transaction Agreements, when executed and delivered by the Company, shall constitute valid and legally binding obligations of the Company, enforceable against the Company in accordance with their respective terms except (a) as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, or other laws of general application relating to or affecting the enforcement of creditors' rights generally, or (b) as limited by laws relating to the availability of specific performance, injunctive relief, or other equitable remedies.

3.5 Valid Issuance of Shares. The Shares, when issued, sold and delivered in accordance with the terms and for the consideration set forth in this Agreement, will be validly issued, fully paid and nonassessable and free of restrictions on transfer other than restrictions on transfer under the Transaction Agreements, applicable state and federal securities laws and liens or encumbrances created by or imposed by any Investor. Assuming the accuracy of the representations of the Investor in Section 4 of this Agreement and subject to Section 3.6 below, the Shares will be issued in compliance with all applicable federal and state securities laws.

3.6 Governmental Consents and Filings. Assuming the accuracy of the representations made by the Investor in Section 4 of this Agreement, no consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any federal, state or local governmental authority is required on the part of the Company in connection with the consummation of the transactions contemplated by this Agreement, except for filings pursuant to applicable federal or state securities laws, which have been made or will be made in a timely manner, and compliance with the HSR Act (as such term is defined in the Option and Collaboration Agreement).

3.7 Litigation There is no claim, action, suit, proceeding, arbitration, complaint, charge or, to the Company's knowledge, investigation pending or, to the Company's knowledge, currently threatened in writing against the Company or any officer or director of the Company that questions the validity of the Transaction Agreements or the right of the Company to enter into them, or to consummate the transactions contemplated by the Transaction Agreements or would reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

3.8 Compliance with Other Instruments. The Company is not in violation or default (a) of any provisions of its Restated Certificate or Bylaws, (b) of any instrument, judgment, order, writ or decree, (c) under any material agreement, note, indenture, deed of trust, license, lease agreement or mortgage where such violation or default would have a Material Adverse Effect, or (d) to its knowledge, of any provision of federal or state statute, rule or regulation applicable to the Company, the violation of which would have a Material Adverse Effect. The execution, delivery and performance of the Transaction Agreements and the consummation of the transactions contemplated by the Transaction Agreements will not result in

any such violation or be in conflict with or constitute, with or without the passage of time and giving of notice, either (x) a default under any such provision, instrument, judgment, order, writ, decree, material agreement, note, indenture, deed of trust, license, lease agreement or mortgage; or (y) an event which results in the creation of any lien, charge or encumbrance upon any assets of the Company or the suspension, revocation, forfeiture, or nonrenewal of any material permit or license applicable to the Company.

3.9 Property. The property and assets that the Company owns are free and clear of all mortgages, deeds of trust, liens, loans and encumbrances, except for statutory liens for the payment of current taxes that are not yet delinquent and encumbrances and liens that arise in the ordinary course of business and do not materially impair the Company's ownership or use of such property or assets. With respect to the property and assets it leases, the Company is in compliance with such leases and, to its knowledge, holds a valid leasehold interest free of any liens, claims or encumbrances other than those of the lessors of such property or assets. The Company does not own any real property.

3.10 SEC Filings; Financial Statements.

(a) The Company's Common Stock is registered pursuant to Section 12(b) or 12(g) of the Exchange Act. The Company has timely and properly filed all forms, schedules, reports, prospectuses, proxy statements and documents required to be filed by the Company with the SEC (the "**Company SEC Reports**"). The Company's Common Stock is currently listed or quoted on the Nasdaq Global Select Market. The Company is not in violation of the listing requirements of the Nasdaq Stock Market LLC and has no knowledge of any facts that would reasonably lead to delisting or suspension of its common stock from the Nasdaq Stock Market LLC in the foreseeable future. The Company SEC Reports (i) at the time they were filed (or if amended or superseded by a filing prior to the date of this Agreement, then on the date of such filing) complied in all material respects with the requirements of the Securities Act or the Exchange Act, as the case may be, and the rules and regulations promulgated thereunder, and (ii) did not at the time they were filed (or if amended or superseded by a filing prior to the date of this Agreement, then on the date of such filing) contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading. The Company makes no representation or warranty whatsoever concerning the Company SEC Reports as of any time other than the time they were filed, amended or superseded.

(b) Each of the consolidated financial statements (including, in each case, any related notes thereto) (the "**Financial Statements**") contained in the Company SEC Reports has been prepared in accordance with GAAP applied on a consistent basis throughout the period involved (except as may be indicated in the notes thereto) and complied in all material respects with the rules and regulations of the SEC. Each of the Financial Statements fairly presents in all material respects the consolidated financial position of the Company at the respective dates thereof and the consolidated results of its operations and cash flows for the periods indicated, except that the unaudited interim financial statements were or are subject to normal and recurring year-end adjustments which have not had or are not expected to have, individually or in the aggregate, a Material Adverse Effect.

3.11 Changes. Except as otherwise disclosed in the Company SEC Reports, since September 30, 2017, there has not been any change in the assets, liabilities, financial condition or operating results of the Company from that reflected in the Financial Statements, except changes in the ordinary course of business that have not caused, in the aggregate, a Material Adverse Effect.

3.12 Option and Collaboration Agreement. The representations and warranties of the Company contained in Article 12 of the Option and Collaboration Agreement are true and correct.

4. Representations and Warranties of the Investor. The Investor hereby represents and warrants to the Company that:

4.1 Authorization. The Investor has full power and authority to enter into the Transaction Agreements. The Transaction Agreements, when executed and delivered by the Investor, will constitute valid and legally binding obligations of Investor, enforceable in accordance with their terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance and any other laws of general application affecting enforcement of creditors' rights generally, and as limited by laws relating to the availability of specific performance, injunctive relief or other equitable remedies.

4.2 Purchase Entirely for Own Account. The Company is entering into this Agreement with the Investor in reliance upon Investor's representation to the Company, which by Investor's execution of this Agreement, Investor hereby confirms that the Shares to be acquired by such Investor will be acquired for investment for Investor's own account, not as a nominee or agent, and not with a view to the resale or distribution of any part thereof, and that Investor has no present intention of selling, granting any participation in, or otherwise distributing the same. By executing this Agreement, Investor further represents that Investor does not presently have any contract, undertaking, agreement or arrangement with any Person to sell, transfer or grant participations to such Person or to any third Person, with respect to any of the Shares. The Investor has not been formed for the specific purpose of acquiring the Shares.

4.3 Disclosure of Information. The Investor has had access to all of the Company's SEC filings that Investor has requested. The Investor has had an opportunity to discuss the Company's business, management, financial affairs and the terms and conditions of the offering of the Shares with the Company's management. The foregoing, however, does not limit or modify the representations and warranties of the Company in Section 3 of this Agreement, or the right of Investor to rely thereon.

4.4 Restricted Securities. The Investor understands that, except as set forth in Section 4 of the Standstill and Stock Restriction Agreement, the Shares have not been, and will not be, registered under the Securities Act, by reason of a specific exemption from the registration provisions of the Securities Act which depends upon, among other things, the bona fide nature of the investment intent and the accuracy of the Investor's representations as expressed herein. The Investor understands that the Shares are "restricted securities" under applicable U.S. federal and state securities laws and that, pursuant to these laws, the Investor must hold the Shares indefinitely unless they are registered with the SEC and qualified by state

authorities, or an exemption from such registration and qualification requirements is available. The Investor acknowledges that, except as set forth in Section 4 of the Standstill and Stock Restriction Agreement, the Company does not have any obligation to register or qualify the Shares for resale. The Investor further acknowledges that if an exemption from registration or qualification is available, it may be conditioned on various requirements including, but not limited to, the time and manner of sale, the holding period for the Shares, and on requirements relating to the Company which, except as set forth in Section 4 of the Standstill and Stock Restriction Agreement, are outside of Investor's control, and which the Company is not under an obligation, and may not be able, to satisfy.

4.5 Legends.

(a) The Investor understands that the Shares may bear the legend set forth in Section 6(b), any legend set forth in, or required by, the other Transaction Agreement, and any legend required by the securities laws of any state to the extent such laws are applicable to the Shares. The Shares, when issued, shall not bear the restrictive legends set forth in Section 6(b) or Section 4.11(d): (i) following a sale of such Shares pursuant to a registration statement covering the resale of such Shares, while such registration statement is effective under the Securities Act, (ii) following any sale of such Shares pursuant to Rule 144 promulgated under the Securities Act ("**Rule 144**"), (iii) if such Shares are eligible for sale under Rule 144, without the requirement for the Company to be in compliance with the current public information required under Rule 144 as to such Shares and without volume or manner-of-sale restrictions or (iv) if such legend is not required under applicable requirements of the Securities Act (including judicial interpretations and pronouncements issued by the staff of the Commission). The Company agrees that at such time as the restrictive legends set forth in Section 6(b) and Section 4.11(d) are no longer required, the Company will (x) no later than five (5) Business Days following the delivery by the Investor to the Company or the Company's transfer agent of a certificate representing Shares issued with such restrictive legend, deliver or cause to be delivered to the Investor a certificate representing such Shares that is free from such restrictive legend, and (y), in the event that such shares are uncertificated, no later than five (5) Business Days following the delivery of a written request by the Investor to the Company to remove such restrictive legend, remove, or cause to be removed, any such restrictive legend in the Company's stock records.

