FOIA Confidential Treatment Requested Pursuant to 17 C.F.R. §200.83

The entity requesting confidential treatment is:

Denali Therapeutics Inc.
151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080

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

CERTAIN PORTIONS OF THIS LETTER HAVE BEEN OMITTED FROM THE VERSION FILED VIA EDGAR. CONFIDENTIAL TREATMENT HAS BEEN REQUESTED WITH RESPECT TO THE OMITTED PORTIONS. INFORMATION THAT WAS OMITTED IN THE EDGAR VERSION HAS BEEN NOTED IN THIS LETTER WITH A PLACEHOLDER IDENTIFIED BY THE MARK "[*]."

November 15, 2017

VIA EDGAR AND OVERNIGHT DELIVERY

Securities and Exchange Commission
Division of Corporation Finance
Office of Healthcare & Insurance
100 F Street, N.E.
Washington, D.C. 20549-3720

Attn: Chris Edwards
Erin Jaskot
Keira Nakada
Jim Rosenberg

RE: Denali Therapeutics Inc.
Registration Statement on Form S-1
File No. 333-221522

Ladies and Gentlemen:

On behalf of our client, Denali Therapeutics Inc. (the "Company"), we submit this letter in response to comments received from the Division of Corporation Finance (the "Staff") of the Securities and Exchange Commission (the "Commission") by letter dated October 5, 2017 (the "Comment Letter"), relating to the Company's Registration Statement on Form S-1 (File No. 333-221522), originally confidentially submitted to the Commission on September 8, 2017 and originally filed by the Company

with the Commission on November 13, 2017 (the "Registration Statement"). In this letter, we are responding only to Comment 10 of the Comment Letter.

Because of the commercially sensitive nature of information contained herein, this submission is accompanied by the Company's request for confidential treatment for selected portions of this letter. The Company has filed a separate letter with the Office of Freedom of Information and Privacy Act Operations in connection with the confidential treatment request, pursuant to Rule 83 of the Commission's Rules on Information and Requests, 17 C.F.R. § 200.83. For the Staff's reference, we have enclosed a copy of the Company's letter to the Office of Freedom of Information and Privacy Act Operations, as well as a copy of this correspondence, marked to show the portions redacted from the version filed via EDGAR and for which the Company is requesting confidential treatment.

For the convenience of the Staff, we have recited the prior comment from the Staff in italicized type and have followed the comment with the Company's response.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Significant Judgments and Estimates
Stock-Based Compensation, page 94

10. We may have additional comments on your accounting for equity issuances including stock based compensation and convertible instruments. Once you have an estimated offering price, please provide us an analysis explaining the reasons for the differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price.

Price Range

To assist the Staff in its evaluation of stock compensation disclosures and certain other matters, the Company advises the Staff that the Company currently estimates a price range of $[*] to $[*] per share (the "Price Range") for the initial public offering (the "IPO") of the Company's common stock, resulting in a midpoint of the Price Range of $[*] per share (the "Midpoint Price"). The Price Range has been estimated based on a number of factors, including recent results from the Company's clinical trials and studies, developments in the Company's business, input received from the Company's "testing the waters meetings," the Company's currently contemplated Series B-2 preferred stock financing in November 2017 at $4.25 per share, current market conditions and input received from Goldman Sachs & Co. LLC, Morgan Stanley & Co. LLC and J.P. Morgan Securities LLC (the "Lead Underwriters"), including discussions that took place on November 10, 2017 among senior management of the Company, members of the board of directors of the Company, and representatives of the Lead Underwriters.

The Price Range does not take into account the current lack of liquidity for the Company's common stock and assumes a successful IPO with no weighting attributed to any other outcome for the Company's business, such as remaining a privately held company or being sold in an acquisition transaction. As is typical for initial public offerings, the Price Range was not derived using a formal determination of fair value, but was determined as a result of discussions among representatives of the Company's management, board of directors, and the Lead Underwriters. During these discussions, the parties considered quantitative factors, as well as non-quantitative factors, such as the valuations of recently completed public offerings and evaluating those issuers' respective stages of development as compared to ours, the current valuations of public companies at a similar stage of clinical development as the Company, and recent market conditions. Prior to November 10, 2017, the Lead Underwriters had not provided the Company with a specific price range.

Please note that the foregoing per-share amounts and the other per-share amounts set forth in this letter do not reflect the impact of an anticipated reverse stock split. The Company expects to include the Price Range, as adjusted for an anticipated reverse stock split, in an amendment to the Registration Statement that would shortly precede the commencement of the Company's road show process and the distribution of any preliminary prospectus relating to the IPO.

