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November 13, 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

Attention: Chris Edwards
Erin Jaskot
Keira Nakada
Jim Rosenberg

Re: Denali Therapeutics Inc.
Amendment No. 1 to the Draft Registration Statement on Form S-1
Submitted on October 13, 2017
CIK No. 0001714899

Ladies and Gentlemen:

On behalf of our client, Denali Therapeutics Inc. ("**Denali**" or the "**Company**"), we submit this letter in response to comments from the staff (the "**Staff**") of the Securities and Exchange Commission (the "**Commission**") contained in its letter dated October 24, 2017 (the "**Comment Letter**"), relating to the above referenced Draft Registration Statement on Form S-1 (the "**Registration Statement**"). We are concurrently submitting via EDGAR this letter and a revised draft of the Registration Statement. For the Staff's reference, we have included both a clean copy of the Registration Statement and a copy marked to show all changes from the version confidentially submitted on October 13, 2017.

In this letter, we have recited the comments from the Staff in italicized, bold type and have followed each comment with the Company's response. Except for the page references contained in the comments of the Staff, or as otherwise specifically indicated, page references herein correspond to the page of the revised draft of the Registration Statement.

Amendment No. 1 to the Draft Registration Statement on Form S-1

Our Strategy, page 2

1. We note your response to prior comment number 3. Please revise this section to include the potential limitations to your strategy to develop patient selection biomarkers for your programs, including the limitation on the size of the potential market for your products and, if applicable, that the FDA may require you to conduct clinical trials on a broader patient population prior to approving your product candidates.

The Company respectfully advises the Staff that it has revised the disclosure on pages 4 and 114 of the Registration Statement to address the Staff's comment to include disclosure of the potential limitations to the Company's strategy to develop patient selection biomarkers for the Company's programs. The Company has included disclosure in the Registration Statement noting that, in certain indications, regulatory approval may limit the market of a product candidate to target patient populations when patient selection biomarkers are used. In these indications, regulatory authorities may require the Company to run additional clinical trials prior to expanding the label for approval that includes a broader patient population.

Our Programs, page 4

2. ***We note your response to our prior comment 4. Please include disclosure in your prospectus summary indicating that DNL201 is subject to a partial clinical hold. Because DNL201 is your most advanced program and you disclose in the prospectus summary that it is in Phase 1 development, the disclosure should be balanced to also inform investors that this program is subject to a partial clinical hold.***

The Company respectfully advises the Staff that it has revised the disclosure on page 5 of the Registration Statement to address the Staff's comment to include disclosure in the prospectus summary indicating that DNL201 is subject to a partial clinical hold.

Risk Factors

We may encounter significant delays in our clinical trials..., page 19

3. ***We note your response to our prior comment 8 and your revised disclosure that if the FDA does not lift the exposure cap you will not be able to evaluate doses and exposures that would potentially achieve higher degrees of LRRK2 kinase inhibition. Please further revise your disclosure to explain the impact of being unable to achieve higher degrees of LRRK2 kinase inhibition, including any impact on the clinical development of DNL201 and whether it could materially impact the prospects for approval of DNL201. To clarify, please explain your ability to continue with clinical trials if the FDA does not lift the exposure cap, and, to the extent you can continue, any material impact on your clinical trials.***

The Company respectfully advises the Staff that it has revised the disclosure on page 20 of the Registration Statement to address the Staff's comment to include disclosure explaining the impact of being unable to achieve higher degrees of LRRK2 kinase inhibition. The Company has included disclosure in the Registration Statement noting that, if the FDA does not lift or change the exposure cap currently imposed, this may negatively impact the development of DNL201 if the Company determines that it must achieve higher degrees of LRRK2 kinase inhibition than what can be achieved with the current exposure cap. If the Company makes such determination and the FDA does not lift the exposure cap, the Company may be unable to continue or complete its clinical trial of DNL201. Any inability to continue or complete the clinical trial of DNL201, as a result of the partial clinical hold or otherwise, will delay or terminate the Company's clinical development plans for DNL201, may require the Company to incur additional clinical development costs and could impair the Company's ability to ultimately obtain FDA approval for DNL201.

Business, page 100

4. ***We note your response to prior comment number 11. Please disclose the number of studies involved and that the studies were designed to demonstrate proof-of-concept of the ATV platform technology.***

The Company respectfully advises the Staff that it has revised the disclosure on pages 4, 103 and 110 of the Registration Statement to address the Staff's comment to disclose the number of studies involved and that the studies were designed to demonstrate proof of concept for the ATV platform technology.

* * * *

Please direct any questions with respect to this confidential submission to 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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