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LEXICON PHARMACEUTICALS, INC./DE  
Form SC 13G/A  
February 14, 2011

SCHEDULE 13G

Amendment No. 1  
LEXICON PHARMACEUTICALS INC  
Common Stock  
Cusip #528872104

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Item 1: Reporting Person - FMR LLC  
Item 4: Delaware  
Item 5: 0  
Item 6: 0  
Item 7: 40,017,988  
Item 8: 0  
Item 9: 40,017,988  
Item 11: 11.855%  
Item 12: HC

Cusip #528872104  
Item 1: Reporting Person - Edward C. Johnson 3d  
Item 4: United States of America  
Item 5: 0  
Item 6: 0  
Item 7: 40,017,988  
Item 8: 0  
Item 9: 40,017,988  
Item 11: 11.855%  
Item 12: IN

SCHEDULE 13G - TO BE INCLUDED IN  
STATEMENTS  
FILED PURSUANT TO RULE 13d-1(b) or 13d-2(b)

Item 1(a). Name of Issuer:  
  
LEXICON PHARMACEUTICALS  
INC

Item 1(b). Name of Issuer's Principal Executive Offices:  
  
8800 Technology Forest Place  
The Woodlands, TX 77381  
USA

Item 2(a). Name of Person Filing:  
  
FMR LLC

Item 2(b). Address or Principal Business Office or, if None,  
Residence:

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82 Devonshire Street, Boston,  
Massachusetts 02109

Item 2(c). Citizenship:

Not applicable

Item 2(d). Title of Class of Securities:

Common Stock

Item 2(e). CUSIP Number:

528872104

Item 3. This statement is filed pursuant to Rule 13d-1(b) or 13d-2(b) and the person filing, FMR LLC, is a parent holding company in accordance with Section 240.13d-1(b)(ii)(G). (Note: See Item 7).

Item 4. Ownership

(a) Amount Beneficially Owned: 40,017,988

(b) Percent of Class: 11.855%

(c) Number of shares as to which such  
person has:

(i) sole power to vote or to direct  
the vote: 0

(ii) shared power to vote or to  
direct the vote: 0

(iii) sole power to dispose or to  
direct the disposition of: 40,017,988

(iv) shared power to dispose or to  
direct the disposition of: 0

Item 5. Ownership of Five Percent or Less of a Class.

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person.

Various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Common Stock of LEXICON PHARMACEUTICALS INC. The interest of one person, Fidelity Growth Company Fund, an investment company registered under the Investment Company Act of 1940, in the Common Stock of LEXICON PHARMACEUTICALS INC, amounted to 30,792,100 shares or 9.122% of the total outstanding Common Stock at December 31, 2010.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent

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Holding Company.

See attached Exhibit A.

Item 8. Identification and Classification of Members of the Group.

Not applicable. See attached Exhibit A.

Item 9. Notice of Dissolution of Group.

Not applicable.

Item 10. Certification.

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired in the ordinary course of business and were not acquired for the purpose of and do not have the effect of changing or influencing the control of the issuer of such securities and were not acquired in connection with or as a participant in any transaction having such purpose or effect.

Signature

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

February 11, 2011  
Date

/s/ Scott C. Goebel  
Signature

Scott C. Goebel  
Duly authorized under Power of Attorney  
effective as of June 1, 2008 by and on behalf of FMR LLC  
and its direct and indirect subsidiaries

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Pursuant to the instructions in Item 7 of Schedule 13G, Fidelity Management & Research Company ("Fidelity"), 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 40,017,988 shares or 11.855% of the Common Stock outstanding of LEXICON PHARMACEUTICALS INC ("the Company") as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940.

The ownership of one investment company, Fidelity Growth Company Fund, amounted to 30,792,100 shares or 9.122% of the Common Stock outstanding. Fidelity Growth

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Company Fund has its principal business office at 82  
Devonshire Street, Boston, Massachusetts 02109.

Edward C. Johnson 3d and FMR LLC, through its  
control of Fidelity, and the funds each has sole power to  
dispose of the 40,017,988 shares owned by the Funds.

Members of the family of Edward C. Johnson 3d,  
Chairman of FMR LLC, are the predominant owners, directly  
or through trusts, of Series B voting common shares of FMR  
LLC, representing 49% of the voting power of FMR LLC.  
The Johnson family group and all other Series B shareholders  
have entered into a shareholders' voting agreement under  
which all Series B voting common shares will be voted in  
accordance with the majority vote of Series B voting common  
shares. Accordingly, through their ownership of voting  
common shares and the execution of the shareholders' voting  
agreement, members of the Johnson family may be deemed,  
under the Investment Company Act of 1940, to form a  
controlling group with respect to FMR LLC.

Neither FMR LLC nor Edward C. Johnson 3d,  
Chairman of FMR LLC, has the sole power to vote or direct  
the voting of the shares owned directly by the Fidelity Funds,  
which power resides with the Funds' Boards of Trustees.  
Fidelity carries out the voting of the shares under written  
guidelines established by the Funds' Boards of Trustees.

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STATEMENTS

FILED PURSUANT TO RULE 13d-1(b) or 13d-2(b)  
RULE 13d-1(f)(1) AGREEMENT

The undersigned persons, on February 11, 2011, agree  
and consent to the joint filing on their behalf of this Schedule  
13G in connection with their beneficial ownership of the  
Common Stock of LEXICON PHARMACEUTICALS INC at  
December 31, 2010.

FMR LLC

By /s/ Scott C. Goebel  
Scott C. Goebel

Duly authorized under Power of Attorney effective as  
of June 1, 2008, by and on behalf of FMR LLC and its direct  
and indirect subsidiaries

Edward C. Johnson 3d

By /s/ Scott C. Goebel  
Scott C. Goebel

Duly authorized under Power of Attorney effective as  
of June 1, 2008, by and on behalf of Edward C. Johnson 3d

Fidelity Management & Research Company

By /s/ Scott C. Goebel  
Scott C. Goebel  
Senior V.P. and General Counsel

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Fidelity Growth Company Fund

By /s/ Scott C. Goebel  
Scott C. Goebel  
Secretary