

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC. 20549**

**SCHEDULE 14A
(Rule 14A-101)**

**INFORMATION REQUIRED IN PROXY STATEMENT
SCHEDULE 14A INFORMATION**

Proxy Statement Pursuant to Section 14(a) of
the Securities Exchange Act of 1934

Filed by the Registrant

Filed by a Party other than the Registrant

Check the appropriate box:

- | | |
|--|---|
| <input checked="" type="checkbox"/> Preliminary Proxy Statement | <input type="checkbox"/> Confidential, for Use of the Commission Only
(as permitted by Rule 14a-6(e)(2)) |
| <input type="checkbox"/> Definitive Proxy Statement | |
| <input type="checkbox"/> Definitive Additional Materials | |
| <input type="checkbox"/> Soliciting Material Pursuant to Rule 14a-11(c) or Rule 14a-12 | |

LEXICON PHARMACEUTICALS, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if Other Than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
 Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

- | | |
|-----|---|
| (1) | Title of each class of securities to which transaction applies: N/A |
| (2) | Aggregate number of securities to which transaction applies: N/A |
| (3) | Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined): N/A |
| (4) | Proposed maximum aggregate value of transaction: N/A |
| (5) | Total fee paid: \$0 |

Fee paid previously with preliminary materials: N/A

Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

- | | |
|-----|---|
| (1) | Amount Previously Paid: |
| (2) | Form, Schedule or Registration Statement No.: |
| (3) | Filing Party: |
| (4) | Date Filed |
-



June __, 2009

TO OUR STOCKHOLDERS:

Our board of directors has called a special meeting of stockholders, as described in the enclosed notice of special meeting of stockholders and proxy statement. The special meeting is being called so that our stockholders may consider and act upon a proposed amendment to our certificate of incorporation to increase the number of authorized shares of our common stock. The increase is intended to permit us to satisfy our obligations under our securities purchase agreement with Invus, L.P. in the event Invus exercises its right to require us to conduct the full amounts of the rights offerings contemplated by that agreement, and to provide us greater flexibility in effecting possible future acquisitions and financings other than the contemplated rights offerings.

The special meeting will be held on Wednesday, July 15, 2009 at 1:30 p.m., local time, at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas.

This proxy statement provides detailed information about the proposed amendment and the special meeting. We encourage you to read the entire proxy statement carefully.

Our board of directors has unanimously approved the amendment to our certificate of incorporation, has determined that the amendment to our certificate of incorporation is advisable and in the best interest of our stockholders, and unanimously recommends that you vote for the amendment to our certificate of incorporation.

Your vote is important, regardless of the number of shares you own. Please vote as soon as possible to make sure that your shares are represented at the special meeting. To vote your shares, please do so electronically on the Internet, by telephone or by signing and returning the enclosed proxy card. You also may cast your vote in person at the special meeting.

Sincerely,

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

LEXICON PHARMACEUTICALS, INC.
8800 Technology Forest Place
The Woodlands, Texas 77381
(281) 863-3000

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS
TO BE HELD JULY 15, 2009

TO OUR STOCKHOLDERS:

A special meeting of the stockholders of Lexicon Pharmaceuticals, Inc. will be held on Wednesday, July 15, 2009 at 1:30 p.m., local time, at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas, to approve an amendment to our certificate of incorporation increasing the number of authorized shares of our common stock from 300,000,000 to 900,000,000.

You are entitled to vote at the special meeting only if you are the record owner of shares of our common stock at the close of business on May 21, 2009.

It is important that your shares be represented at the special meeting whether or not you plan to attend. **Please cast your vote electronically on the Internet, by telephone or by signing and returning the enclosed proxy card as promptly as possible.** If you are present at the special meeting, and wish to do so, you may revoke the proxy and vote in person.

By order of the board of directors,

Jeffrey L. Wade
Secretary

The Woodlands, Texas
June __, 2009

LEXICON PHARMACEUTICALS, INC.
8800 Technology Forest Place
The Woodlands, Texas 77381
(281) 863-3000

PROXY STATEMENT
FOR
SPECIAL MEETING OF STOCKHOLDERS

To Be Held July 15, 2009

GENERAL INFORMATION

Purpose of this Proxy Statement

We have prepared this proxy statement to solicit proxies on behalf of our board of directors for use at a special meeting of stockholders called so that our stockholders may consider and act upon an amendment to our certificate of incorporation to increase the number of authorized shares of our common stock, and at any adjournment or postponement of the special meeting.

