



DIVISION OF  
CORPORATION FINANCE

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

November 20, 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: Registration Statement on Form S-1**  
**Filed November 13, 2017**  
**File No. 333-221522**

Dear Dr. Watts:

We have reviewed your amended 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 amending your registration statement and providing the requested information. 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 any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments. Unless we note otherwise, our references to prior comments are to comments in our October 24, 2017 letter.

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

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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.

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.

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 Christopher 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