

[LEXICON PHARMACEUTICALS, INC. LETTERHEAD]

September 16, 2009

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

Attention: Ms. Laura Crotty

Re: Request for acceleration of effectiveness of registration statement on Form S-3 (File No. 333-161696) of Lexicon Pharmaceuticals, Inc.

Ladies and Gentlemen:

Pursuant to Rule 461 under the Securities Act of 1933, as amended, we hereby request that the effectiveness of the above-captioned registration statement be accelerated so that such registration statement will become effective on Friday, September 18, 2009 at 12:00 p.m., Eastern time, or as soon thereafter as practicable.

In connection with such request, we hereby acknowledge that:

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

Please call the undersigned at (281) 863-3321 with any questions regarding this matter.

Very truly yours,

LEXICON PHARMACEUTICALS, INC.

By: /s/ JEFFREY L. WADE  
Name: Jeffrey L. Wade  
Title: Executive Vice President and General Counsel