4.6 Accredited Investor. The Investor is an Accredited Investor.

4.7 Foreign Investor. If the Investor is not a United States person (as defined by Section 7701(a)(30) of the Code), Investor hereby represents that it has satisfied itself as to the full observance of the laws of its jurisdiction in connection with any invitation to subscribe for the Shares or any use of this Agreement, including (a) the legal requirements within its jurisdiction for the purchase of the Shares, (b) any foreign exchange restrictions applicable to such purchase, (c) any governmental or other consents that may need to be obtained, and (d) the income tax and other tax consequences, if any, that may be relevant to the purchase, holding, redemption, sale, or transfer of the Shares. The Investor's subscription and payment for and continued beneficial ownership of the Shares will not violate any applicable securities or other laws of Investor's jurisdiction.

4.8 No General Solicitation. Neither the Investor, nor any of its officers, directors, employees, agents, stockholders or partners has either directly or indirectly, including, through a broker or finder (a) engaged in any general solicitation, or (b) published any advertisement in connection with the offer and sale of the Shares.

4.9 Exculpation. The Investor acknowledges that it is not relying upon any Person, other than the Company and its officers and directors, in making its investment or decision to invest in the Company.

4.10 Residence. The office or offices of the Investor in which its principal place of business is identified in the address or addresses of the Investor set forth on its signature page hereto.

4.11 Non-U.S. Investors. If Investor is not a U.S. person (as defined in Securities Act Rule 902(k)), it also represents and warrants as follows: Investor is not a U.S. person and is not acquiring the Shares for the account or benefit of any U.S. person.

(b) Investor understands and acknowledges that the Shares have not been registered under the Securities Act and are being offered and transferred in reliance upon the exemptions provided in Regulation S of the Securities Act and the rules and regulations adopted thereunder. Accordingly, the Shares may not be offered or sold in the U.S. or to U.S. persons unless the securities are registered under the Securities Act, or an exemption for the regulation requirements is available. Furthermore, hedging transactions involving the Shares may not be conducted unless in compliance with the Securities Act.

(c) Investor will not offer or sell the Shares to a U.S. person or to for the account or benefit of a U.S. person prior to the expiration of the one-year period after the date on which the Investor purchased such shares.

(d) Investor further acknowledges and agrees that the Shares acquired by such Investor hereunder may bear a legend in substantially the following form:

> "The shares represented by this certificate have not been registered under the Securities Act of 1933, as amended (the "Securities Act"), and may not be offered, sold, pledged or otherwise transferred (nor may the holder otherwise hedge its exposure with respect to the shares) except (a)(1) in an offshore transaction complying with Rule 903 or Rule 904 of Regulation S under the Securities Act, (2) if they have been registered under the Securities Act or (3) if the Corporation has been furnished with an opinion of legal counsel, reasonably satisfactory to the Corporation, to the effect that such sale or transfer is exempt from the registration requirements of the Securities Act, and (b) in accordance with all applicable securities laws of the United States."

(e) Investor acknowledges and agrees that, notwithstanding anything in this Agreement to the contrary, the Company shall, and shall instruct its transfer agent to, refuse to register any transfer of Shares that is not made in accordance with the provisions of Regulation S, pursuant to registration under Securities Act or pursuant to an available exemption from registration required under the Securities Act.

5. Market Stand-off Agreement. Investor 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 initial public offering (the "**IPO**") or any other equity securities under the Securities Act on a registration statement on Form S-1 or Form S-3 filed within eighteen (18) months after the Closing, and ending on (x) one hundred eighty (180) days in the case of the IPO, or (y) in the case of a registration other than the IPO, the date specified by the Company and the managing underwriter, such period not to exceed ninety (90) days, or such other period in each case as may be requested by the Company or an underwriter to accommodate regulatory restrictions, (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 underwriters in connection with such registration are intended third-party beneficiaries of this Section 5 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto. Investor further agrees to execute such agreements as may be reasonably requested by the underwriters in connection with such registration that are consistent with this Section 5 or that are necessary to give further effect thereto.

6. Restrictions on Transfer.

(a) The Shares 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. Investor will cause any proposed purchaser, pledgee, or transferee of the Shares 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 Shares and any other securities issued in respect of such Shares, upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Section 6(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.

Investor consents to the Company making a notation in its records and giving instructions to any transfer agent of the Company's securities in order to implement the restrictions on transfer set forth in this Section 6.

(c) Before any proposed sale, pledge, or transfer of any Shares, unless there is in effect a registration statement under the Securities Act covering the proposed transaction, Investor shall give oral notice to the Company of its intention to effect such sale, pledge, or transfer (which notice shall not be required following the expiration or earlier termination of the Option and Collaboration Agreement) and, if reasonably requested by the Company, cause to be delivered at Investor's expense 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 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 securities may be effected without registration under the Securities Act, whereupon Investor shall be entitled to sell, pledge, or transfer such securities in accordance with the terms of the notice given by Investor to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with Rule 144; or (y) in any transaction in which such Holder distributes 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 Agreement, including Section 5 and Section 6. Each certificate, instrument, or book entry representing the Shares transferred as above provided shall be notated with, except if such transfer is made pursuant to Rule 144, the appropriate restrictive legend set forth in Section 6(b), except that such certificate instrument, or book entry shall not be notated with such restrictive legend if, in the opinion of counsel for Investor and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act

(d) Notwithstanding anything herein to the contrary, any transfer of Shares shall be subject to the Standstill and Stock Restriction Agreement.

7. Conditions to the Investor's Obligations. The obligation of Investor to purchase Shares at the Closing is subject to the fulfillment, on or before the Closing, of each of the conditions set forth below.

7.1 Representations and Warranties. The representations and warranties of the Company contained in Section 3 hereof shall have been true and correct in all respects as of the date hereof.

7.2 Performance. The Company shall have performed and complied, in all material respects, with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by the Company on or before such Closing.

7.3 Option and Collaboration Agreement. The Company shall have executed the Option and Collaboration Agreement and the Effective Date of the Option and Collaboration Agreement shall have occurred.

7.4 Standstill and Stock Restriction Agreement. The Company shall have executed and delivered the Standstill and Stock Restriction Agreement.

7.5 Proceedings and Documents. All corporate and other proceedings in connection with the transactions contemplated at the Closing and all documents incident thereto shall be reasonably satisfactory in form and substance to the Investor, and Investor (or its counsel) shall have received all such counterpart original and certified or other copies of such documents as reasonably requested.

7.6 Qualifications. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement shall be obtained and effective as of the Closing.

7.7 Compliance Certificate. The President of the Company shall deliver to Investor a certificate certifying that the conditions specified in Section 7.1 and Section 7.2 with respect to the Company have been fulfilled.

7.8 Secretary's Certificate. The Secretary of the company shall deliver to Investor a certificate certifying as to (a) the Company's certificate of incorporation and bylaws, (b) the resolutions of the Board approving this Agreement and the transactions contemplated hereby, and (c) good standing certificates with respect to the Company from the applicable authority(ies) in Delaware and any other jurisdiction in which the Company is qualified to do business, dated within three (3) Business Days of the closing.

7.9 Legal Opinion. Investor shall have received from Wilson Sonsini Goodrich and Rosati P.C., counsel for the Company, an opinion, dated as of the Closing, in a form reasonably satisfactory to the Investor.

8. Conditions of the Company's Obligations at Closing. The obligations of the Company to sell Shares to the Investor at the Closing are subject to the fulfillment, on or before the Closing, of each of the following conditions, unless otherwise waived:

8.1 Representations and Warranties. The representations and warranties of the Investor contained in Section 4 shall be true and correct in all respects as of the Closing.

8.2 Performance. The Investor shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by them on or before such Closing.

8.3 Compliance Certificate. An authorized officer of Investor shall deliver to the Company a certificate certifying that the conditions specified in Section 8.1 and Section 8.2 with respect to the Investor have been fulfilled.

8.4 Qualifications. All authorizations, approvals or permits, if any, of any governmental authority or regulatory body of the United States or of any state that are required in connection with the lawful issuance and sale of the Shares pursuant to this Agreement shall be obtained and effective as of the Closing.

8.5 Market Standoff Agreement. The Investor shall have executed and delivered the Market Standoff Agreement.

8.6 Standstill and Stock Restriction Agreement. The Investor shall have executed and delivered the Standstill and Stock Restriction Agreement.

9. Miscellaneous.

9.1 Successors and Assigns. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and assigns 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 assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

9.2 Governing Law. This Agreement shall be governed by the internal law of the State of Delaware without regard to principles of conflicts of law.

