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

DIVISION OF
CORPORATION FINANCE

October 5, 2017

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

Re: Denali Therapeutics Inc.
Draft Registration Statement on Form S-1
Submitted on September 8, 2017
CIK No. 0001714899

Dear Dr. Watts:

We have reviewed your 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.

Draft Registration Statement on Form S-1

Prospectus Summary, page 1

1. Please balance the statement that you discover and develop therapeutics to defeat degeneration with the fact that you are a clinical stage biopharmaceutical company and that your lead product candidate is in Phase 1 clinical development.

2. Please clarify the meaning of any significant scientific or technical terms the first time they are used in the prospectus in order to ensure that lay readers will understand the disclosure. For example, and without limitation, please define each of the following at their first use in this section or where appropriate in the prospectus:

   - biomarkers
   - kinase
   - RNA
   - proteinopathy
   - metabolic homestasis
   - reagents and assays
   - IDS
   - CSF
   - PK/PD

   Further, we note your use of the term degenogenes. Please tell us whether this is a commonly used scientific term or whether it is a term you developed. To the extent you developed this term, please clearly state this in your disclosure.

Our Strategy, page 2

3. We note your discussion of biomarker-driven development and your intention to select the "right" patient population. Please explain whether this approach will limit the potential market for your product candidates as it appears your product candidates may only be tested on a subset of patients with the disease indications you are targeting.

Our Programs, page 4

4. Please revise the pipeline chart on page 5 and 101 to indicate the three phases of clinical development and that DNL201 is in the beginning of Phase 1. Please also indicate that the Phase 1 trial is subject to a partial clinical hold instituted by the FDA, including the circumstances leading to the clinical hold.

5. We note your statement that data from your Phase 1 study for DNL201 will, if positive, demonstrate your ability to safely deliver DNL201 to the brain and drive therapeutic efficiency. Safety and efficacy determinations are solely within the FDA's authority. As your product candidate has not received FDA approval, it is premature to state that Phase 1 data will show that it is safe or effective.

6. Please balance your disclosure that you have a broad patent portfolio supporting your core programs with the fact that you do not own or in-license any issued patents relating to certain of your antibodies and enzymes and certain aspects of your BBB platform technology.

Implications of Being an Emerging Growth Company, page 7

7. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

Risk Factors
We may encounter substantial delays in our clinical trials . . ., page 19

8. Please disclose the particular findings that led to the FDA's institution of a partial clinical hold in your Phase 1 trial of DNL201. Please also state the anticipated impact on the clinical development of DNL201 if the FDA does not lift or change the exposure cap. Please also disclose, to the extent material, any potential adverse effect of a similar exposure cap in your DNL151 trial, given that you plan to proactively propose such a cap.

Use of Proceeds, page 70

9. It appears from your disclosure that the proceeds from the offering will not be sufficient to fund development of your product candidates through regulatory approval and commercialization. Please revise to make this clear and disclose the sources of other funds needed to reach regulatory approval and commercialization for each product candidate. Refer to Instruction 3 to Item 504 of Regulation S-K.

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.

Business, page 100

11. We note your statement on page 102, and elsewhere in the prospectus, that an antibody engineered with your ATV technology demonstrated over 20-fold greater brain penetration than a control antibody not enabled by the technology. Please balance your disclosure by indicating whether you have consistently demonstrated such an increase in brain penetration throughout your studies, or if this is a single incident limited to this study. To the extent that you have achieved materially different increases in brain penetration, please also disclose those results.

Intellectual Property, page 139

12. Please expand your disclosure of your patents licensed from F-star and VIB and the patents covering DNL151 to discuss the type of patent protection you have (e.g., composition of matter, use or process).

Scientific Advisory Board, page 159

13. Please expand your disclosure to clarify how and to what extent members of the advisory board are compensated.

Notes to Consolidated Financial Statements
5. License and Collaboration Agreements
F-Star, page F-15

14. On page F-18, you state that the upfront payments of $0.5 million and $5.5 million and the obligation to fund certain future research costs represent your maximum exposure to loss under the arrangements with F-star. Please tell us why you do not consider the technical milestone payments for each Accepted Fcab Target and monthly exclusivity fees for each Accepted Fcab Target in your exposure under the agreement. In this regard, your upfront payment included selection of the first Accepted Fcab Target.

General

15. We note that you have requested confidential treatment for agreements that will be filed as exhibits to the registration statement. We will send any comments on your application for confidential treatment under separate cover.

16. Please provide us proofs of all graphics, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

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