

[LEXICON PHARMACEUTICALS, INC. LETTERHEAD]

August 6, 2012

Securities and Exchange Commission  
Division of Corporate Finance  
100 F Street, N.E.  
Washington, D.C. 20549

Attention: Mr. Johnny Gharib

Re: Lexicon Pharmaceuticals, Inc.  
Registration Statement and Pre-Effective Amendment No. 1 on Form S-3  
Filed July 26 and August 1, 2012  
File No. 333-182859

Dear Mr. Gharib:

On behalf of Lexicon Pharmaceuticals, Inc., we submit the following response to the comment received on August 3, 2012 from the Securities and Exchange Commission's staff with respect to Lexicon's Registration Statement and Pre-Effective Amendment No. 1 on Form S-3 (File No. 333-182859). Your comment and our response to that comment are set forth below. We are filing an amendment to the registration statement reflecting the change described below concurrently with our submission of this letter.

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.

*Response:* We have filed a revised legal opinion reflecting the issuance of the Shares on July 30, 2012.

Please do not hesitate to contact the undersigned at (281) 863-3443 with any comments or questions concerning this letter or the above-referenced registration statement.

Very truly yours,

/s/ Brian T. Crum

Brian T. Crum  
*Vice President and General Counsel*