9.3 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 (including .pdf or any electronic signature) 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.

9.4 Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

9.5 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 (a) personal delivery to the party to be notified, (b) when sent, if sent by electronic mail or facsimile during normal business hours of the recipient, and if not sent during normal business hours, then on the recipient's next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) business day after deposit with a nationally recognized overnight courier, freight prepaid, specifying next business day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their address as set forth on the signature page hereto, or to such e-mail address, facsimile number or address as subsequently modified by written notice given in accordance with this Section 9.5. If notice is given to the Company, a copy shall also be

sent to Wilson Sonsini Goodrich and Rosati, P.C., 650 Page Mill Road, Palo Alto, CA 94304, Attn: Tony Jeffries, Esq., and if notice is given to the Investor, a copy shall also be given to (i) Millennium Pharmaceuticals, Inc., 300 Massachusetts Ave, Cambridge, MA 02139, Attn: Head of Global R&D Finance; and (ii) Cooley LLP, 3175 Hanover Street, Palo Alto, CA 94304, Attn: Lila Hope, Esq.

9.6 No Finder's Fees. Each party represents that it neither is nor will be obligated for any finder's fee or commission in connection with this transaction. The Investor agrees to indemnify and to hold harmless the Company from any liability for any commission or compensation in the nature of a finder's or broker's fee arising out of this transaction (and the costs and expenses of defending against such liability or asserted liability) for which the Investor or any of its officers, employees or representatives is responsible. The Company agrees to indemnify and hold harmless the Investor from any liability for any commission or compensation in the nature of a finder's or broker's fee arising out of this transaction (and the costs and expenses of defending against such liability or asserted liability) for which the Company or any of its officers, employees or representatives is responsible.

9.7 Amendments and Waivers. Any term of this Agreement may be amended, terminated or waived only with the written consent of the Company and the Investor. Any amendment or waiver effected in accordance with this Section 9.7 shall be binding upon the Investor and each transferee of the Shares, each future holder of all such securities, and the Company.

9.8 Severability. The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

9.9 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 non-breaching or non-defaulting party nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in 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. Any waiver, permit, consent or approval of any kind or character on the part of any party of any breach or default under this Agreement, or any waiver on the part of any party of any provisions or conditions of this Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

9.10 Entire Agreement. This Agreement (including the Exhibits hereto), the Option and Collaboration Agreement, and the other Transaction Agreements, constitute the full and entire understanding and agreement between 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 are expressly canceled.

9.11 Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of the state 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 the state 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 AGREEMENT, 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.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Common Stock Purchase Agreement as of the date first written above.

COMPANY:
DENALI THERAPEUTICS INC.

By: /s/ Ryan Watts, Ph.D.
Name: Ryan Watts, Ph.D.
Title: President and CEO

151 Oyster Point Boulevard
South San Francisco, CA 94080

IN WITNESS WHEREOF, the parties have executed this Common Stock Purchase Agreement as of the date first written above.

INVESTOR:
TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: /s/ Fumihiko Sato
Name: Fumihiko Sato
Title: Head of Portfolio Strategic Relations

Address:
1-1, Doshomachi
4-chome, Chuo-ku, Osaka, Japan

EXHIBIT A

Form of Market Standoff Agreement

Denali Therapeutics Inc.

Lock-Up Agreement

[insert date]

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

c/o Goldman Sachs & Co. LLC
200 West Street
New York, NY 10282

c/o Morgan Stanley & Co. LLC
1585 Broadway
New York, NY 10036

c/o J.P. Morgan Securities LLC
383 Madison Avenue
New York, NY 10179

Re: Denali Therapeutics Inc. - Lock-Up Agreement

Ladies and Gentlemen:

The undersigned understands that you, as representatives (the "Representatives"), propose to enter into an Underwriting Agreement on behalf of the several Underwriters named in Schedule I to such agreement (collectively, the "Underwriters"), with Denali Therapeutics Inc., a Delaware corporation (the "Company"), providing for a public offering (the "Public Offering") of shares of the Common Stock of the Company, par value $0.01 per share, (the "Shares") pursuant to a Registration Statement on Form S-1 (the "Registration Statement") to be filed with the Securities and Exchange Commission (the "SEC").

In consideration of the agreement by the Underwriters to offer and sell the Shares, and of other good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, the undersigned agrees that, during the period beginning from the date of this Lock-Up Agreement and continuing to and including the date 180 days after the date set forth on the final prospectus (the "Prospectus") used to sell the Shares (the "Public Offering Date") pursuant to the Underwriting Agreement (the "Lock-Up Period"), the undersigned will not offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of ("Transfer") any shares of Common Stock of the Company, or any options or warrants to purchase any shares of Common Stock of the Company, or any securities convertible into, exchangeable for or that represent the right to receive shares of Common Stock of the Company (collectively, the "Equity Securities"), whether now owned or hereinafter acquired, owned directly by the undersigned (including holding as a custodian) or with respect to which the undersigned has beneficial ownership within the rules and regulations of the SEC (collectively the "Undersigned's Shares") or make any public announcement or SEC filing relating to any proposed Transfer or intent to engage in such a Transfer, other than any Shares sold to the Underwriters

pursuant to the Underwriting Agreement or as otherwise provided herein. In addition, the undersigned also agrees that it will not, during the Lock-Up Period, without the prior written consent of the Representatives on behalf of the Underwriters, make any demand for or exercise any right with respect to, the registration of any of the Undersigned's Shares. Notwithstanding the foregoing or any other agreement or waiver to which the undersigned is a party, the undersigned may make a demand under any registration rights agreement with the Company described in the Prospectus for, and exercise its rights under any such registration rights agreement with respect to, the registration after the expiration of the Lock-Up Period of Equity Securities that does not require the filing of a registration statement or any public announcement or activity regarding the registration by the undersigned, the Company or any third party during the Lock-Up Period (and no such public announcement or activity shall be voluntarily made or taken during the Lock-Up Period). The foregoing restrictions are expressly agreed to preclude the undersigned from engaging in any hedging or other transaction which is designed to or which reasonably could be expected to lead to or result in a sale or disposition of the Undersigned's Shares even if such Shares would be disposed of by someone other than the undersigned. Such prohibited hedging or other transactions would include without limitation any short sale or any purchase, sale or grant of any right (including without limitation any put or call option) with respect to any of the Undersigned's Shares or with respect to any security that includes, relates to, or derives any significant part of its value from such Shares. If the undersigned is an officer or director of the Company, the undersigned further agrees that the foregoing provisions shall be equally applicable to any issuer-directed Shares the undersigned may purchase in the Public Offering.

Notwithstanding the foregoing, the undersigned may:

(a) Transfer the Undersigned's Shares or make an SEC filing related to any such Transfer:

(i) as a *bona fide* gift or gifts, including without limitation to a charitable organization or educational institution, or for *bona fide* estate planning purposes;

(ii) to any member of the undersigned's immediate family or to any trust or other legal entity for the direct or indirect benefit of the undersigned or the immediate family of the undersigned, or if the undersigned is a trust, to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, provided that any such transfer shall not involve a disposition for value;

(iii) by will, other testamentary document or the laws of intestate succession;

(iv) in connection with a sale of the Undersigned's Shares acquired in the Public Offering (other than any issuer-directed shares of Common Stock purchased in the Public Offering by an officer or director of the Company) or in open market transactions on or after the Public Offering Date;

(v) if the undersigned is a corporation, partnership, limited liability company, trust or other business entity, (A) to another corporation, member, partner, partnership, limited liability company, trust or other business entity that is an affiliate (as defined in Rule 405 as promulgated by the SEC under the Securities Act of 1933, as amended) of the undersigned, or to any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the undersigned or affiliates of the undersigned (including, for the avoidance of doubt, where the undersigned is a partnership, to its general partner or a successor partnership or fund, or any other funds managed by such partnership), or (B) as

part of a distribution, transfer or disposition by the undersigned to its or its affiliates' directors, officers, employees, managers, managing members, members, stockholders, partners, beneficiaries (or the estates thereof) or other equity holders;

(vi) (a) surrender or forfeiture to the Company of shares of Common Stock of the Company in connection with the "net" or "cashless" exercise or settlement of stock options, other rights to purchase shares of Common Stock or other awards expiring during the Lock-Up Period (collectively, the "Expiring Awards") or for the payment of tax withholdings or remittance payments due as a result of the vesting, settlement, or exercise of such Expiring Awards, in all such cases, pursuant to an equity incentive plan, stock purchase plan or other employee benefit plan described in the Registration Statement and the Prospectus, or (b) surrender or forfeiture to the Company of shares of Common Stock of the Company upon the conversion of a convertible security of the Company described in the Registration Statement and the Prospectus in order to cover withholding tax obligations in connection with such conversion;

(vii) to the Company in connection with any contractual arrangement in effect on the date of the Prospectus that provides for the repurchase of the undersigned's Equity Securities by the Company in connection with the termination of the undersigned's service with the Company;