Notice of Internet Availability of Proxy Materials

As permitted by rules adopted by the Securities and Exchange Commission, we are providing access to our proxy materials over the Internet. Accordingly, on or about June 1, 2009, we are mailing to our stockholders a notice containing instructions on how to access our proxy materials and vote electronically over the Internet. The notice also provides instructions on how stockholders may request a paper copy of our proxy materials free of charge. Our proxy materials may be accessed by stockholders at any time after the date of mailing of the notice.

Time and Place of the Special Meeting

The special meeting will be held on Wednesday, July 15, 2009 at 1:30 p.m., local time, at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas.

Matter to Be Considered at the Special Meeting

At the special meeting, our stockholders will be asked to consider and act upon a proposal to approve an amendment to our certificate of incorporation increasing the number of authorized shares of our common stock from 300,000,000 to 900,000,000.

Record Date for Determining Entitlement to Vote

You are entitled to vote at the special meeting if you were the record owner of shares of our common stock as of the close of business on May 21, 2009, the record date for the special meeting established by our board of directors.

How to Vote Your Shares

You may vote in person at the special meeting or by proxy. To ensure that your shares are represented at the special meeting, we recommend you vote by proxy even if you plan to attend the special meeting in person. Even if you vote by proxy, if you wish, you can revoke your proxy and vote in person at the special meeting. If you want to vote at the special meeting but your shares are held by an intermediary, such as a broker or bank, you will need to obtain a proxy from such intermediary authorizing you to vote your shares at the meeting.

You may receive more than one proxy depending on how you hold your shares. If you hold your shares through an intermediary, such as a broker or bank, you may receive materials from them asking you how you want your shares to be voted at the special meeting.

Voting by Proxy

By Internet or Telephone. You may vote electronically on the Internet or by telephone by following the instructions contained on the notice of Internet availability of our proxy materials. If you hold your shares through an intermediary, such as a broker or bank, please follow the voting instructions contained on the voting card used by the intermediary.

By Mail. If you request a paper copy of our proxy materials, you may vote by mail by completing, dating and signing the proxy card provided and mailing it in the pre-addressed envelope enclosed with the paper copy of our proxy materials.

Quorum

We must have a quorum to conduct any business at the special meeting. This means that at least a majority of our outstanding shares eligible to vote at the special meeting must be represented at the special meeting, either in person or by proxy. Abstentions are counted for purposes of determining whether a quorum is present.

Outstanding Shares

On the record date, we had 137,330,254 shares of our common stock outstanding. If you were the record owner of shares of our common stock on the record date, you will be entitled to one vote for each share of stock that you own on the matter to be voted on at the special meeting.

Vote Needed to Approve the Proposal

The approval of the proposed amendment to our certificate of incorporation will require the affirmative vote, in person or by proxy, of the holders of a majority of the outstanding shares of our common stock as of the record date. Any abstention from voting with respect to the proposed amendment to our certificate of incorporation will have the same effect as a vote against the proposed amendment.

How Your Proxy Will Be Voted

Giving us your proxy means that you are authorizing us to vote your shares at the special meeting in the manner you direct. You may vote for or against the proposal to approve the amendment to our certificate of incorporation to increase the number of authorized shares of our common stock, or abstain from voting on such proposal.

If you vote by proxy but do not specify how you want your shares voted, your shares will be voted in favor of the approval of the proposed amendment to our certificate of incorporation.

How to Revoke Your Proxy

You may revoke your proxy at any time before your shares are voted by providing our corporate secretary with either a new proxy with a later date or a written notice of your desire to revoke your proxy at the following address:

Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands, Texas 77381
Attention: Corporate Secretary

You may also revoke your proxy at any time prior to your shares having been voted by attending the special meeting in person and notifying the inspector of election of your desire to revoke your proxy. Your proxy will not automatically be revoked merely because you attend the special meeting.