Additionally, the actual *bona fide* price range to be included in a subsequent amendment to the Registration Statement has not yet been determined and remains subject to adjustment based on factors outside of the Company's control. However, the Company believes that the actual *bona fide* price range will be within the Price Range. In addition, the actual price range to be included in such amendment will comply with the Staff's interpretation regarding the parameters of a *bona fide* price range.

Stock Option Grants and Common Stock Valuation

As stated in the Registration Statement, the Company has granted stock-based awards, consisting of stock options and restricted stock, to its employees, certain non-employee consultants and certain members of its board of directors. The Company measures stock-based compensation expense for restricted stock and stock options granted to its employees and directors on the date of grant and recognizes the corresponding compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. The Company has also granted stock options that vest in conjunction with certain performance and market conditions to certain key employees. At each reporting date, the Company evaluates whether the achievement of the performance or market condition is probable. Compensation expense is recorded over the appropriate service period based on management's assessment of accomplishing each performance or market provision or the occurrence of other events that may have caused the awards to accelerate and vest. The Company accounts 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 non-employee options with vesting conditions is affected in each reporting period by changes in the estimated fair value of common stock. The Company adjusts for actual forfeitures as they occur.

The Registration Statement describes the Company's use of the Black-Scholes option-pricing model for the purpose of calculating the estimated fair value of the stock options. In the preceding twelve months, the Company's board of directors, with input from management, determined the estimated fair value of the Company's common stock to be $1.32 as of December 31, 2016, $1.62 as of March 31, 2017, $2.40 as of June 30, 2017, and $2.91 as of September 30, 2017, after considering valuation reports from an independent third-party valuation specialist as well as the other objective and subjective factors described in the Registration Statement. Set forth below in this letter is a discussion of each valuation and option grant in the preceding twelve months, along with a comparison of the estimated fair value of the Company's common stock at September 30, 2017 to the Midpoint Price.

The following table presents a summary of equity awards in the preceding twelve months:

Grant date	Type of award	Number of shares	Exercise price of options per share	Estimated fair value of common stock per share on grant date
11/10/16	Options	555,000	$ 1.32	$ 1.32
12/9/16	Options	1,102,500	$ 1.32	$ 1.32
1/12/17	Options	295,000	$ 1.32	$ 1.32
2/10/17	Options	507,500	$ 1.32	$ 1.32
3/8/17	Options	2,250,000	$ 1.32	$ 1.32
3/10/17	Options	1,010,000	$ 1.32	$ 1.32
5/19/17	Options	305,000	$ 1.62	$ 1.62
6/9/17	Options	555,000	$ 1.62	$ 1.62
8/22/17	Options	1,320,000	$ 2.40	$ 2.40
9/10/17	Options	248,000	$ 2.40	$ 2.40
11/2/17	Options	806,000	$ 2.91	$ 2.91

September 30, 2016

In preparing the September 30, 2016 valuation, the Company determined the enterprise value using the option pricing method ("OPM"). The resulting estimated fair value of the Company's common stock was $1.32, selected from a valuation range of $1.28-1.32 per share, and consistent with the valuation price previously determined as of June 30, 2016.

Under the OPM, the Company used a back-solve method so that the enterprise value equaled the contemplated value of the Company determined by the Series B-1 preferred stock financing transaction with both existing and new third-party investors, which closed in June 2016 and August 2016. A discount for lack of marketability ("DLOM") of 23% and 25% was applied to derive the high and low points of the valuation price range, respectively. The DLOMs used were derived from the then-current estimates of the time to a liquidity event made by the Company's board of directors, with input from the Company's senior management.

November 10, 2016, December 9, 2016 and January 12, 2017 Grants

At each grant date listed above, the Company's board of directors determined that the estimated fair value of the Company's common stock was $1.32 per share in consideration of the valuation analysis as of September 30, 2016 and the other objective and subjective factors described in the Registration Statement. As part of this determination, the Company's board of directors concluded that no significant internal or external value-generating events had taken place between the September 30, 2016 valuation date and each grant date listed above.

December 31, 2016 Valuation

In preparing the December 31, 2016 valuation, the Company determined the enterprise value using the OPM. The resulting estimated fair value of the Company's common stock was $1.32, selected from a valuation range of $1.30-1.33 per share, and consistent with the valuation price previously determined as of September 30, 2016.