(viii) in connection with the conversion of any convertible security into shares of Common Stock in a manner consistent with the description of such securities contained in the Prospectus, provided that for the avoidance of doubt such shares of Common Stock shall remain subject to the provisions of this Lock-Up Agreement;

(ix) to a nominee or custodian of a person or entity to whom a Transfer would be permissible under (i), (ii), (iii) or (v) above;

(x) pursuant to a bona fide third-party tender offer, merger, consolidation or other similar transaction that is approved by the board of directors of the Company and made to all holders of the Company's capital stock involving a Change of Control of the Company, provided that in the event that such tender offer, merger, consolidation or other similar transaction is not completed, the Undersigned's Shares shall remain subject to the provisions of this Lock-Up Agreement;

(xi) in connection with the conversion or reclassification of the outstanding preferred stock or other classes of common stock of the Company into shares of Common Stock, provided that any such shares of Common Stock received upon such conversion or reclassification shall be subject to the terms of this Lock-Up Agreement;

(xii) by operation of law, including pursuant to orders of a court, a qualified domestic order or in connection with a divorce settlement; or

(xiii) with the prior written consent of the Representatives on behalf of the Underwriters;

provided that (A) in the case of (i), (ii), (iii), (v), (ix) and (xii) above, it shall be a condition to the transfer or distribution that the donee, transferee or distributee, as

the case may be, agrees in writing to be bound by the restrictions set forth herein, (B) in the case of (i), (ii), (iii), (iv) and (v) above, no filing under Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of Common Stock shall be required or shall be voluntarily made during the Lock-Up Period (other than a required filing on Form 5, Schedule 13G (or Schedule 13G/A) or Schedule 13F), (C) in the case of (vi) above, if the undersigned is required to file a report under Section 16 of the Exchange Act during the Lock-Up Period, the undersigned shall include a statement in any such report to the effect that such report relates to the circumstances described in (vi) above, (D) in the case of (i), (ii), (iii) and (v) above, it shall be a condition to the transfer or distribution that such transfer or distribution does not involve a disposition for value and (E) in the case of (vii) above, no filing under Section 16 of the Exchange Act, or other public filing, report or announcement reporting a reduction in beneficial ownership of shares of Common Stock shall be voluntarily made during the Lock-Up Period and, if the undersigned is required to file a report under Section 16 of the Exchange Act during the Lock-Up Period, the undersigned shall include a statement in such report to the effect that such transfer is to the Company in connection with the repurchase of shares of Common Stock, as the case may be.

(b) receive from the Company shares of Common Stock in connection with the exercise of options or other rights granted under a stock incentive plan or other equity award plan, which plan is described in the Registration Statement; or

(c) enter into a written plan meeting the requirements of Rule 10b5-1 under the Exchange Act after the date of this Lock-Up Agreement relating to the sale of the Undersigned's Shares, provided that (i) the securities subject to such plan may not be transferred until after the expiration of the Lock-Up Period and (ii) no public announcement or filing under the Exchange Act shall be voluntarily made regarding the establishment of such plan during the Lock-Up Period and any required report under Section 16 of the Exchange Act shall clearly indicate in the footnotes thereto that the filing relates to the circumstances described in this clause (c).

For purposes of this Lock-Up Agreement, "immediate family" shall mean any relationship by blood, current or former marriage, domestic partnership or adoption, not more remote than first cousin. For purposes of this Lock-Up Agreement, "Change of Control" shall mean the transfer (whether by tender offer, merger, consolidation or other similar transaction) in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an Underwriter pursuant to the Public Offering), of the Company's voting securities if, after such transfer, such person or group of affiliated persons would hold a majority of the outstanding voting securities of the Company (or the surviving entity).

The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the transfer of the Undersigned's Shares except in compliance with the foregoing restrictions.

In addition, the Representatives agree that should a discretionary release or waiver be granted to a holder of Equity Securities, then the undersigned will be released on the same terms on a pro rata basis, based on the number of Equity Securities held by the undersigned on the date hereof on an as-converted basis, from the restrictions set forth in this Lock-Up Agreement (such

release, a "Pro-rata Release"); provided, however, that such Pro-rata Release shall not be applied in the event of (a) releases granted from such lockup restrictions to all parties by the Representatives constitute in the aggregate an amount less than or equal to 1% of the Company's total outstanding stock (determined as of the closing date of the Public Offering for, and giving effect to, the Public Offering) and no releases are granted to any officer or director of the Company, or (b) any primary or secondary public offering or sale that is underwritten (the "Underwritten Sale") of the Company's Common Stock during the Lock-Up Period; provided further, that the undersigned is offered the opportunity to participate on a pro rata basis with and otherwise on the same terms as any other equity holders in such Underwritten Sale and, if the undersigned so elects to participate in such Underwritten Sale, the undersigned is hereby released from the restrictions herein with respect to the Undersigned's Shares included in such Underwritten Sale; provided further, that any of the Undersigned's Shares that are released for such Underwritten Sale but not sold in such Underwritten Sale shall be subject to this Lock-Up Agreement immediately following such Underwritten Sale. The Representatives shall use their commercially reasonable efforts to provide at least three business days' notice to the Chief Financial Officer of the Company prior to the effective date of such release or waiver (the effective date of such release or waiver, the "Release Date"), stating the percentage of shares held by such person or entity to be released, and the Company shall use commercially reasonable efforts to send notice within two business days thereafter to the undersigned stating the same percentage of shares of Common Stock held by the undersigned as is held by the release on an as-converted basis shall be released from the restrictions set forth herein on the Release Date; provided that the failure to provide such notices shall not give rise to any claim or liability against the Representatives or the Underwriters. The Company has agreed or will agree in the Underwriting Agreement to announce the impending release or waiver by press release through a major news service at least two business days before the Release Date, if required by FINRA Rule 5131 (or any successor provision thereto). The provisions of this paragraph will not apply if (1) the release or waiver is effected solely to permit a transfer not for consideration and (2) the transferee agrees to be bound in writing by the restrictions set forth herein.

Notwithstanding anything to the contrary contained herein, this Lock-Up Agreement will automatically terminate and the undersigned shall automatically, and without any action on the part of any other party, be released from all obligations hereunder upon the earliest to occur, if any, of (i) the Company advises the Representatives in writing prior to the execution of the Underwriting Agreement that it has determined not to proceed with the Public Offering, (ii) the withdrawal of the Registration Statement prior to the execution of the Underwriting Agreement, (iii) the Underwriting Agreement is executed but is terminated (other than the provisions thereof which survive termination) prior to payment for and delivery of the Shares to be sold thereunder, or (iv) March 31, 2018, in the event that the Underwriting Agreement has not been executed by such date.

In the event that any Representative withdraws from or declines to participate in the Public Offering, all references to the Representatives contained in this Lock-Up Agreement shall be deemed to refer to the remaining Representatives that continue to participate in the Public Offering (the "Remaining Representatives"), and, in such event, any written consent, waiver or notice given or delivered in connection with this Lock-Up Agreement by the Remaining Representatives shall be deemed to be sufficient and effective for all purposes under this Lock-Up Agreement.

The undersigned hereby consents to receipt of this Lock-Up Agreement in electronic form and understands and agrees that execution and delivery of this Lock-Up Agreement by facsimile transmission, electronic mail or other electronic transmission is legal, valid and binding for all purposes.

The undersigned understands that the Company and the Underwriters are relying upon this Lock-Up Agreement in proceeding toward consummation of the offering. The undersigned further understands that this Lock-Up Agreement is irrevocable and shall be binding upon the undersigned's heirs, legal representatives, successors, and assigns.

Very truly yours,

_____

Exact Name of Shareholder

_____

Authorized Signature

_____

Title

EXHIBIT B

Form of Standstill and Stock Restriction Agreement

DENALI THERAPEUTICS INC.

STANDSTILL AND STOCK RESTRICTION AGREEMENT

This Standstill and Stock Restriction Agreement (this "**Agreement**") is made as of **[**DATE] ("**Effective Date**") by and among Denali Therapeutics Inc., a Delaware corporation (the "**Company**") and Takeda Pharmaceutical Company Limited, a corporation organized under the laws of Japan (the "**Investor**").

WHEREAS, the Investor has agreed to purchase shares of the Company's Common Stock (the "**Shares**") pursuant to that certain Common Stock Purchase Agreement of even date herewith, by and between the Company and the Investor (the "**Purchase Agreement**").

WHEREAS, it is a condition to the Closing (as defined in the Purchase Agreement) of the sale of the Shares that the Company and Investor execute and deliver this Agreement.

