



DIVISION OF
CORPORATION FINANCE

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

February 8, 2011

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer
Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands, Texas 77381-1160

**Re: Lexicon Pharmaceuticals, Inc.
Registration Statement on Form S-3
Filed January 28, 2011
File No. 333-171953**

Dear Dr. Sands:

We have limited our review of your registration statement to the issues we have addressed in our comments below. In our comments we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

General

1. It does not appear that you are eligible to conduct a primary offering on Form S-3 under General Instruction I.B.1 to Form S-3 based on your public float. If you disagree, please provide us with a detailed analysis supporting your conclusion. Alternatively, if you are eligible to conduct a primary offering on Form S-3 under General Instruction I.B.6, please provide the information required pursuant to Instruction 7 to General Instruction I.B.6 on the cover page of the filing. Otherwise, please withdraw your registration statement and file it on a form on which you are eligible to conduct a primary offering.
2. In the event you believe you are eligible to conduct a primary offering on Form S-3, please amend your filing to incorporate by reference each of the two Form 8-Ks filed by the company on March 16, 2010.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and

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all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Please contact Laura Crotty at (202) 551-3563 or me at (202) 551-3715 with any questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director

cc: David P. Oelman (Vinson & Elkins L.L.P.)