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

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**FORM S-8**  
**REGISTRATION STATEMENT**  
*UNDER*  
*THE SECURITIES ACT OF 1933*

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

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**46-3872213**  
(I.R.S. Employer  
Identification No.)

**161 Oyster Point Blvd.**  
**South San Francisco, CA, 94080**  
**(650) 866-8548**  
(Address of principal executive offices, including zip code)

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**2017 Equity Incentive Plan**  
**2017 Employee Stock Purchase Plan**  
(Full title of the plan)

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

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*Copies to:*

**Tony Jeffries**  
**Jennifer Knapp**  
**Wilson Sonsini Goodrich & Rosati, P.C.**  
**650 Page Mill Road**  
**Palo Alto, California 94304**  
**(650) 493-9300**

**Steve E. Krognes**  
**Chief Financial Officer and Treasurer**  
**Denali Therapeutics Inc.**  
**161 Oyster Point Blvd.**  
**South San Francisco, California 94080**  
**(650) 866-8548**

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

Emerging growth company

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

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**CALCULATION OF REGISTRATION FEE**

<b>Title of Securities to be Registered</b>	<b>Amount to be Registered <sup>(1)</sup></b>	<b>Proposed Maximum Offering Price Per Share</b>	<b>Proposed Maximum Aggregate Offering Price</b>	<b>Amount of Registration Fee</b>
Common Stock, \$0.01 par value per share, reserved for issuance pursuant to the 2017 Equity Incentive Plan	4,757,573 <sup>(2)</sup>	\$20.58 <sup>(3)</sup>	\$97,910,852	\$11,867
Common Stock, \$0.01 par value per share, reserved for issuance pursuant to the 2017 Employee Stock Purchase Plan	951,514 <sup>(4)</sup>	\$17.49 <sup>(5)</sup>	\$16,641,980	\$2,017
<b>TOTAL:</b>			<b>\$114,552,832</b>	<b>\$13,884</b>

- (1) Pursuant to Rule 416(a) of the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall also cover any additional shares of the Registrant's common stock that become issuable under the 2017 Equity Incentive Plan (the "2017 Plan") and the 2017 Employee Stock Purchase Plan (the "2017 ESPP") by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without receipt of consideration that increases the number of the Registrant's outstanding shares of common stock.
- (2) Represents shares of common stock reserved for issuance under that were automatically added on January 1, 2019 to the shares of common stock reserved for issuance under the 2017 Plan. The 2017 Plan provides for an automatic annual increase in the number of shares reserved and available for issuance under the 2017 Plan as follows: the number of shares of common stock available for issuance under the 2017 Plan will be increased on the first day of each fiscal year beginning with the 2019 fiscal year, in an amount equal to the least of (i) 10,000,000 shares, (ii) five percent (5%) of the outstanding shares on the last day of the immediately preceding fiscal year, or (iii) such number of shares determined by the administrator of the 2017 Plan.
- (3) Estimated in accordance with Rule 457(h) solely for the purpose of calculating the registration fee on the basis of \$20.58 per share, which represents the average of the high and low selling prices per share of the Registrant's common stock on March 7, 2019 as reported by The NASDAQ Global Select Market.
- (4) Represents shares of common stock reserved for issuance under that were automatically added on January 1, 2019 to the shares of common stock reserved for issuance under the 2017 ESPP. The 2017 ESPP provides for an automatic annual increase in the number of shares reserved and available for issuance under the 2017 ESPP as follows: the number of shares of common stock available for issuance under the 2017 ESPP will be increased on the first day of each fiscal year beginning with the 2019 fiscal year, in an amount equal to the least of (i) 2,000,000 shares, (ii) one percent (1%) of the outstanding shares on the last day of immediately preceding fiscal year, or (iii) an amount determined by the administrator of the 2017 ESPP.
- (5) Estimated in accordance with Rule 457(h) solely for the purpose of calculating the registration fee on the basis of 85% of \$20.58, which represents the average of the high and low selling prices per share of the Registrant's common stock on March 7, 2019 as reported by The NASDAQ Global Selected Market. Pursuant to the 2017 ESPP, the purchase price of the shares of common stock reserved for issuance thereunder will be 85% of the lower of the fair market value of the common stock on (i) the first trading day of the offering period or (ii) the exercise date.