NOW, THEREFORE, in consideration of the mutual promises and covenants herein contained, and other consideration, the receipt and adequacy of which is hereby acknowledged, the parties hereto agree as follows:

1. Standstill. Investor hereby agrees that, without the prior approval of the Board (as defined in the Purchase Agreement), Investor shall not and shall not permit or cause any Affiliate (as defined in the Purchase Agreement) or Representative of Investor to:

(a) acting alone or with others, acquire, offer to acquire, or agree to acquire, directly or indirectly, by purchase, merger, business combination or in any other manner, any voting securities or direct or indirect rights to acquire any securities of the Company or any subsidiary thereof, or of any successor to or person in control of the Company if after such acquisition Investor, together with its Affiliates, would own more than 10% of the outstanding capital stock of the Company or voting power of the Company, or any assets of the Company or any subsidiary or division thereof or of any such successor or controlling person; provided that any investment by Investor or an Affiliate of Investor in third-party mutual funds or other similar passive investment vehicles that hold interests in securities of the Company or any of its Affiliates shall not be taken into account for the purpose of this subparagraph (a);

(b) enter into any voting agreements, trusts or similar arrangements with respect to voting securities of the Company other than as set forth herein;

(c) make, or in any way participate, directly or indirectly, in any "solicitation" of "proxies" to vote (as such terms are used in the rules promulgated by the Securities and Exchange Commission (the "**Commission**")), or seek to advise or influence any person or entity with respect to the voting by any third party of any voting securities of the Company;

(d) make any public announcement, directly or indirectly, with respect to, or submit a proposal for, or offer of (with or without conditions) any extraordinary transaction involving the Company or any of its securities or assets;

(e) form, join or in any way participate in a "group" as defined in Section 13(d)(3) (a "**13D Group**") of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**") , in connection with any of the foregoing;

(f) act, alone or in concert with others, to seek to control, advise, change or influence the management, Board, governing instruments, policies or affairs of the Company;

(g) disclose any intention, plan or arrangement inconsistent with the foregoing;

(h) have any discussions or enter into any arrangement with, or advise, assist or encourage any other person in connection with any of the foregoing events;

(i) take any action that could reasonably be expected to require the Company to make a public announcement regarding the possibility of any of the events described in clauses (a) through (h) above; or

(j) request the Company or any of its agents or Representatives, directly or indirectly, in any public manner, to amend or waive any of the foregoing provisions.

For the purposes of this Agreement, "**Representatives**" means as to any person, its directors, officers, employees, agents and advisors (including, without limitation, financial advisors, attorneys and accountants) and debt and/or equity financing sources and their advisors.

Notwithstanding the foregoing, it is understood and agreed that Investor shall not be prohibited from entering into an agreement and having discussions with legal, accounting or financial advisors for the limited purposes of evaluating any of the transactions contemplated by this Section 1, and Investor and/or its Affiliates may initiate private discussions with the Company that Investor and/or its Affiliates alone, and not in concert with any third party, would be interested in engaging in discussions with the Company that could result in a negotiated transaction otherwise prohibited by this Section 1; *provided, however*, that any such discussions shall be expressly conditioned on approval of such proposal by the Board and will not reasonably be expected to require public disclosure.

2. Transfer Restrictions.

(a) Notwithstanding anything to the contrary in the Purchase Agreement, Investor shall not, directly or indirectly, sell, transfer, pledge, 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, transfer the economic risk of ownership of, or otherwise dispose of (each, a "**Transfer**" any securities of the Company except:

(i) to the Company;

(ii) in response to a bona fide public tender offer or exchange offer subject to Regulation 14D or Rule 13e-3 of the rules promulgated under the Exchange Act by the Commission, for cash or other consideration which is made by or on behalf of the Company;

(iii) in connection with a Change in Control (as defined below) of the Company which has received the Board's approval; or

(iv) to an Affiliate of Investor in one or more transactions, so long as prior to or concurrent with any such Transfer such Affiliate agrees in writing to be bound by the terms of this Agreement.

3. Termination of Standstill and Transfer Restrictions.

(a) The restrictions set forth in Section 1 (Standstill) shall terminate upon the earliest to occur of the following:

(i) merger, consolidation or other business combination or transaction to which the Company is a party if the stockholders of the Company immediately prior to the effective date of such merger, consolidation or other business combination or transaction, as a result of such share ownership, have beneficial ownership of voting securities of the Company representing less than 50% of the total number of votes which may be cast in the election of members of the Board if all securities entitled to vote in the election of such directors are present and voted ("**Total Voting Power**") of the surviving entity following such merger, consolidation or other business combination or transaction; (ii) an acquisition by any person, entity or 13D Group (other than a 13D Group of which Investor or any of its Affiliates is a member) of direct or indirect beneficial ownership of voting securities of the Company representing 50% or more of the Total Voting Power; (iii) a sale of all or substantially all of the assets of the Company; or (iv) a liquidation or dissolution of the Company (collectively, a "**Change of Control**"); or

(ii) the 18 month anniversary of the Effective Date.

(b) The restrictions set forth in Section 2 (Transfer Restrictions) shall terminate upon the earliest to occur of the following:

(i) a Change of Control;

(ii) the expiration or earlier termination of the Option and Collaboration Agreement (as defined in the Purchase Agreement); or

(iii) the 18 month anniversary of the Effective Date.

(c) The restrictions set forth in Section 1 (Standstill) and the restrictions set forth in Section 2 (Transfer Restrictions) shall be suspended and shall not apply to or otherwise restrict the Investor's actions in respect of the Company's securities for so long as a Significant Event has occurred and is continuing. For purposes of this Section 3(c), a "**Significant Event**" of the following not involving a violation of Section 1: (i) the public announcement of a proposal to acquire, or the acquisition, by any person or 13D Group of beneficial ownership of voting securities of the Company representing 15% or more of the then outstanding voting securities of the Company, or all or substantially all of the assets of the Company; (ii) the commencement, by any person or 13D Group of a tender or exchange offer, to acquire voting securities of the Company which, if successful, would result in such person or 13D Group owning, when combined with any other voting securities of the Company owned by such person or 13D Group, 15% or more of the then outstanding voting securities of the Company; or (iii) the entry into by the Company, or the public announcement by the Company of a determination to enter into or commence or continue any discussions relating to, any merger, sale or other business combination transaction, or an agreement therefor, pursuant to which the outstanding shares of capital stock of the Company would be converted into cash, other consideration or securities of another person or 13D Group or 50% or more of the then outstanding shares of capital stock of the Company would be owned by persons other than the then current holders of shares of capital stock of the Company, or which would result in all or a substantial portion of the Company's assets being sold to any person or 13D Group.

4. Registration Rights

(a) *Rule 144 Reporting*. With a view to making available to the Investor the benefits of certain rules and regulations of the Commission which may permit the sale of the Shares to the public without registration, the Company agrees to use commercially reasonable efforts to:

(i) make and keep public information available, as those terms are understood and defined in Rule 144 promulgated under the Securities Act of 1933, as amended (the "**Securities Act**");

(ii) file with the Commission in a timely manner all reports and other documents required of the Company under the Exchange Act; and

(iii) furnish the Investor forthwith upon request (A) a written statement by the Company as to its compliance with the public information requirements of said Rule 144, (B) a copy of the most recent annual or quarterly report of the Company, and (C) such other reports and documents as may be reasonably requested in availing the Investor of any rule or regulation of the Commission permitting the sale of any such securities without registration.

(b) *Registration*.

(i) If, upon termination of the restrictions set forth in Section 2 (Transfer Restrictions) pursuant to the terms hereof, the Shares cannot be sold without restriction pursuant to Rule 144 promulgated under the Securities Act, then upon Investor's written

request, the Company will use commercially reasonable efforts to register the Shares of resale under the Securities Act on a Registration Statement on Form S-3 (the "**Registration Statement**"), filed within 90 days of such written request, and will use commercially reasonable efforts to have such Registration Statement promptly declared effective by the Commission.

(ii) The Company will use commercially reasonable efforts to keep the Registration Statement continuously effective under the Securities Act for one hundred eighty (180) days following the initial effectiveness of such Registration Statement or, if earlier, until the date all of the Shares covered by such Registration Statement have been sold or can be sold publicly without restriction or limitation under Rule 144.

(iii) The Investor shall furnish to the Company such information regarding the Investor, and the distribution proposed by the Investor, as the Company may reasonably request in writing and as shall be required in connection with the Registration Statement.

(iv) The Company shall pay all fees and expenses incident to the performance of or compliance with this Section 4(b) by the Company.

(v) Notwithstanding the foregoing obligations, if the Company furnishes to Investor a certificate signed by faith judgment of the Board 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 (a) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (b) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (c) 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 Investor 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 (1) 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; (2) a registration relating to an SEC Rule 145 transaction; (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 the Shares; or (4) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered).

(vi) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Section 4(b) (a) during the period that is thirty (30) days before the Company's good faith estimate of the date of the 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 previously effected one registration pursuant to this Section 4(b).

(vii) This Section 4 (Registration Rights) shall terminate upon the earliest to occur of the following: (a) a Change of Control or (b) the 18 month anniversary of the termination of the restrictions set forth in Section 2 (Transfer Restrictions).