Under the OPM, the Company used a back-solve method so that the enterprise value equaled the contemplated value of the Company determined by the Series B-1 preferred stock financing transaction with both existing and new third-party investors, which closed in June 2016 and August 2016. A DLOM of 21% and 23% was applied to derive the high and low points of the valuation price range, respectively. The DLOMs used were derived from the then-current estimates of the time to a liquidity event made by the Company's board of directors, with input from the Company's senior management.

February 10, 2017, March 8, 2017 and March 10, 2017 Grants

At each grant date listed above, the Company's board of directors determined that the estimated fair value of the Company's common stock was $1.32 per share in consideration of the valuation analysis as of December 31, 2016 and the other objective and subjective factors described in the Registration Statement. As part of this determination, the Company's board of directors concluded that no significant internal or external value-generating events had taken place between the December 31, 2016 valuation date and each grant date listed above.

March 31, 2017 Valuation

In preparing the March 31, 2017 valuation, the Company allocated enterprise value using a hybrid of the OPM and the probability-weighted expected return model (the "PWERM") that incorporates three allocation methods: the OPM utilizing a market multiple approach to estimate the Company's equity value, an IPO model, and an OPM back-solve method to a potential private round financing. Both the OPM and the PWERM utilize the enterprise value determined using market multiple approaches. The IPO scenario was assigned a weight of 5%, the OPM scenario was assigned a weight of 70%, and the potential private round back-solve scenario was assigned a weight of 25%. The resulting estimated fair value of the Company's common stock was $1.62 per share.

The IPO scenario assumed that the Company would complete an IPO within 18 months, which represented management's then-current best estimate of time to IPO at that time. For the OPM scenario, the Company used the then-current capitalization table to solve for the Company's total equity value. For the OPM back-solve scenario, the Company's estimated private round price was used to solve for the

Company's total equity value. A DLOM of 20% was applied to the private round back-solve, a DLOM of 28% was applied to the OPM, and a DLOM of 30% was applied to the IPO scenario. The DLOMs used for all scenarios were derived from the then-current estimates of the time to a liquidity event made by the Company's board of directors, with input from the Company's senior management.

May 19, 2017 and June 9, 2017 Grants

At each grant date listed above, the Company's board of directors determined that the estimated fair value of the Company's common stock was $1.62 per share in consideration of the valuation analysis as of March 31, 2017 and the other objective and subjective factors described in the Registration Statement. As part of this determination, the Company's board of directors concluded that no significant internal or external value-generating events had taken place between the March 31, 2017 valuation date and each grant date listed above.

June 30, 2017 Valuation

In preparing the June 30, 2017 valuation, the Company allocated enterprise value using a hybrid of the OPM and the PWERM that incorporates four allocation methods: the OPM utilizing a market multiple approach to estimate the Company's equity value, two IPO models (one with an IPO price assuming the Company reached a strategic partnership agreement in advance of an IPO, and one assuming that the Company did not), and an OPM back-solve method to a potential private round financing. Both the OPM and the PWERM utilize the enterprise value determined using market approaches. The IPO without a partnership scenario was assigned a weight of 30%, the IPO with a partnership was assigned a weight of 10%, the OPM scenario was assigned a weight of 50%, and the private round back-solve scenario was assigned a weight of 10%. The increased probability ascribed to the two IPO scenarios reflected, among other things, the Company's efforts during the quarter to prepare for a potential IPO, including the selection of the Lead Underwriters and commencement of drafting of the Registration Statement, as well as the Company's plans to confidentiality submit the Registration Statement to the Commission in the third quarter of 2017. The resulting estimated fair value of the Company's common stock was $2.40 per share (the "June Valuation Price").

The IPO without a partnership scenario assumed that the Company would complete an IPO within six months, while the IPO with partnership scenario assumed that the Company would complete an IPO within 12 months. For the OPM scenario, the Company used the current capitalization table to solve for the Company's total equity value. For the OPM back-solve scenario, the Company's estimated private round price was used to solve for the Company's total equity value. A DLOM of 20% was applied to the private round financing back-solve, a DLOM of 25% was applied to the OPM, and a DLOM of 30% was applied to the IPO scenarios. The DLOMs used for all scenarios were derived from the then-current estimates of the time to a liquidity event made by the Company's board of directors, with input from the Company's senior management.

