

[Lexicon Pharmaceuticals, Inc. Letterhead]

February 21, 2008

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

Attention: Mr. Mark Brunhofer
Division of Corporate Finance

Re: Lexicon Pharmaceuticals, Inc.
Form 10-K for the fiscal year ended December 31, 2006
Form 10-Q for the quarterly period ended September 30, 2007
File No. 000-30111

Dear Mr. Brunhofer:

On behalf of Lexicon Pharmaceuticals, Inc., we have set forth our responses to the oral comments received from the Securities and Exchange Commission's staff on February 13, 2008 regarding our annual report on Form 10-K for the fiscal year ended December 31, 2006 and our quarterly report on Form 10-Q for the quarterly period ended September 30, 2007. For your convenience, we have summarized each comment prior to the response.

Form 10-Q for the Quarterly Period Ended September 30, 2007

Notes to Consolidated Financial Statements

Note 7: Arrangements with Symphony Icon, Inc., page 9

1. Please provide us the disclosure you intend to include in your future filings with respect to the recording of the value of the purchase option as an asset rather than a charge to minority interests.

Response: In future filings beginning in the Form 10-K for the year ended December 31, 2007, we propose to disclose in a footnote to our financial statements the following statement:

Lexicon has calculated the value of the Purchase Option as the difference between the fair value of the common stock issued to Holdings of \$23.6 million and the \$15.0 million in cash received from Holdings for the issuance of the common stock. Lexicon has recorded the value of the Purchase Option as an asset, and is amortizing this asset over the four-year option period. The unamortized balance of \$7.4 million is recorded in other assets in the accompanying consolidated balance sheet as of December 31, 2007, and the amortization expense of \$1.2 million is recorded in other expense, net in the accompanying consolidated statement of operations for the year ended December 31, 2007.

Note 8: Agreements with Invus, L.P., page 10

2. Please provide us the disclosure you intend to include in your future filings indicating that you assessed whether the rights offerings should be treated as liabilities or equity instruments under EITF 00-19.

Response: In future filings beginning in the Form 10-K for the year ended December 31, 2007, we propose to disclose in a footnote to our financial statements the following statement:

Lexicon has determined that the First Rights Offering and the Second Rights Offering should be treated as equity instruments in accordance with EITF 00-19, "Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock," and accordingly has not recorded a liability for the future settlement of any rights offerings.

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 and
General Counsel