



DIVISION OF  
CORPORATION FINANCE

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

August 3, 2012

Via E-mail

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

**Re: Lexicon Pharmaceuticals, Inc.  
Registration Statement on Form S-3  
Filed July 26, 2012  
File No. 333-182859**

Dear Dr. Sands:

We have limited our review of your registration statement to the issue we have addressed in our comment. Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comment applies 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 this comment, we may have additional comments.

1. We note that the legal opinion states that counsel is “of the opinion that when the Shares are issued in accordance with the terms of the Purchase Option Agreement, the Shares will be validly issued, fully paid and non-assessable.” Since the Shares were already issued on July 30, 2012, please revise the legal opinion accordingly.

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 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 comment, 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;

Arthur T. Sands  
Lexicon Pharmaceuticals, Inc.  
August 3, 2012  
Page 2

- 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 Johnny Gharib at (202) 551-3170, Daniel Greenspan at (202) 551-3170 or me at (202) 551-3715 with any questions.

Sincerely,

/s/ Daniel Greenspan for

Jeffrey Riedler  
Assistant Director

cc: David P. Oelman, Esq.  
Vinson & Elkins LLP  
1001 Fannin Street  
2500 First City Tower  
Houston, Texas 77002