[Lexicon Pharmaceuticals logo]

July 16, 2007

Securities and Exchange Commission
Division of Corporate Finance
Judiciary Plaza
450 Fifth Street, N.W.
Washington, D.C. 20549

Attention: Mr. Greg Belliston
Division of Corporate Finance

Re: *Lexicon Pharmaceuticals, Inc.*
Schedule 14A filed July 5, 2007
File Number: 0-30111

Dear Mr. Belliston:

On behalf of Lexicon Pharmaceuticals, Inc., we submit the following responses to the comments received on July 12, 2007 from the Securities and Exchange Commission's staff with respect to Lexicon's preliminary proxy statement filed on July 5, 2007 (File No. 0-30111). Your comments and our responses to those comments are set forth below. We have attached as Exhibit A to this letter a revised "Use of Proceeds" section reflecting the changes described below.

Use of Proceeds

1. We note you plan to use some of the proceeds "to implement a long-term financial strategy to fund [your] extensive drug discovery and development pipeline." Please briefly describe what this strategy is.

   Response: We have revised the Use of Proceeds disclosure to be more specific and concrete and to provide more detail with respect to our planned funding of our drug discovery and development pipeline.

2. We note you plan to use some of the proceeds "to help fund [your] strategic goal of transitioning into an integrated biopharmaceutical company." Please briefly describe the aspects of this transition that will require funding.

   Response: We have revised the Use of Proceeds disclosure to include brief descriptions of the significant aspects of our transition into an integrated biopharmaceutical company.

3. Please identify more specifically the uses currently described as "working capital and general corporate expenses."

   Response: We have eliminated the reference to "working capital and general corporate expenses" and have provided a more detailed description of "other corporate purposes."

4. After you have revised the Use of Proceeds disclosure in accordance with the above comments, please state an approximate dollar amount for each specific use.

Response: We have revised the Use of Proceeds disclosure to include approximate dollar amounts we expect to allocate to research and development and other general corporate purposes.

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

Exhibit A

Use of Proceeds

We currently intend to use the net proceeds from the Invus transaction to help fund our extensive drug discovery and development pipeline and further our strategic goal of transitioning into an integrated biopharmaceutical company. Our currently planned operations are focused on drug discovery and development activities related to our 10TO10 program, an ongoing initiative with the goal of advancing ten drug candidates into human clinical trials by the end of 2010. Currently planned activities in support of our 10TO10 program include:

- the scheduled completion of our Genome5000 ™ program, in which we are using our gene knockout and evaluative technologies to discover the physiological and behavioral functions of 5,000 human genes;
- the expansion of our medicinal chemistry, biotherapeutics and preclinical research operations; and
- the initiation and conduct of additional preclinical development activities and human clinical trials for our drug candidates.

We expect to receive approximately $198 million in net proceeds from the initial investment of the Invus transaction after deducting estimated fees and expenses of $7.5 million incurred in connection with the initial investment. We currently anticipate that we will apply the net proceeds as follows: $165 million to research and development and $33 million to other general corporate purposes such as general and administrative expenses and capital expenditures to support our research and development efforts. However, we caution you that the amounts that we actually expend will vary significantly depending on a number of factors, including future revenue growth, if any, the amount of cash we generate from operations and the progress of our preclinical and clinical development efforts. Accordingly, our management will retain broad discretion in the allocation of net proceeds from the initial investment.