5. Indemnification. If the Shares are included in a registration statement pursuant to Section 4(b), then, subject to the provisions of this Section 5, the Company will indemnify and hold the Investor and its directors, officers, shareholders, members, partners, employees and agents, each person or entity who controls the Investor (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act) and the directors, officers, shareholders, agents, members, partners or employees of such controlling persons (each, an "**Indemnified Person**") harmless from any and all Indemnified Losses (as defined below), provided that the Company shall not be liable for any Indemnified Losses 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 Investor, controlling person, or other aforementioned person expressly for use in connection with a registration of securities. Promptly after receipt by any Indemnified Person of notice of any demand or claim from any person or entity that would or might give rise to a claim or the commencement of any action, proceeding or investigation in respect of which indemnification may be sought pursuant to this Section 5 (a "**Third Party Claim"),** such Indemnified Person shall promptly notify the Company in writing, and in reasonable detail, of such Third Party Claim, but in no event shall the Company be liable for any Indemnified Losses to the extent such Indemnified Losses arose from any delay in the Indemnified Person providing notice the Company. Thereafter, the Indemnified Person will deliver to the Company, within five (5) business days after the Indemnified Person's receipt thereof, copies of all notices and documents (including court papers) received by the Indemnified Person relating to the Third Party Claim. If notice of a Third Party Claim is delivered to the Company, the Company will be entitled, if it so chooses, to assume the defense thereof (subject to a reservation of rights) with counsel selected by the Company by giving the Indemnified Person written notice within twenty (20) days of the Company's receipt of notice of the Third Party Claim pursuant to this Section 5. If the Company does not give such notice to the Indemnified Person of the Company's intent to assume the defense of the Third Party Claim, the Indemnified person shall be entitled to assume the defense thereof. Should the Company so elect to assume the defense of a Third Party Claim, the Company will not be liable to the Indemnified Person for legal expenses subsequently incurred by the Indemnified Person in connection with the defense thereof. If the Company assumes such defense, the Indemnified Person will have the right to participate in the defense thereof and to employ counsel, at its own expense, separate from the counsel employed by the Company, it being understood, however, that the Company will control such defense, except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is a material conflict on any material issue between the

position of the Company and the position of such Indemnifier Person, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel for all Indemnified Persons entitled to indemnification hereunder. If the Company chooses to defend any Third Party Claim, then all the Parties will cooperate in the defense or prosecution of such Third Party Claim. The Indemnified Person will not admit any liability with respect to, or settle, compromise or discharge, any Third Party Claim without the prior written consent of the Indemnified Person (which consent shall not be unreasonably withheld), unless such settlement requires only the payment of money that the Company is obligated to pay. For purposes of this Section 5, "**Indemnified Losses**" means any loss, damage, claim or liability (joint or several) to which an Indemnified Person 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 of 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 Company (or any of its agents or Affiliated) 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. For the avoidance of doubt, nothing contained in this Section 5 shall diminish or otherwise affect the rights of Investor or any other Indemnified Party (as defined in the Option and Collaboration Agreement) of Investor to indemnification pursuant to the terms of the Option and Collaboration Agreement.

6. Miscellaneous Provisions.

(a) *Amendment*. Any term of this Agreement may be amended, terminated or waived only with the written consent of the Company and the Investor. Any amendment or waiver effected in accordance with this Section 6(a) shall be binding upon the Investor and each transferee of the Shares, each future holder of all such securities, and the Company.

(b) *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 (a) personal delivery to the party to be notified, (b) when sent, if sent by electronic mail or facsimile during normal business hours of the recipient, and if not sent during normal business hours, then on the recipient s next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) business day after deposit with a nationally recognized overnight courier, freight prepaid, specifying next business day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their address as set forth on the signature page or otherwise furnished to the Company at Closing, or to such e-mail address, facsimile number or address as subsequently modified by written notice given in accordance with this Section 6(b). If notice is given to the Company, a copy shall also be sent to Wilson Sonsini Goodrich and Rosati, PC, 650 Page Mill Road, Palo Alto, CA 94304, Attn: Tony Jeffries, Esq., and if notice is given to the Investor, a copy shall also be given to: (i) Millennium Pharmaceuticals, Inc., 300 Massachusetts Ave, Cambridge, MA 02139, Attn: Head of Global R&D Finance; and (ii) Cooley LLP, 3175 Hanover Street, Palo Alto, 94304, Attn: Lila Hope, Esq.

(c) *Governing Law*. This Agreement shall be governed by the internal law of the State of Delaware without regard to principles of conflicts of law.

(d) *Dispute Resolution*. The parties (i) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of the state 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, (ii) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of the state of Delaware or the United States District Court for the District of Delaware, and (iii) 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 AGREEMENT, 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.

(e) *Successors and Assigns*. Except as otherwise provided herein, the provisions of this Agreement shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors and administrators of the parties hereto.

(f) *Entire Agreement*. This Agreement, the Option and Collaboration Agreement, and the other Transaction Agreements (each as defined in the Purchase Agreement), constitute the full and entire understanding and agreement between 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 are expressly canceled.

(g) *Delays or Omissions*. Except as expressly provided herein, no delay or omission to exercise any right, power or remedy accruing to any party to this Agreement upon any breach or default of any other party under this Agreement shall impair any such right, power or remedy of such non-defaulting party, nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in 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. Any waiver, permit, consent or approval of any kind or character on the part of any party of any breach or default under this Agreement, or any waiver on the part of any party of any provisions or conditions of this Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement or by law or otherwise afforded to any party to this Agreement, shall be cumulative and not alternative.

(h) *Severability*. If any provision of this Agreement becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, portions of such provision, or such provision in its entirety, to the extent necessary, shall be severed from this Agreement, and such court will replace such illegal, void or unenforceable provision of this Agreement with a valid and enforceable provision that will achieve, to the extent possible, the same economic, business and other purposes of the illegal, void or unenforceable provision. The balance of this Agreement shall be enforceable in accordance with its terms.

(i) *Counterparts*. This Agreement may be executed in any number of counterparts, each of which shall be enforceable against the parties that execute such counterparts, and all of which together shall constitute one instrument.

(j) *Telecopy, Execution and Delivery*. A facsimile, telecopy or other reproduction of this Agreement may be executed by one or more parties hereto and delivered by such party by facsimile or any similar electronic transmission device pursuant to which the signature of or on behalf of such party can be seen. Such execution and delivery shall be considered valid, binding and effective for all purposes. At the request of any party hereto, all parties hereto agree to execute and deliver an original of this Agreement as well as any facsimile, telecopy or other reproduction hereof.

(k) *Further Assurances*. Each party hereto agrees to execute and deliver, by the proper exercise of its corporate, limited liability company, partnership or other powers, all such other and additional instruments and documents and do all such other acts and things as may be necessary to more fully effectuate this Agreement.

(l) *Stop Transfer Instructions.* The Company may issue appropriate :stop transfer" instructions to enforce the covenants set forth in this Agreement.

[Remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have executed this Standstill and Stock Restriction Agreement as of the Effective Date.

COMPANY:

DENALI THERAPEUTICS INC.
a Delaware corporation

By: _____
Ryan Watts, Ph.D.
President and CEO

151 Oyster Point Boulevard
South San Francisco, CA 94080

IN WITNESS WHEREOF, the parties have executed this Standstill and Stock Restriction Agreement as of the Effective Date.

INVESTOR:

TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: _____
Name: _____
Title: _____

Address:

_____

_____

(*Signature Page to Standstill and Stock Restriction Agreement*)

Exhibit 10.18

DENALI THERAPEUTICS INC.

STANDSTILL AND STOCK RESTRICTION AGREEMENT

This Standstill and Stock Restriction Agreement (this "**Agreement**") is made as of February 23, 2018 ("**Effective Date**") by and among Denali Therapeutics Inc., a Delaware corporation (the "**Company**") and Takeda Pharmaceutical Company Limited, a corporation organized under the laws of Japan (the "**Investor**").

WHEREAS, the Investor has agreed to purchase shares of the Company's Common Stock (the "**Shares**") pursuant to that certain Common Stock Purchase Agreement of even date herewith, by and between the Company and the Investor (the "**Purchase Agreement**").

WHEREAS, it is a condition to the Closing (as defined in the Purchase Agreement) of the sale of the Shares that the Company and Investor execute and deliver this Agreement.

