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

DIVISION OF
CORPORATION FINANCE

October 24, 2017

Ryan J. Watts, Ph.D.
President and Chief Executive Officer
Denali Therapeutics Inc.
151 Oyster Point Blvd., 2nd Floor
South San Francisco, California 94080

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

Dear Dr. Watts:

We have reviewed your amended draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

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 biomakers 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.

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.

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.

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.

You may contact Keira Nakada at (202) 551-3659 or Jim Rosenberg at (202) 551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Chris Edwards at (202) 551-6761 or Erin Jaskot at (202) 551-3442 with any other questions.

Division of Corporation Finance
Office of Healthcare & Insurance

cc: Tony Jeffries