August 22, 2017 and September 10, 2017 Grants

At each grant date listed above, the Company's board of directors determined that the fair value of the Company's common stock was $2.40 per share in consideration of the valuation analysis as of June 30, 2017 and the other objective and subjective factors described in the Registration Statement. As part of this determination, the Company's board of directors concluded that no significant internal or external value-

generating events had taken place between the June 30, 2017 valuation date and each grant date listed above.

September 30, 2017 Valuation

In preparing the September 30, 2017 valuation, the Company allocated enterprise value using a hybrid of the OPM and the PWERM that incorporates four allocation methods: the OPM utilizing a market multiple approach to estimate the Company's equity value, two IPO models (one with an IPO price assuming the Company reaches a strategic partnership agreement in advance of an IPO, and one assuming that the Company does not), and an OPM back-solve method to a potential private round financing. Both the OPM and the PWERM utilize the enterprise value determined using market approaches. The IPO without a partnership scenario was assigned a weight of 30%, the IPO with a partnership was assigned a weight of 15%, the OPM scenario was assigned a weight of 40%, and the private round financing back-solve scenario was assigned a weight of 15%. The increased probability ascribed to the IPO scenarios reflected, among other things, the Company's confidential submission of the Registration Statement to the Commission on September 8, 2017. The increased probability ascribed to the private round financing back-solve scenario reflected, among other things, the Company's identification of a potential lead investor for a private round financing. The resulting estimated fair value of the Company's common stock was $2.91 per share (the "September Valuation Price").

The IPO without a partnership scenario assumed that the Company would complete an IPO within three months, while the IPO with partnership scenario assumed that the Company would complete an IPO within nine months. For the OPM scenario, the Company used the then-current capitalization table to solve for the Company's total equity value. For the OPM back-solve scenario, the Company's estimated private round financing price was used to solve for the Company's total equity value. A DLOM of 20% was applied to the private round financing back-solve, and a DLOM of 25% was applied to all other scenarios. The DLOMs used for all scenarios were derived from the then-current estimates of the time to a liquidity event made by the Company's board of directors, with input from the Company's senior management.

November 2, 2017 Grants

On November 2, 2017, the Company granted options to purchase 806,000 shares of common stock. The Company has not granted any other equity awards since November 2, 2017. At November 2, 2017, the Company's board of directors determined that the estimated fair value of the Company's common stock was $2.91 per share in consideration of the valuation analysis as of September 30, 2017 and the other objective and subjective factors described in the Registration Statement. As part of this determination, the Company's board of directors concluded that no significant internal or external value-generating events had taken place between the September 30, 2017 valuation date and November 2, 2017.

Comparison of the September Valuation Price and the Midpoint Price

As is typical in an initial public offering, the estimated price range for the offering was not derived using a formal determination of estimated fair value, but was determined primarily by negotiation between the Company and the Lead Underwriters. Among the factors that were considered in setting the Price Range were the following:

- an analysis of the typical valuation ranges seen in recent initial public offerings for clinical-stage biopharmaceutical companies;

- the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies;
- an assumption that there would be a receptive public trading market for pre-commercial, clinical-stage biopharmaceutical companies such as the Company; and
- an assumption that there would be sufficient demand for the Company's common stock to support an offering of the size contemplated by the Company.

The Midpoint Price exceeds the September Valuation Price of $2.91 per share, which was determined as described above, by $[*] per share. The Company respectfully submits that the difference between the September Valuation Price and the Midpoint Price is primarily attributable to the following factors:

- Feedback from potential investors following the "testing the waters" meetings that occurred between October 25, 2017 and November 3, 2017.
- On November 6, 2017, the Company and a certain outside lead investor reached an agreement in principle on the sale of shares of the Company's Series B-2 preferred stock at $4.25 per share (the "Series B-2 Financing"). The Series B-2 Financing is currently expected to be completed by November 20, 2017. Given the arm's length nature of and due diligence associated with the Series B-2 Financing, the Company and the Lead Underwriters consider this financing round to be a meaningful indicator of total equity value.
- The methodology for determining the September Valuation Price incorporated multiple liquidity scenarios, not all of which allocate value to the Company's stockholders on a fully diluted, as-converted to common stock basis. The Midpoint Price assumes with 100% probability that the Company completes an IPO, in connection with which all of the Company's convertible preferred stock will be converted into common stock. This factor is significant because the holders of the Company's preferred stock currently enjoy substantial economic rights and preferences over the holders of the Company's common stock, including (i) the right to receive dividends prior to any dividends declared or paid on any shares of the Company's common stock and (ii) liquidation payments in preference to holders of the Company's common stock. The Midpoint Price assumes the conversion of all of the Company's convertible preferred stock upon the completion of its IPO. The corresponding elimination of the preferences and rights enjoyed by the holders of such preferred stock results in a higher valuation.
- The successful completion of the IPO would strengthen the Company's balance sheet, provide access to public equity, increase the Company's strategic flexibility and provide enhanced operational flexibility to potentially obtain regulatory approval for and commercialize its product candidates.
- The valuation report prepared by management and the Company's third-party valuation specialist in determining the September Valuation Price utilized a quantitative methodology to determine the estimated fair value of the Company's common stock, which may differ from the more qualitative and subjective methodology used by some public market investors to determine the price that they are willing to pay in the IPO. The quantitative methods used in the valuation report