NOW, THEREFORE, in consideration of the mutual promises and covenants herein contained, and other consideration, the receipt and adequacy of which is hereby acknowledged, the parties hereto agree as follows:

1. Standstill. Investor hereby agrees that, without the prior approval of the Board (as defined in the Purchase Agreement), Investor shall not and shall not permit or cause any Affiliate (as defined in the Purchase Agreement) or Representative of Investor to:

(a) acting alone or with others, acquire, offer to acquire, or agree to acquire, directly or indirectly, by purchase, merger, business combination or in any other manner, any voting securities or direct or indirect rights to acquire any securities of the Company or any subsidiary thereof, or of any successor to or person in control of the Company if after such acquisition Investor, together with its Affiliates, would own more than 10% of the outstanding capital stock of the Company or voting power of the Company, or any assets of the Company or any subsidiary or division thereof or of any such successor or controlling person; provided that any investment by Investor or an Affiliate of Investor in third-party mutual funds or other similar passive investment vehicles that hold interests in securities of the Company or any of its Affiliates shall not be taken into account for the purpose of this subparagraph (a);

(b) enter into any voting agreements, trusts or similar arrangements with respect to voting securities of the Company other than as set forth herein;

(c) make, or in any way participate, directly or indirectly, in any "solicitation" of "proxies" to vote (as such terms are used in the rules promulgated by the Securities and Exchange Commission (the "**Commission**")), or seek to advise or influence any person or entity with respect to the voting by any third party of any voting securities of the Company;

(d) make any public announcement, directly or indirectly, with respect to, or submit a proposal for, or offer of (with or without conditions) any extraordinary transaction involving the Company or any of its securities or assets;

(e) form, join or in any way participate in a "group" as defined in Section 13(d)(3) (a "**13D Group**") of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), in connection with any of the foregoing;

(f) act, alone or in concert with others, to seek to control, advise, change or influence the management, Board, governing instruments, policies or affairs of the Company;

(g) disclose any intention, plan or arrangement inconsistent with the foregoing;

(h) have any discussions or enter into any arrangement with, or advise, assist or encourage any other person in connection with any of the foregoing events;

(i) take any action that could reasonably be expected to require the Company to make a public announcement regarding the possibility of any of the events described in clauses (a) through (h) above; or

(j) request the Company or any of its agents or Representatives, directly or indirectly, in any public manner, to amend or waive any of the foregoing provisions.

For the purposes of this Agreement, "**Representatives**" means as to any person, its directors, officers, employees, agents and advisors (including, without limitation, financial advisors, attorneys and accountants) and debt and/or equity financing sources and their advisors.

Notwithstanding the foregoing, it is understood and agreed that Investor shall not be prohibited from entering into an agreement and having discussions with legal, accounting or financial advisors for the limited purposes of evaluating any of the transactions contemplated by this Section 1, and Investor and/or its Affiliates may initiate private discussions with the Company that Investor and/or its Affiliates alone, and not in concert with any third party, would be interested in engaging in discussions with the Company that could result in a negotiated transaction otherwise prohibited by this Section 1; *provided, however*, that any such discussions shall be expressly conditioned on approval of such proposal by the Board and will not reasonably be expected to require public disclosure.

2. Transfer Restrictions.

(a) Notwithstanding anything to the contrary in the Purchase Agreement, Investor shall not, directly or indirectly, sell, transfer, pledge, 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, transfer the economic risk of ownership of, or otherwise dispose of (each, a "**Transfer**") any securities of the Company except:

(i) to the Company;

(ii) in response to a bona fide public tender offer or exchange offer subject to Regulation 14D or Rule 13e-3 of the rules promulgated under the Exchange Act by the Commission, for cash or other consideration which is made by or on behalf of the Company;

(iii) in connection with a Change in Control (as defined below) of the Company which has received the Board's approval; or

(iv) to an Affiliate of Investor in one or more transactions, so long as prior to or concurrent with any such Transfer such Affiliate agrees in writing to be bound by the terms of this Agreement.

3. Termination of Standstill and Transfer Restrictions.

(a) The restrictions set forth in Section 1 (Standstill) shall terminate upon the earliest to occur of the following:

(i) merger, consolidation or other business combination or transaction to which the Company is a party if the stockholders of the Company immediately prior to the effective date of such merger, consolidation or other business combination or transaction, as a result of such share ownership, have beneficial ownership of voting securities of the Company representing less than 50% of the total number of votes which may be cast in the election of members of the Board if all securities entitled to vote in the election of such directors are present and voted ("**Total Voting Power**") of the surviving entity following such merger, consolidation or other business combination or transaction; (ii) an acquisition by any person, entity or 13D Group (other than a 13D Group of which Investor or any of its Affiliates is a member) of direct or indirect beneficial ownership of voting securities of the Company representing 50% or more of the Total Voting Power; (iii) a sale of all or substantially all of the assets of the Company; or (iv) a liquidation or dissolution of the Company (collectively, a "**Change of Control**"); or

(ii) the 18 month anniversary of the Effective Date.

(b) The restrictions set forth in Section 2 (Transfer Restrictions) shall terminate upon the earliest to occur of the following:

(i) a Change of Control;

(ii) the expiration or earlier termination of the Option and Collaboration Agreement (as defined in the Purchase Agreement); or

(iii) the 18 month anniversary of the Effective Date.

(c) The restrictions set forth in Section 1 (Standstill) and the restrictions set forth in Section 2 (Transfer Restrictions) shall be suspended and shall not apply to or otherwise restrict the Investor's actions in respect of the Company's securities for so long as a Significant Event has occurred and is continuing. For purposes of this Section 3(c), a "**Significant Event**" shall mean any of the following not involving a violation of Section 1: (i) the public announcement of a proposal to acquire, or the acquisition, by any person or 13D Group of beneficial ownership of voting securities of the Company representing 15% or more of the then outstanding voting securities of the Company, or all or substantially all of the assets of the Company; (ii) the commencement, by any person or 13D Group of a tender or exchange offer, to acquire voting securities of the Company which, if successful, would result in such person or 13D Group owning, when combined with any other voting securities of the Company owned by such person or 13D Group, 15% or more of the then outstanding voting securities of the Company; or (iii) the entry into by the Company, or the public announcement by the Company of a determination to enter into or commence or continue any discussions relating to, any merger, sale or other business combination transaction, or an agreement therefor, pursuant to which the outstanding shares of capital stock of the Company would be converted into cash, other consideration or securities of another person or 13D Group or 50% or more of the then outstanding shares of capital stock of the Company would be owned by persons other than the then current holders of shares of capital stock of the Company, or which would result in all or a substantial portion of the Company's assets being sold to any person or 13D Group.

4. Registration Rights

(a) Rule 144 Reporting. With a view to making available to the Investor the benefits of certain rules and regulations of the Commission which may permit the sale of the Shares to the public without registration, the Company agrees to use commercially reasonable efforts to:

(i) make and keep public information available, as those terms are understood and defined in Rule 144 promulgated under the Securities Act of 1933, as amended (the "**Securities Act**");

(ii) file with the Commission in a timely manner all reports and other documents required of the Company under the Exchange Act; and

(iii) furnish the Investor forthwith upon request (A) a written statement by the Company as to its compliance with the public information requirements of said Rule 144, (B) a copy of the most recent annual or quarterly report of the Company, and (C) such other reports and documents as may be reasonably requested in availing the Investor of any rule or regulation of the Commission permitting the sale of any such securities without registration.

(b) Registration.

(i) If, upon termination of the restrictions set forth in Section 2 (Transfer Restrictions) pursuant to the terms hereof, the Shares cannot be sold without restriction pursuant to Rule 144 promulgated under the Securities Act, then upon Investor's written request, the Company will use commercially reasonable efforts to register the Shares for

resale under the Securities Act on a Registration Statement on Form S-3 (the "**Registration Statement**"), filed within 90 days of such written request, and will use commercially reasonable efforts to have such Registration Statement promptly declared effective by the Commission.

(ii) The Company will use commercially reasonable efforts to keep the Registration Statement continuously effective under the Securities Act for one hundred eighty (180) days following the initial effectiveness of such Registration Statement or, if earlier, until the date all of the Shares covered by such Registration Statement have been sold or can be sold publicly without restriction or limitation under Rule 144.

(iii) The Investor shall furnish to the Company such information regarding the Investor, and the distribution proposed by the Investor, as the Company may reasonably request in writing and as shall be required in connection with the Registration Statement.

(iv) The Company shall pay all fees and expenses incident to the performance of or compliance with this Section 4(b) by the Company.

(v) Notwithstanding the foregoing obligations, if the Company furnishes to Investor a certificate signed by the Company's chief executive officer stating that in the good faith judgment of the Board 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 (a) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (b) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (c) 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 Investor 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 (1) 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; (2) a registration relating to an SEC Rule 145 transaction; (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 the Shares; or (4) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered).

(vi) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Section 4(b) (a) 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 previously effected one registration pursuant to this Section 4(b).

(vii) This Section 4 (Registration Rights) shall terminate upon the earliest to occur of the following: (a) a Change of Control or (b) the 18 month anniversary of the termination of the restrictions set forth in Section 2 (Transfer Restrictions).