Inspector of Election

Broadridge Financial Solutions, Inc. will count votes and provide a representative who will serve as an inspector of election for the special meeting.

List of Stockholders Entitled to Vote

A list of our stockholders entitled to vote at the special meeting will be available for inspection at the special meeting. The stockholder list will also be available for inspection for ten days prior to the special meeting at our corporate offices located at 8800 Technology Forest Place, The Woodlands, Texas. Any inspection of this list at our offices will need to be conducted during ordinary business hours. If you wish to conduct an inspection of the stockholder list, we request that you please contact our corporate secretary before coming to our offices.

Solicitation of Proxies and Expenses

We are asking for your proxy on behalf of our board of directors. We will bear the entire cost of preparing, printing and soliciting proxies. We will send notices of Internet availability of proxy materials and, if requested, paper copies of our proxy materials to all of our stockholders of record as of the record date and to all intermediaries, such as brokers and banks, that held any of our shares on that date on behalf of others. These intermediaries will then forward the notices and, if requested, paper copies of our proxy materials to the beneficial owners of our shares, and we will reimburse them for their reasonable out-of-pocket expenses for forwarding such materials.

We have retained Innisfree M&A Incorporated, a proxy solicitation firm, to assist us in the solicitation of proxies for the special meeting and our directors, officers and employees may solicit proxies by mail, in person or by telephone or other electronic communication. We have agreed to pay Innisfree a fee of approximately \$10,000 and to reimburse its out-of-pocket expenses incurred in connection with its services. Our directors, officers and employees will not receive additional compensation for their solicitation efforts, but they will be reimbursed for any out-of-pocket expenses they incur.

Adjournments and Postponements

Although it is not expected, the special meeting may be adjourned or postponed for the purpose of soliciting additional proxies. Any adjournment or postponement may be made without notice, other than by announcement made at the special meeting, by approval of the holders of a majority of the outstanding shares of our common stock present in person or represented by proxy at the special meeting, whether or not a quorum exists. Any signed proxies received by us prior to the special meeting will be voted in favor of an adjournment or postponement in these circumstances. Any adjournment or postponement of the special meeting for the purpose of soliciting additional proxies will allow those of our stockholders who have already sent in their proxies to revoke them at any time prior to their use.

Householding

As permitted by rules adopted by the Securities and Exchange Commission, we are delivering a single notice of Internet availability of proxy materials and proxy statement, as applicable, to any household at which two or more stockholders reside if we believe the stockholders are members of the same family, unless otherwise instructed by one or more of the stockholders. We will promptly deliver separate copies of these documents upon the written or oral request of any stockholder at a shared address to which a single copy of the documents were delivered.

If your household received a single set of any of these documents, but you would prefer to receive your own copy, or if you share an address with another stockholder and together both of you would like to receive only a single set of these documents, please follow these instructions:

- If your shares are registered in your own name, please contact our transfer agent, BNY Mellon Shareowner Services, and inform them of your request by calling them at (800) 635-9270 or writing them at 480 Washington Boulevard., Jersey City, New Jersey 07310.
- If an intermediary, such as a broker or bank, holds your shares, please contact Broadridge and inform them of your request by calling them at (800) 542-1061 or writing them at Householding Department, 51 Mercedes Way, Edgewood, New York 11717. Be sure to include your name, the name of your brokerage firm and your account number.

Increase in Authorized Shares of our Common Stock

Our board of directors believes that it is advisable to amend Article IV of our certificate of incorporation to increase the number of authorized shares of our common stock from 300,000,000 shares to 900,000,000 shares. As of May 21, 2009, of the 300,000,000 shares of our common stock authorized by our certificate of incorporation, 137,330,254 shares were issued and outstanding and 31,510,782 shares were reserved for issuance under our stock incentive plans. The remaining 131,158,964 shares that were authorized but not issued or reserved for issuance as of such date would not be sufficient, at currently prevailing market prices for our common stock, to permit us to satisfy our obligations under our securities purchase agreement with Invus, L.P. in the event Invus were to exercise its right to require us to conduct the full amounts of the rights offerings contemplated by that agreement, as described below. After the proposed increase in the number of authorized shares of our common stock to 900,000,000 shares, 731,158,964 shares of our common stock would be authorized but not issued or reserved for issuance, which we believe should be sufficient to permit us both to satisfy such obligations and to provide us greater flexibility in effecting possible future acquisitions and financings other than the contemplated rights offerings.