are both commonly accepted and applied in the valuation community, and are consistent with the methods and guidance in the AICPA Practice Guide on Valuing Equity Securities.

- The inclusion of other factors by the Lead Underwriters in their valuation models of indicated market values in determining the Price Range, which factors may not have been expressly considered in the Company's valuations as a private company, or are not quantifiable in the Company's valuation models as a private company, or are not objectively determinable by the Company.
- The Price Range represents a future price for shares of the Company's common stock that, if issued in the IPO, will be immediately freely tradable in a public market, whereas the estimated fair value of the Company's common stock as of the November 2, 2017 grant date represents a contemporaneous estimate of the fair value of shares that were then illiquid, might never become liquid and, even if an IPO were successfully completed, would remain illiquid at least until the expiration of the 180-day lockup period following the IPO. This illiquidity accounts for a substantial portion of the difference between the September Valuation Price and the Midpoint Price.
- The increase in the value of the Company's common stock subsequent to the September 30, 2017 valuation reflects the effects detailed above. However, the Company also notes that it has made significant progress in its business from the time of the September Valuation Price through the determination of the Price Range. These developments include the following:
  - During the fourth quarter of 2017, the Company received further favorable clinical safety data from the Company's ongoing, blinded Phase 1 clinical trials in healthy volunteers for DNL 201. Based on this data, the Company expects to request in November 2017 that the FDA increase the exposure cap to permit additional dose escalation in this trial.
  - The Company received a written indication on November 13, 2017 that its CTA to the Netherlands Health Authority for DNL151 had been approved without any amendments to its submitted proposal. The CTA for DNL151 allows for doses that enable exposures that the Company believes will achieve adequate inhibition of LRRK2 activity.
  - During the fourth quarter of 2017, the Company received initial validating data from an ongoing study in nonhuman primates designed to show proof of concept for its ATV platform. These data demonstrate a robust and sustained pharmacodynamic effect in the brain after intravenous dosing of an ATV-enabled antibody, while a standard antibody had minimal pharmacodynamic effect. The Company believes these *in vivo* proof of concept data in nonhuman primates provide further support for the translatability of its ATV platform for human studies.
  - In November 2017, the Company demonstrated robust brain uptake of its ETV:IDS fusions in its human TfR knock-in mouse model.
  - In November 2017, the Company took various steps to expand its patent portfolio and intellectual property protection for certain of its core programs:

- ATV/ETV Programs: The Company filed multiple new provisional patent applications on November 8, 2017 relating to its ATV/ETV programs.
- LRRK2: One of Genentech's European patent cases, which covers both DNL201 and DNL151, has been granted and validated in a large number of European countries, resulting in an increased number of granted foreign patents related to DNL201 and DNL151.
- RIPK1: The Company's non-provisional patent application covering DNL747 has been allowed and was issued on November 14, 2017. The Company has also filed a continuation application to broaden the scope of its patent application to further cover DNL747.

In conclusion, the Company respectfully submits that the differences between the estimated IPO price (i.e., the Midpoint Price), the latest valuation (i.e., the September Valuation Price) and the prior valuations (i.e., the June Valuation Price) are reasonable in light of all of the considerations outlined above. In addition, the Company will continue to update its disclosure for all equity-related transactions through the effective date of the Registration Statement. Based on the foregoing, the Company respectfully seeks confirmation that the Staff has no further comments with respect to the matters discussed in this letter.

* * *

If you require any additional information on the matters contained in this letter, or if we can provide you with any other information that will facilitate your review, please advise us at your earliest convenience. You may reach me at (650) 849-3223 or tjeffries@wsgr.com.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

/s/ Tony Jeffries

Tony Jeffries

cc: Ryan J. Watts, Ph.D., Denali Therapeutics Inc.
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