

[LEXICON PHARMACEUTICALS, INC. LETTERHEAD]

February 2, 2017

Securities and Exchange Commission
Division of Corporate Finance
100 F Street, N.E.
Washington, D.C. 20549

Attention: Mr. Jim Rosenberg
Division of Corporate Finance
Office of Healthcare and Insurance

Re: Lexicon Pharmaceuticals, Inc.
Form 10-K for the Year Ended December 31, 2015
Filed March 11, 2016 and Amended June 14, 2016
File No. 000-30111

Dear Mr. Rosenberg:

On behalf of Lexicon Pharmaceuticals, Inc., we have set forth our amended response to one of the comments received from the Securities and Exchange Commission's staff regarding our annual report on Form 10-K for the year ended December 31, 2015 reflecting changes discussed in telephonic conversations with the staff on January 18, 2017 and February 1, 2017.

Form 10-K for the Year Ended December 31, 2015

Notes to Consolidated Financial Statements

16. Collaboration and License Agreements

Sanofi, page F-20

1. Regarding amounts that you are eligible to receive from Sanofi of up to an aggregate of \$430 million upon the achievement of specified development and regulatory milestones and up to an aggregate of \$990 million upon the achievement of specified sales milestones, please:
 - Clarify for us which milestones meet the definition of a milestone in ASC 605-28-20.
 - Provide for us each milestone meeting the definition in ASC 605-28-20 the information required by ASC 605-28-50-2.b.c.d. and e.
 - Tell us your accounting policy for recognizing non-substantive milestones and milestones that do not meet the definition in ASC 605-28-20.

Response: In the Sanofi agreement, there are (a) three different objectively-based development milestones that total \$210 million, (b) four different regulatory milestones that total \$220 million, and (c) six different commercial milestones that total \$990 million.

Upon entering into the agreement with Sanofi, we reviewed each milestone, and we believe that each development and regulatory milestone meets the definition of a milestone in ASC 605-28-20. For each milestone, there is substantive uncertainty at the inception of the arrangement that the event will be achieved; each event can only be achieved in whole or in part by our performance (in that regard, Lexicon is responsible for performing and funding all of the clinical development activities relating to type 1 diabetes; for funding a significant portion, up to \$100 million, of the clinical development activities relating to type 2 diabetes; and for reviewing development plans and reports and jointly overseeing all development activities performed under the collaboration by participating with Sanofi on the joint steering committee and the development and regulatory committee) or a specific outcome resulting from our performance; and achievement of the event results in additional payments being due to Lexicon. As a result, each development and regulatory milestone meets all of the criteria set forth in ASC 605-28-20. The commercial milestones do not meet the definition of a milestone, and therefore will not be treated as milestones under generally accepted accounting principles and will instead be accounted for as royalties.

Each of the development and regulatory milestones also meets the definition of substantive set forth in ASC 605-28-25-2. First, each of the development and regulatory milestones is commensurate with either 1) Lexicon's performance to achieve the milestone, or 2) the enhancement of the value of the delivered item as a result of a specific outcome resulting from Lexicon's performance to achieve the milestone. The development and regulatory milestones are triggered by clinical trial and regulatory outcomes, respectively, that enhance the value of the licensed product. Each of these milestones were negotiated between Lexicon and Sanofi with the intent of assigning the commensurate value to each of the milestones in order to appropriately reward Lexicon for its performance to achieve each milestone and the additional value attributed to the licensed product as a result of such milestones. Second, each of the development and regulatory milestones is non-refundable once received, and therefore contingent solely on Lexicon's past performance. Finally, each milestone payment is reasonable relative to the effort and risk involved as well as relative to all of the other deliverables and payment terms within the arrangement. As a result, each development and regulatory milestone meets all of the criteria required to be considered substantive.

The commercial milestones are achieved based on levels of sales, and they are designed to reward Lexicon for additional commercial value attributed to the licensed product evidenced by high volumes of sales. Commercial milestones will be accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria were met.

None of the referenced milestones have been earned to date; therefore, no disclosure was made for the year ended December 31, 2015, and no revenue relating to these milestones was earned during the year ended December 31, 2016. As we earn the milestones, we plan to disclose the amount and nature of the milestones recognized during each period.

We considered the guidance in ASC 605-28-50-2 regarding the disclosure required for milestones, and we have aggregated the milestones as indicated below. We considered disclosing each specific milestone outlined in the agreement; however, taking into account (a) the significant level of uncertainty about achievability and timing of the milestones and (b) our belief that the proposed aggregated disclosure provides investors with sufficient detail (both

with respect to the milestone amounts and the underlying milestone events) to properly understand the Sanofi agreement and assess the potential impact of such milestones on our business and financial condition, we determined that the specifics of each milestone were not meaningful or useful to the users of the financial statements in making an investment decision. We acknowledge the Staff's comment, and in future filings beginning in the Form 10-K for the year ended December 31, 2016, we will disaggregate the development and regulatory milestones in our disclosures. We propose to disclose the following in Footnote 16, Collaboration and License Agreements, with the additional passages that were not included in the Form 10-K for the year ended December 31, 2015 underlined:

Under the Sanofi Agreement, Sanofi paid Lexicon an upfront payment of \$300 million. In addition, Lexicon is eligible to receive from Sanofi (a) up to an aggregate of \$110 million upon the achievement of two development milestones relating to the achievement of positive results in certain Phase 3 clinical trials in type 2 diabetes patients, with such aggregate amount being predominantly allocated to one of the two development milestones, (b) up to an aggregate of \$220 million upon the achievement of four regulatory milestones relating to the first commercial sale following regulatory approval of sotagliflozin for type 1 and type 2 diabetes, respectively, in each of the United States and Europe, of which two milestones representing the substantial majority of such aggregate amount relate to type 2 diabetes and the remaining two milestones relate to type 1 diabetes, (c) \$100 million upon the achievement of a milestone based on the results of an outcomes study in type 2 diabetes patients, the completion of which would likely occur after initial regulatory approval, and (d) up to an aggregate of \$990 million upon the achievement of six commercial milestones that will be achieved upon reaching specified levels of sales. The Company believes that each of the development and regulatory milestones under the Sanofi Agreement is substantive. Due to the uncertainty surrounding the achievement of the future development and regulatory milestones, these payments will not be recognized as revenue unless and until they are earned, as the Company is not able to reasonably predict if and when the milestones will be achieved. Commercial milestones, which are not encompassed within the definition of milestones under generally accepted accounting principles, will be accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria were met.

If you have any further questions or require additional information, please do not hesitate to contact me at (281) 863-3321.

Very truly yours,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
*Executive Vice President,
Corporate and Administrative Affairs, and
Chief Financial Officer*