The right of Invus, at its option, to require us to conduct such rights offerings arises under a June 2007 securities purchase agreement under which Invus purchased 50,824,986 shares of our common stock for approximately \$205.4 million in August 2007. Our stockholders approved the transactions contemplated by the securities purchase agreement, including Invus' August 2007 stock purchase and the potential issuance of additional shares of common stock in the rights offerings, at a special meeting held on August 23, 2007. Pursuant to the securities purchase agreement, Invus has the right to require us to initiate up to two pro rata rights offerings to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount of up to \$344.5 million, less the proceeds of any "qualified offerings" that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share. Invus may exercise its right to require us to conduct the first rights offering by giving us notice within a period of 90 days beginning on November 28, 2009 (which we refer to as the first rights offering trigger date), although we and Invus may agree to change the first rights offering trigger date to as early as August 28, 2009 with the approval of the members of our board of directors who are not affiliated with Invus. Invus may exercise its right to require us to conduct the second rights offering by giving us notice within a period of 90 days beginning on the date that is 12 months after Invus' exercise of its right to require us to conduct the first rights offering or, if Invus does not exercise its right to require us to conduct the first rights offering, within a period of 90 days beginning on the first anniversary of the first rights offering trigger date. The initial investment and subsequent rights offerings, combined with any qualified offerings, were designed to achieve up to \$550 million in proceeds to us. Invus would participate in each rights offering for up to its pro rata portion of the offering, and would commit to purchase the entire portion of the offering not subscribed for by other stockholders.

In addition to allowing us to meet our obligations under the securities purchase agreement in the event Invus were to exercise its right to require us to conduct the full amounts of the rights offerings contemplated by that agreement, our board of directors believes that the increase in the number of authorized shares of our common stock will provide us with greater flexibility in effecting future acquisitions and financings without the delay and expense associated with obtaining the approval or consent of our stockholders at the same time the shares are needed. We expect that our future growth may require the use of our common stock from time to time either as consideration for acquisitions or as part of a financing for us either through the use of our common stock or securities convertible into our common stock. Such shares may be issued in conjunction with both public offerings and private placements of shares of our common stock which issuances, depending on the circumstances, may or may not require future stockholder approval under the rules of The Nasdaq Global Market. Such shares could also be used for our stock-based compensation plans, subject to appropriate stockholder approval. Our stockholders other than Invus do not have any preemptive rights to purchase additional shares of our common stock. Other than the securities purchase agreement with Invus, we do not have any current plans, proposals or understandings that would require the use of the additional authorized shares of our common stock to be issued.

The text of the amendment to increase the number of authorized shares of our common stock from 300,000,000 shares to 900,000,000 shares can be found in the form of the third certificate of amendment to our restated certificate of incorporation, which is attached as Annex A to this proxy statement.

Recommendation of our Board of Directors

Our board of directors has unanimously approved the amendment to our certificate of incorporation to increase the number of authorized shares of our common stock from 300,000,000 shares to 900,000,000 shares, has determined that this amendment to our certificate of incorporation is advisable and in the best interest of our stockholders, and recommends that our stockholders vote for its approval.

Effects of the Amendment to our Certificate of Incorporation

Stockholders should consider the following factors which may affect them, as well as the other information contained in this proxy statement, in evaluating the proposal to approve the amendment to our certificate of incorporation to increase the number of authorized shares of our common stock.

Possible Dilution from Future Issuance of Additional Shares. Any future issuance of additional authorized shares of our common stock could dilute future earnings per share, book value per share and voting power of existing stockholders. Depending upon the circumstances under which such shares are issued, such issuance may reduce stockholders equity per share and may reduce the percentage ownership of common stock of existing stockholders.

