

[LEXICON PHARMACEUTICALS, INC. LETTERHEAD]

January 5, 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 responses to the comments received from Securities and Exchange Commission's staff in its December 21, 2016 letter regarding our annual report on Form 10-K for the year ended December 31, 2015. For your convenience, we have listed our responses in the same order as the comments were presented and have repeated each comment prior to the response.

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

Notes to Consolidated Financial Statements

2. Summary of Significant Accounting Policies

Revenue Recognition, page F-9

1. Please tell us how your criteria for milestone being substantive as disclosed on page F-9 complies with ASC 605-28-25-2.

Response: ASC 605-28-25-2 states that all of the following must be met for the milestone to be considered substantive:

(a) It is commensurate with either of the following:

1. The vendor's performance to achieve the milestone
2. The enhancement of the value of the delivered item or items as a result of a specific outcome resulting from the vendor's performance to achieve the milestone.

(b) It relates solely to past performance.

(c) It is reasonable relative to all of the deliverables and payment terms (including other potential milestone consideration) within the arrangement.

Upon review, we acknowledge that our disclosure on page F-9 refers primarily to the definition of a milestone discussed in ASC 605-28-20 rather than to the requirements for a milestone to be considered substantive discussed in ASC 605-28-25-2. In future filings, beginning with the Form 10-K for the year ended December 31, 2016, we propose to disclose the following criteria for milestones to be considered substantive:

- The consideration payable to the Company is commensurate with the Company's performance necessary to achieve the milestone or the increase in value to the collaboration resulting from the Company's performance;
- Relates solely to the Company's past performance; and
- Is reasonable relative to all of the other deliverables and payments within the arrangement.

We will also state in future filings that 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.

16. Collaboration and License Agreements

Sanofi, page F-20

2. 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 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 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 milestone meets all of the criteria set forth in ASC 605-28-20.

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 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 milestones and the 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 milestone 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 by using the development and regulatory milestone category and the sales milestone category. We considered disclosing each specific milestone outlined in the agreement; however, there is significant uncertainty about achievability and timing of the milestones, and therefore we accordingly determined that the specifics of each milestone were not meaningful or useful to the users of the financial statements in understanding the agreement with Sanofi. 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 \$210 million upon the achievement of three clinical development milestones, (b) up to an aggregate of \$220 million upon the achievement of four regulatory milestones and (c) 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 substantive, 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*