**PART I**

**INFORMATION REQUIRED IN THE PROSPECTUS**

The information specified in Item 1 and Item 2 of Part I of Form S-8 is omitted from this Registration Statement on Form S-8 (the "Registration Statement") in accordance with the provisions of Rule 428 under the Securities Act and the introductory note to Part I of Form S-8. The documents containing the information specified in Part I of Form S-8 will be delivered to the participants in the equity benefit plans covered by this Registration Statement as specified by Rule 428(b)(1) under the Securities Act.

**PART II**

**INFORMATION REQUIRED IN REGISTRATION STATEMENT**

**Item 3. Incorporation of Documents by Reference.**

Denali Therapeutics Inc. (the "Registrant") hereby incorporates by reference into this Registration Statement the following documents previously filed with the Securities and Exchange Commission (the "Commission"):

(1) The Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the Commission on March 12, 2019 pursuant to Section 13(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act");

(2) All other reports filed with the Commission pursuant to Sections 13(a) or 15(d) of the Exchange Act since the end of the fiscal year covered by the Registrant's Annual Report referred to in (1) above; and

(3) The description of the Registrant's Common Stock contained in the Company's Registration Statement on Form 8-A (File No 001-38311) filed with the Commission on November 30, 2017, pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

All documents filed by the Registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act on or after the date of this Registration Statement and prior to the filing of a post-effective amendment to this Registration Statement that indicates that all securities offered have been sold or that deregisters all securities then remaining unsold shall be deemed to be incorporated by reference in this Registration Statement and to be part hereof from the date of filing of such documents; *provided, however*, that documents or information deemed to have been furnished and not filed in accordance with the rules of the Commission shall not be deemed incorporated by reference into this Registration Statement. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any subsequently filed document which also is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

**Item 4. Description of Securities.**

Not applicable.

**Item 5. Interests of Named Experts and Counsel.**

Not applicable.

## **Item 6. Indemnification of Directors and Officers.**

Section 145 of the Delaware General Corporation Law empowers a corporation to indemnify its directors and officers and to purchase insurance with respect to liability arising out of their capacity or status as directors and officers, provided that the person acted in good faith and in a manner the person reasonably believed to be in our best interests, and, with respect to any criminal action, had no reasonable cause to believe the person's actions were unlawful. The Delaware General Corporation Law further provides that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The certificate of incorporation of the registrant to be in effect upon the completion of this offering provides for the indemnification of the registrant's directors and officers to the fullest extent permitted under the Delaware General Corporation Law. In addition, the bylaws of the registrant to be in effect upon the completion of this offering require the registrant to fully indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of the registrant, or is or was a director or officer of the registrant serving at the registrant's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, to the fullest extent permitted by applicable law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for payments of unlawful dividends or unlawful stock repurchases or redemptions or (4) for any transaction from which the director derived an improper personal benefit. The registrant's certificate of incorporation to be in effect upon the completion of this offering provides that the registrant's directors shall not be personally liable to it or its stockholders for monetary damages for breach of fiduciary duty as a director and that if the Delaware General Corporation Law is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of the registrant's directors shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, the registrant has entered into separate indemnification agreements with each of the registrant's directors and certain of the registrant's officers which require the registrant, among other things, to indemnify them against certain liabilities which may arise by reason of their status as directors, officers or certain other employees.

The registrant expects to obtain and maintain insurance policies under which its directors and officers are insured, within the limits and subject to the limitations of those policies, against certain expenses in connection with the defense of, and certain liabilities which might be imposed as a result of, actions, suits or proceedings to which they are parties by reason of being or having been directors or officers. The coverage provided by these policies may apply whether or not the registrant would have the power to indemnify such person against such liability under the provisions of the Delaware General Corporation Law.

These indemnification provisions and the indemnification agreements entered into between the registrant and the registrant's officers and directors may be sufficiently broad to permit indemnification of the registrant's officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act of 1933, as amended.

The underwriting agreement between the registrant and the underwriters to be filed as Exhibit 1.1 to this registration statement provides for the indemnification by the underwriters of the registrant's directors and officers and certain controlling persons against specified liabilities, including liabilities under the Securities Act with respect to information provided by the underwriters specifically for inclusion in the registration statement.

**Item 7. Exemption from Registration Claimed.**

Not applicable.