Possible Anti-Takeover Effect from Future Issuances of Additional Shares. Any future issuance of additional shares also may have an anti-takeover effect by making it more difficult to engage in a merger, tender offer, proxy contest or assumption of control of a large voting block of our common stock. Our board of directors could impede a takeover attempt by issuing additional shares and thereby diluting the voting power of other outstanding shares and increasing the cost of a takeover. A future issuance of additional shares of common stock could render more difficult an attempt to obtain control of us, even if it appears to be desirable to a majority of stockholders, and it may be more difficult for our stockholders to obtain an acquisition premium for their shares or to remove incumbent management. Although the increase in the number of authorized shares of our common stock may have an anti-takeover effect, the amendment to our certificate of incorporation has been proposed for the reasons stated above under the heading “—Increase in Authorized Shares of our Common Stock,” and our board of directors has no present intention to use the proposed increase in the authorized shares of common stock as a measure aimed at discouraging takeover efforts.

STOCK OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table presents information regarding the beneficial ownership of our common stock as of May 21, 2009 by:

- each of the individuals listed in “Executive and Director Compensation — Summary Compensation Table” in our proxy statement for our 2009 annual meeting;
- each of our directors;
- each person, or group of affiliated persons, who is known by us to own beneficially five percent or more of our common stock; and
- all current directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission computing the number of shares beneficially owned by a person and the percentage ownership of that person. Shares of common stock under options held by that person that are currently exercisable or exercisable within 60 days of May 21, 2009 are considered outstanding. These shares, however, are not considered outstanding when computing the percentage ownership of each other person.

Except as indicated in the footnotes to this table and pursuant to state community property laws, each stockholder named in the table has sole voting and investment power for the shares shown as beneficially owned by them. Percentage of ownership is based on 137,330,254 shares of common stock outstanding on May 21, 2009. Unless otherwise indicated in the footnotes, the address of each of the individuals named below is: c/o Lexicon Pharmaceuticals, Inc., 8800 Technology Forest Place, The Woodlands, Texas 77381.

	Beneficial Ownership		
	Number of Shares Beneficially Owned	Shares Issuable Pursuant to Options Exercisable within 60 Days of February 23, 2009	Percentage Ownership
Invus, L.P., Invus Public Equities, L.P. and related parties ⁽¹⁾	55,385,146	—	40.3%
Royce & Associates, LLC ⁽²⁾	9,205,777	—	6.7%
Arthur T. Sands, M.D., Ph.D. ⁽³⁾	1,663,562	1,993,776	2.6%
Alan J. Main, Ph.D.	44,800	704,802	*
Jeffrey L. Wade, J.D.	47,800	669,876	*
Brian P. Zambrowicz, Ph.D.	156,800	936,922	*
James F. Tessmer	25,800	103,066	*
Julia P. Gregory ⁽⁴⁾	51,983	1,003,994	*
Samuel L. Barker, Ph.D. ⁽⁵⁾	47,000	137,333	*
Philippe J. Amouyal	—	22,666	*
Raymond Debbane ⁽⁶⁾	55,385,146	22,666	40.3%
Robert J. Lefkowitz, M.D.	—	89,666	*
Alan S. Nies, M.D.	5,000	80,166	*
Frank P. Palantoni	—	59,666	*
Christopher J. Sobecki	1,000	22,666	*
Judith L. Swain, M.D.	—	22,166	*
Kathleen M. Wiltsey	—	25,666	*
All directors and executive officers as a group ⁽³⁾⁽⁵⁾⁽⁶⁾ (16 persons)	57,414,408	5,079,245	43.9%

* Represents beneficial ownership of less than 1 percent.

⁽¹⁾ Based upon a Schedule 13D filed with the SEC on June 27, 2007, and amended on August 24 and August 29, 2007, and certain representations made to us by Invus, L.P. Reflects the beneficial ownership of (a) 51,494,038 shares of our common stock by Invus, L.P., Invus Advisors, L.L.C., Ulys, L.L.C. and Raymond Debbane, each of which may be deemed to have sole voting and investment power with respect to such shares, and (b) 3,891,108 shares of our common stock by Invus Public Equities, L.P., Invus Public Equities Advisors, LLC, Ulys, L.L.C. and Mr. Debbane, each of which may be deemed to have sole voting and investment power with respect to such shares. Such shares are subject to certain voting restrictions pursuant to our stockholders' agreement with Invus, L.P. described under the heading "Agreements with Invus." The address for Invus, L.P., Invus Advisors, L.L.C., Invus Public Equities, L.P., Invus Public Equities Advisors, LLC, Ulys, L.L.C. is 750 Lexington Avenue, 30th Floor, New York, New York 10022. The address for Mr. Debbane is c/o Ulys, L.L.C., 750 Lexington Avenue, 30th Floor, New York, New York 10022.

