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Wilson Sonsini Goodrich & Rosati
PROFESSIONAL CORPORATION

November 27, 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.
Registration Statement on Form S-1
Filed on November 13, 2017
CIK No. 0001714899
File No. 333-221522

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 November 20, 2017 (the "**Comment Letter**"), relating to the above referenced 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 filed on November 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.

Registration Statement on Form S-1

Business

RIPK1 Inhibitor Program, page 127

1. We note your disclosure of immune-mediated histopathology findings during the 28-day GLP study of DNL747 in monkeys. Please revise your disclosure to explain which doses you tested during the study, the doses at which such findings occurred, the length of time from first administering DNL747 until such findings were observed, and the dose given to the animal that was euthanized. Please also revise to explain the significance of the safety margins

discussed in this section. In addition, please revise your disclosure in Figure 24 on page 130, including the labels used on the graphs, to explain which doses were tested and the reduction in p-RIPK1 at such doses. Please also revise your Summary to include a discussion of the histopathology findings for DNL747.

The Company respectfully advises the Staff that it has revised the disclosure on pages 5, 6, 131,132 and 133 of the Registration Statement to address the Staff's comment and provide the additional disclosure requested. Specifically, the Company has revised the disclosure on page 132 to clarify that the Company tested doses of 20 mg/kg BID to 500 mg/kg BID during the 28-day GLP study of DNL747 in cynomolgus monkeys, and the disclosure now specifically identifies the doses at which specific findings occurred and the dose given to the animal that was euthanized. The Company has also clarified, on page 132, that the timing of observation was on histopathology (28 days) and clinical findings in the recovery period.

Additionally, the Company has revised the disclosure on pages 6 and 133 to further clarify the significance of the safety margins. Because IC90 coverage at trough should allow for robust inhibition of RIPK1 activity, the Company believes that these margins provide an adequate safety window to explore a robust pharmacodynamic range in humans. The Company intends to file a CTA with a protocol-defined maximum exposure not to exceed two fold over that which enables 90% inhibition at trough.

The Company has also revised its disclosure in Figure 24 on page 131 to clarify that this is an *in vitro* experiment. Because Figure 24 is describing *in vitro* data with a dose response curve with *in vitro* drug concentrations, the Company is unable to provide a specific dose that would correspond with *in vivo* dose. However, the Company has modified the labels in Figure 24 to clarify that the ratio depicted is a percent reduction in p-RIPK1 and IL-1b, respectively. The Company has also provided additional disclosure on page 131 to provide further context for how the range of concentrations studied in the *in vitro* experiment compares to exposures tested in the rat pilot toxicity studies.

Finally, the Company has revised the disclosure on pages 5 and 6 of the Registration Statement to provide a discussion of the histopathology findings for DNL747.

Notes to Consolidated Financial Statements

Unaudited Pro Forma Information, page F-1

2. Please tell us whether you expect to meet the IPO conditions described on page F-24 to trigger the automatic conversion of the preferred shares or you have received the enforceable written consent of the holders of at least a majority of the outstanding preferred stock to assume the automatic conversion upon the IPO.

The Company respectfully advises the Staff that it currently expects that the price range for its initial public offering of the Company's common stock will be within the price range (the "**Price Range**") previously submitted by the Company to the Staff by a letter dated November 15, 2016. The Company has obtained the affirmative written consent of the holders of a majority of its outstanding shares of preferred stock to automatically convert all shares of preferred stock into common stock immediately prior to the completion of an initial public offering, provided that the offering price per share is not less

than the bottom of the Price Range (subject to appropriate adjustment in the event of any stock split). The Company further submits to the Staff that it would not seek to complete an initial public offering absent the above-mentioned election of the holders of preferred stock or other binding arrangement to cause the existing preferred stock to convert to common stock.

* * * *

Please direct any questions with respect to this response 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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