Filed pursuant to Rule 433 Registration No.: 333-161696 March 15, 2010

Lexicon Pharmaceuticals, Inc. \$100,875,000 87,717,391 Shares of Common Stock

Levicon Dharmacouticals Inc

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Symbol:	LXRX
Size:	\$100,875,000
Total Shares Offered:	87,717,391 Shares of Common Stock
Greenshoe Offered by Issuer:	8,804,348 Shares of Common Stock
Price to Public:	\$1.15 per share
Trade Date:	March 15, 2010
Closing Date:	March 19, 2010
CUSIP No:	528872104
Underwriters:	Morgan Stanley & Co. Incorporated J.P. Morgan Securities Inc. Cowen and Company, LLC Thomas Weisel Partners LLC

Invus Participation

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To maintain its pro rata ownership of the common stock of Lexicon Pharmaceuticals, Inc., Invus, L.P., the largest shareholder of Lexicon, has agreed to separately purchase in a concurrent private placement 59,296,749 shares of common stock offered directly from Lexicon at the per share price to the public set forth above for proceeds to Lexicon of \$68,191,261. Additionally, an affiliate of Invus has agreed to purchase from the underwriters 29,021,739 shares of the 87,717,391 shares of common stock offered pursuant to this offering at the per share price to the public set forth above.

To the extent the underwriters exercise their over-allotment option, Invus will have the right to purchase up to an aggregate of 5,951,718 additional shares of common stock pursuant to Invus' right to purchase shares sufficient to maintain its pro rata ownership of Lexicon's common stock.

Following completion of this offering Invus and its affiliated entities will own approximately 49.3% of the outstanding shares of Lexicon's common stock, or 48.9% if the underwriters exercise their over-allotment option in full and Invus exercises its right to purchase additional shares sufficient to maintain its pro rata ownership of Lexicon's common stock.

Net Proceeds

Total net proceeds to Lexicon from this offering and the Invus private placement will be approximately \$164,953,761 following the deduction of underwriting discounts and commissions and estimated expenses payable by Lexicon, or \$181,366,361 if the underwriters exercise their over-allotment option in full and Invus exercises its right to purchase additional shares sufficient to maintain its pro rata ownership of Lexicon's common stock.

Dilution

New investors purchasing shares of common stock in this offering will experience immediate dilution in net tangible book value of \$0.21 per share.

Supplements to Agreements with Invus

In connection with this offering and the concurrent private placement, Lexicon entered into an agreement with Invus and its affiliate supplementing the terms of the transaction agreements between Lexicon and Invus, including the securities purchase and stockholders' agreements with Invus, dated June 17, 2007, in the case of the securities purchase agreement, as previously amended.

The supplement to these transaction agreements:

- Extends the period during which Invus may exercise its right to require Lexicon to conduct the first rights offering under the securities purchase agreement from one year beginning on November 28, 2009 to fifteen months following November 28, 2009.
- Provides that the 29,021,739 shares of common stock purchased from the underwriters in this offering by Invus and its affiliates will not be restricted shares under the stockholders' agreement. As a result, the shares will not be subject to the voting restrictions in the stockholders agreement and will be included in determining whether Invus exceeds the 50% ownership threshold with respect to our common stock under the stockholders agreement, thereby terminating certain rights thereunder.
- Reduces the maximum amount of the first and second rights offerings under the securities purchase agreement by the net proceeds to Lexicon from this offering and the concurrent private placement, or by approximately \$165.0 million. Pursuant to the securities purchase agreement prior to giving effect to the supplement, Invus had the right to require Lexicon to initiate the first rights offering to all of Lexicon's stockholders in an aggregate amount to be designated by Invus not to exceed approximately \$172.3 million. As a result, after giving effect to the supplement, the maximum amount subject to the first rights offering will not exceed approximately \$7.3 million.

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The issuer has filed a registration statement (including a prospectus) with the SEC for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and other documents the issuer has filed with the SEC for more complete information about the issuer and this offering. You may get these documents for free by visiting EDGAR on the SEC Web site at www.sec.gov. Alternatively, the issuer, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by calling toll-free 1-(866) 718-1649, or by emailing prospectus@morganstanley.com.