⁽²⁾ Based upon a Schedule 13G filed with the SEC on January 26, 2009, reflecting the beneficial ownership of our common stock by Royce & Associates, LLC. The address for Royce & Associates, LLC is 1414 Avenue of the Americas, New York, New York 10019.

⁽³⁾ The number of shares beneficially owned by Dr. Sands includes 60,000 shares held in the name of minor children and 817,500 shares owned by Sands Associates LP. The general partners of Sands Associates LP are ATS Associates, L.L.C., owned by Dr. Sands, and MES Associates, L.L.C., owned by Dr. Sands' wife.

⁽⁴⁾ Based on certain representations made to us by Ms. Gregory. The number of shares beneficially owned by Ms. Gregory includes 4,847 shares held in trusts for the benefit of her children, of which she serves as trustee.

⁽⁵⁾ The number of shares beneficially owned by Dr. Barker includes 35,000 shares held in grantor retained annuity trusts for the benefit of his children, of which he serves as trustee.

⁽⁶⁾ Based upon a Schedule 13D filed with the SEC on June 27, 2007, and amended on August 24 and August 29, 2007, and certain representations made to us by Mr. Debbane. Mr. Debbane disclaims beneficial ownership of these shares. The address for Mr. Debbane is c/o Ulys, L.L.C., 750 Lexington Avenue, 30th Floor, New York, New York 10022.

AGREEMENTS WITH INVUS

Securities Purchase Agreement. In June 2007, we entered into a securities purchase agreement with Invus, L.P., pursuant to which Invus purchased 50,824,986 shares of our common stock for approximately \$205.4 million in August 2007. This purchase resulted in Invus' ownership of 40% of the post-transaction outstanding shares of our common stock. Pursuant to the securities purchase agreement, Invus also has the right to require us to initiate up to two pro rata rights offerings to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount of up to \$344.5 million, less the proceeds of any "qualified offerings" that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share.

Invus may exercise its right to require us to conduct the first rights offering by giving us notice within a period of 90 days beginning on November 28, 2009 (which we refer to as the first rights offering trigger date), although we and Invus may agree to change the first rights offering trigger date to as early as August 28, 2009 with the approval of the members of our board of directors who are not affiliated with Invus. If Invus exercises its right to require us to initiate such first rights offering, it will have the right to designate the amount of such first rights offering up to \$172.3 million, less the proceeds of any “qualified offerings” that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share. Invus may exercise its right to require us to conduct the second rights offering by giving us notice within a period of 90 days beginning on the date that is 12 months after Invus’ exercise of its right to require us to conduct the first rights offering or, if Invus does not exercise its right to require us to conduct the first rights offering, within a period of 90 days beginning on the first anniversary of the first rights offering trigger date. If Invus exercises its right to require us to initiate such second rights offering, it will have the right to designate the amount of such second rights offering up to \$344.5 million, less the proceeds of the first rights offering, if any, and less the proceeds of any “qualified offerings” that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share. Invus would participate in each rights offering for up to its pro rata portion of the offering, and would commit to purchase the entire portion of the offering not subscribed for by other stockholders.

Board of Directors. Concurrently with the execution of the securities purchase agreement, we entered into a stockholders’ agreement with Invus under which Invus has the right to designate the greater of three members or 30% (or the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, if less than 30%) of all members of our board of directors, rounded up to the nearest whole number of directors, and pursuant to which Invus has designated Philippe J. Amouyal, Raymond Debbane and Christopher J. Sobecki. Mr. Debbane is president and chief executive officer of The Invus Group, LLC, an affiliate of Invus, and Mr. Amouyal and Mr. Sobecki are each managing directors of The Invus Group, LLC.