**Item 8. Exhibits.**

Exhibit Number	Description	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
4.1	Specimen common stock certificate of the Registrant	S-1/A	333-221522	4.2	11/27/2017
4.2	2017 Equity Incentive Plan and forms of agreements thereunder	S-1/A	333-221522	10.3	11/27/2017
4.3	2017 Employee Stock Purchase Plan and form of agreement thereunder	S-1/A	333-221522	10.4	12/7/2017
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation				
23.1	Consent of Independent Registered Public Accounting Firm				
23.2	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (contained in Exhibit 5.1 hereto)				
24.1	Power of Attorney (contained on signature page hereto)				

**Item 9. Undertakings.**

A. The undersigned Registrant hereby undertakes that:

- (1) It will file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:
  - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act;
  - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
  - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement.

*Provided, however,* that paragraphs (A)(1)(i) and (A)(1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in this Registration Statement.

- (2) For the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) It will remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

- B. The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- C. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## EXHIBIT INDEX

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24.1	<a href="#">Power of Attorney (contained on signature page hereto)</a>				

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 12th day of March 2019.

### DENALI THERAPEUTICS INC.

By: /s/ Ryan J. Watts  
Ryan J. Watts, Ph.D.  
*President and Chief Executive Officer*

## POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Ryan J. Watts, Ph.D. and Steve E. Krognnes, and each of them, as his true and lawful attorney-in-fact and agent with full power of substitution, for him in any and all capacities, to sign any and all amendments to this registration statement on Form S-8 (including post-effective amendments), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact, proxy and agent 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 for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact, proxy and agent, or his substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement on Form S-8 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Ryan J. Watts</u> Ryan J. Watts, Ph.D.	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 12, 2019
<u>/s/ Steve E. Krognnes</u> Steve E. Krognnes	Chief Financial Officer and Treasurer <i>(Principal Financial and Accounting Officer)</i>	March 12, 2019
<u>/s/ Vicki Sato</u> Vicki Sato, Ph.D.	Chairperson of our Board of Directors	March 12, 2019
<u>/s/ Marc Tessier-Lavigne</u> Marc Tessier-Lavigne, Ph.D.	Director	March 12, 2019
<u>/s/ Douglas Cole</u> Douglas Cole, M.D.	Director	March 12, 2019
<u>/s/ Jennifer Cook</u> Jennifer Cook	Director	March 12, 2019
<u>/s/ Jay Flatley</u> Jay Flatley	Director	March 12, 2019
<u>/s/ Peter Klein</u> Peter Klein	Director	March 12, 2019
<u>/s/ Robert Nelsen</u> Robert Nelsen	Director	March 12, 2019
<u>/s/ David Schenkein</u> David Schenkein, M.D.	Director	March 12, 2019



March 12, 2019

Denali Therapeutics Inc,  
161 Oyster Point Blvd.  
South San Francisco, California 94080  
(650) 866-8548

**Re: Registration Statement on Form S-8**

Ladies and Gentlemen:

We have examined the Registration Statement on Form S-8 (the "Registration Statement") to be filed by Denali Therapeutics Inc., a Delaware corporation, with the Securities and Exchange Commission on or about the date hereof, in connection with the registration under the Securities Act of 1933, as amended, of (i) 4,757,573 shares of Common Stock reserved for issuance pursuant to the 2017 Equity Incentive Plan and (ii) 951,514 shares of Common Stock reserved for issuance pursuant to the 2017 Employee Stock Purchase Plan (which plans are referred to herein as the "Plans" and which shares of Common Stock are referred to herein as the "Shares").

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when issued and sold in the manner referred to in the Plans and pursuant to the agreements that accompany the Plans, will be legally and validly issued, fully paid, and nonassessable.

We consent to the use of this opinion as an exhibit to the Registration Statement, and further consent to the use of our name wherever appearing in the Registration Statement and any amendments thereto.

Very truly yours,

/s/ Wilson Sonsini Goodrich & Rosati, P.C.  
WILSON SONSINI GOODRICH & ROSATI  
Professional Corporation

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2017 Equity Incentive Plan and 2017 Employee Stock Purchase Plan of Denali Therapeutics Inc. of our report dated March 12, 2019, with respect to the consolidated financial statements of Denali Therapeutics Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2018, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Redwood City, California

March 12, 2019