



June 1, 2009

Securities and Exchange Commission
Division of Corporate Finance
100 F Street, N.E.
Washington, D.C. 20549
Attention: Ms. Jennifer Riegel
Division of Corporate Finance

Re: *Lexicon Pharmaceuticals, Inc.*
Preliminary Proxy Statement on Schedule 14A filed May 22, 2009
File Number: 000-30111

Dear Ms. Riegel:

On behalf of Lexicon Pharmaceuticals, Inc., we submit the following response to the comment received on May 29, 2009 from the Securities and Exchange Commission's staff with respect to Lexicon's preliminary proxy statement filed on May 22, 2009 (File No. 000-30111). Your comment and our response to that comment are set forth below.

Proposed Amendment to Our Certificate of Incorporation, page 4

1. Please expand your disclosure on page 4 to state the price at which the shares under the securities purchase agreement will be issued and the number of shares that could be issued under the agreement.

Response: We will include the following additional disclosure on page 4 of our definitive proxy statement:

The price per share of each rights offering would be designated by Invus in a range between \$4.50 and a then-current average market price of our common stock, and the number of shares to be issued in each rights offering would be determined by the dollar amount of the rights offering and the designated price per share. For purposes of illustration, if we were to conduct both rights offerings for the maximum dollar amounts contemplated by the securities purchase agreement at an assumed price equal to the \$1.39 closing price per share of our common stock on the Nasdaq Global Market on May 29, 2009, we would issue a total of 247,841,727 shares in the rights offerings.

As requested by the staff, we are providing the following acknowledgements:

- we are responsible for the adequacy and accuracy of the disclosure in the filing;
 - staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
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· we may not assert staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please do not hesitate to contact the undersigned at (281) 863-3321 with any comments or questions concerning this letter or the above-referenced registration statement.

Very truly yours,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
*Executive Vice President and
General Counsel*