



DIVISION OF  
CORPORATION FINANCE

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

August 17, 2011

Via E-mail

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

**Re: Lexicon Pharmaceuticals, Inc.  
Post-Effective Amendment No. 2 to Form S-3 on Form S-1  
Filed August 12, 2011  
File No. 333-171953**

Dear Dr. Sands:

We have limited our review of your registration statement to those issues we have addressed in our comments.

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. Please disclose prior to effectiveness the amount of securities to be sold in the rights offering and the number of shares each subscription right will be entitled to purchase.

Exhibit 5.1

2. The legal opinion of Vinson & Elkins L.L.P. filed as Exhibit 5.1 to your registration statement improperly assumes that at the time of any offering or sale of the Rights Shares, the Company will have a sufficient number of authorized shares available for issuance. Please amend your registration statement to include a revised legal opinion that avoids assumption of material facts underlying the opinion.

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 all applicable Securities Act rules require. Since the company and its management are in

Arthur T. Sands  
Lexicon Pharmaceuticals, Inc.  
August 17, 2011  
Page 2

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 Karen Ubell, Staff Attorney, at (202) 551-3873 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Jeffrey Riedler

Jeffrey Riedler  
Assistant Director