5. Indemnification. If the Shares are included in a registration statement pursuant to Section 4(b), then, subject to the provisions of this Section 5, the Company will indemnify and hold the Investor and its directors, officers, shareholders, members, partners, employees and agents, each person or entity who controls the Investor (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act) and the directors, officers, shareholders, agents, members, partners or employees of such controlling persons (each, an "**Indemnified Person**") harmless from any and all Indemnified Losses (as defined below), provided that the Company shall not be liable for any Indemnified Losses 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 Investor, controlling person, or other aforementioned person expressly for use in connection with a registration of securities. Promptly after receipt by any Indemnified Person of notice of any demand or claim from any person or entity that would or might give rise to a claim or the commencement of any action, proceeding or investigation in respect of which indemnification may be sought pursuant to this Section 5 (a "**Third Party Claim**"), such Indemnified Person shall promptly notify the Company in writing, and in reasonable detail, of such Third Party Claim, but in no event shall the Company be liable for any Indemnified Losses to the extent such Indemnified Losses arose from any delay in the Indemnified Person providing notice the Company. Thereafter, the Indemnified Person will deliver to the Company, within five (5) business days after the Indemnified Person's receipt thereof, copies of all notices and documents (including court papers) received by the Indemnified Person relating to the Third Party Claim. If notice of a Third Party Claim is delivered to the Company, the Company will be entitled, if it so chooses, to assume the defense thereof (subject to a reservation of rights) with counsel selected by the Company by giving the Indemnified Person written notice within twenty (20) days of the Company's receipt of notice of the Third Party Claim pursuant to this Section 5. If the Company does not give such notice to the Indemnified Person of the Company's intent to assume the defense of the Third Party Claim, the Indemnified Person shall be entitled to assume the defense thereof. Should the Company so elect to assume the defense of a Third Party Claim, the Company will not be liable to the Indemnified Person for legal expenses subsequently incurred by the Indemnified Person in connection with the defense thereof. If the Company assumes such defense, the Indemnified Person will have the right to participate in the defense thereof and to employ counsel, at its own expense, separate from the counsel employed by the Company, it being understood, however, that the Company will control such defense, except to the extent that (i) the employment thereof has been specifically authorized by the Company in writing, (ii) the Company has failed after a reasonable period of time to assume such defense and to employ counsel or (iii) in such action there is a material conflict on any material issue between the position of the Company and the position of such Indemnified Person, in which case the Company shall be responsible for the reasonable fees and expenses of no more than one such separate counsel

for all Indemnified Persons entitled to indemnification hereunder. If the Company chooses to defend any Third Party Claim, then all the Parties will cooperate in the defense or prosecution of such Third Party Claim. The Indemnified Person will not admit any liability with respect to, or settle, compromise or discharge, any Third Party Claim without the prior written consent of the Company. Notwithstanding any other provision of this Agreement, the Company shall not enter into settlement of any Third Party Claim without the prior written consent of the Indemnified Person (which consent shall not be unreasonably withheld), unless such settlement requires only the payment of money that the Company is obligated to pay. For purposes of this Section 5, "**Indemnified Losses**" means any loss, damage, claim or liability (joint or several) to which an Indemnified Person 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 Company (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. For the avoidance of doubt, nothing contained in this Section 5 shall diminish or otherwise affect the rights of Investor or any other Indemnified Party (as defined in the Option and Collaboration Agreement) of Investor to indemnification pursuant to the terms of the Option and Collaboration Agreement.

6. Miscellaneous Provisions.

(a) *Amendment*. Any term of this Agreement may be amended, terminated or waived only with the written consent of the Company and the Investor. Any amendment or waiver effected in accordance with this Section 6(a) shall be binding upon the Investor and each transferee of the Shares, each future holder of all such securities, and the Company.

(b) *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 (a) personal delivery to the party to be notified, (b) when sent, if sent by electronic mail or facsimile during normal business hours of the recipient, and if not sent during normal business hours, then on the recipient's next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) business day after deposit with a nationally recognized overnight courier, freight prepaid, specifying next business day delivery, with written verification of receipt. All communications shall be sent to the respective parties at their address as set forth on the signature page or otherwise furnished to the Company at Closing, or to such e-mail address, facsimile number or address as subsequently modified by written notice given in accordance with this Section 6(b). If notice is given to the Company, a copy shall also be sent to Wilson Sonsini Goodrich and Rosati, PC, 650 Page Mill Road, Palo Alto, CA 94304, Attn: Tony Jeffries, Esq., and if notice is given to the Investor, a copy shall also be given to: (i) Millennium Pharmaceuticals, Inc., 300 Massachusetts Ave, Cambridge, MA 02139, Attn: Head of Global R&D Finance; and (ii) Cooley LLP, 3175 Hanover Street, Palo Alto, 94304, Attn: Lila Hope, Esq.

(c) *Governing Law*. This Agreement shall be governed by the internal law of the State of Delaware without regard to principles of conflicts of law.

(d) *Dispute Resolution*: The parties (i) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of the state 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, (ii) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of the state of Delaware or the United States District Court for the District of Delaware, and (iii) 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 AGREEMENT, 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.

(e) *Successors and Assigns*. Except as otherwise provided herein, the provisions of this Agreement shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors and administrators of the parties hereto.

(f) *Entire Agreement*. This Agreement, the Option and Collaboration Agreement, and the other Transaction Agreements (each as defined in the Purchase Agreement), constitute the full and entire understanding and agreement between 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 are expressly canceled.

(g) *Delays or Omissions*. Except as expressly provided herein, no delay or omission to exercise any right, power or remedy accruing to any party to this Agreement upon any breach or default of any other party under this Agreement shall impair any such right, power or remedy of such non-defaulting party, nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in 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. Any waiver, permit, consent or approval of any kind or character on the part of any party of any breach or default under this Agreement, or any waiver on the part of any party of any provisions or conditions of this Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Agreement or by law or otherwise afforded to any party to this Agreement, shall be cumulative and not alternative.

(h) *Severability*. If any provision of this Agreement becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, portions of such provision, or such provision in its entirety, to the extent necessary, shall be severed from this Agreement, and such court will replace such illegal, void or unenforceable provision of this Agreement with a valid and enforceable provision that will achieve, to the extent possible, the same economic, business and other purposes of the illegal, void or unenforceable provision. The balance of this Agreement shall be enforceable in accordance with its terms.

(i) *Counterparts*. This Agreement may be executed in any number of counterparts, each of which shall be enforceable against the parties that execute such counterparts, and all of which together shall constitute one instrument.

(j) *Telecopy, Execution and Delivery*. A facsimile, telecopy or other reproduction of this Agreement may be executed by one or more parties hereto and delivered by such party by facsimile or any similar electronic transmission device pursuant to which the signature of or on behalf of such party can be seen. Such execution and delivery shall be considered valid, binding and effective for all purposes. At the request of any party hereto, all parties hereto agree to execute and deliver an original of this Agreement as well as any facsimile, telecopy or other reproduction hereof.

(k) *Further Assurances*. Each party hereto agrees to execute and deliver, by the proper exercise of its corporate, limited liability company, partnership or other powers, all such other and additional instruments and documents and do all such other acts and things as may be necessary to more fully effectuate this Agreement.

(l) *Stop Transfer Instructions*. The Company may issue appropriate “stop transfer” instructions to enforce the covenants set forth in this Agreement.

[Remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have executed this Standstill and Stock Restriction Agreement as of the Effective Date.

COMPANY:

DENALI THERAPEUTICS INC.
a Delaware corporation

By: /s/ Ryan Watts, Ph.D.
Ryan Watts, Ph.D.
President and CEO

151 Oyster Point Boulevard
South San Francisco, CA 94080

IN WITNESS WHEREOF, the parties have executed this Standstill and Stock Restriction Agreement as of the Effective Date.

INVESTOR:

TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: /s/ Fumihiko Sato
Name: Fumihiko Sato
Title: Head of Portfolio Strategic Relations

Address:
1-1, Doshomachi
4-chome, Chuo-ku, Osaka, Japan

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-221946) pertaining to the 2017 Equity Incentive Plan, the 2017 Employee Stock Purchase Plan and the 2015 Stock Incentive Plan of Denali Therapeutics Inc. of our report dated March 19, 2018, with respect to the consolidated financial statements of Denali Therapeutics Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Redwood City, California
March 19, 2018

Exhibit 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Ryan J. Watts, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Denali Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 19, 2018

/s/ Ryan J. Watts
Ryan J. Watts, Ph.D.
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Steve E. Krognes, certify that:

1. I have reviewed this Annual Report on Form 10-K of Denali Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 19, 2018

/s/ Steve E. Krognes
Steve E. Krognes
Chief Financial Officer and Treasurer

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Ryan J. Watts, Ph.D., President and Chief Executive Officer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 19, 2018

By: /s/ Ryan J. Watts
Name: Ryan J. Watts, Ph.D.
Title: President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), I, Steve E. Krognes, Chief Financial Officer and Treasurer of Denali Therapeutics Inc. (the "Company"), hereby certify that:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, to which this Certification is attached as Exhibit 32.2 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 19, 2018

By:	/s/ Steve E. Krognes
Name:	Steve E. Krognes
Title:	Chief Financial Officer and Treasurer