In the event that the number of shares of our common stock owned by Invus and its affiliates ever exceeds 50% of the total number of shares of our common stock then outstanding (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders’ agreement), from and after that time, Invus will have the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders’ agreement), rounded up to the nearest whole number of directors. The directors appointed by Invus have proportionate representation on the compensation committee and corporate governance committee of our board of directors.

Invus’ rights with respect to the designation of members of our board of directors and its compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus will also have the right to terminate these provisions at any time following the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders’ agreement).

Preemptive Rights. Invus has preemptive rights under the stockholders’ agreement to participate in future equity issuances by us (including any qualified offering), subject to certain exceptions, so as to maintain its then-current percentage ownership of our capital stock. Subject to certain limitations, Invus will be required to exercise its preemptive rights in advance with respect to certain marketed offerings, in which case it will be obligated to buy its pro rata share of the number of shares being offered in such marketed offering, including any overallocation (or such lesser amount specified in its exercise of such rights), so long as the sale of the shares were priced within a range within 10% above or below the market price on the date we notified Invus of the offering and we met certain other conditions.

The provisions of the stockholders’ agreement relating to preemptive rights will terminate on the earlier to occur of August 28, 2017 and the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%.

Standstill Provisions. Invus is subject to standstill provisions restricting its ability to purchase or otherwise acquire additional shares of common stock from third parties to an amount that would result in its ownership of our common stock not exceeding 49% of the total number of shares outstanding. These standstill provisions will not apply to the acquisitions of securities by way of stock splits, stock dividends, reclassifications, recapitalizations, or other distributions by us, acquisitions contemplated by the securities purchase agreement and the stockholders' agreement, including in the rights offerings and upon Invus' exercise of preemptive rights under the stockholders' agreement.

Except for acquisitions pursuant to the provisions described above, and subject to certain exceptions, Invus has agreed that it will not, and will cause its affiliates not to, without the approval of our unaffiliated board, directly or indirectly:

- solicit proxies to vote any of our voting securities or any voting securities of our subsidiaries;
- submit to our board of directors a written proposal for any merger, recapitalization, reorganization, business combination or other extraordinary transaction involving an acquisition of us or any of our subsidiaries or any of our or our subsidiaries' securities or assets by Invus and its affiliates;
- enter into discussions, negotiations, arrangements or understandings with any third party with respect to any of the foregoing; or
- request us or any of our representatives, directly or indirectly, to amend or waive any of these standstill provisions.

The standstill provisions of the stockholders' agreement will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all of the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), (d) the date on which any third party makes a public proposal to acquire (by purchase, exchange, merger or otherwise) assets or business constituting 50% or more of our revenues, net income or assets or 50% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction or (e) the date on which any third party acquires beneficial ownership (by purchase, exchange, merger or otherwise) of assets or business constituting 20% or more of our revenues, net income or assets or 20% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction.

Sales to Third Parties. Subject to certain exceptions, Invus has agreed that neither it nor its affiliates will sell any shares of common stock to third parties that are not affiliated with Invus if, to Invus' knowledge, such transfer would result in any such third party (or any person or group including such third party) owning more than 14.9% of the total number of outstanding shares of our common stock.

The provisions of the stockholders' agreement relating to sales to third parties will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, and (c) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders' agreement).

Voting of Shares. In any election of persons to serve on our board of directors, Invus will be obligated to vote all of the shares of common stock held by it and its affiliates in favor of the directors nominated by our board of directors, as long as we have complied with our obligation with respect to the designation of members of our board of directors described above and the individuals designated by Invus for election to our board of directors have been nominated, and, if applicable, are serving on our board of directors. With respect to all other matters submitted to a vote of the holders of our common stock, Invus will be obligated to vote any shares that it acquired from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement, in the same proportion as all the votes cast by other holders of our common stock, unless Invus and we (acting with the approval of the unaffiliated board) agree otherwise. Invus may vote all other shares of our common stock held by it in its sole discretion.

The provisions of the stockholders' agreement relating to voting will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock held by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the provisions of the stockholders' agreement), and (d) the termination of the standstill provisions in accordance with the stockholders' agreement.

Minority Protections. Invus is entitled to certain minority protections, including consent rights over (a) the creation or issuance of any new class or series of shares of our capital stock (or securities convertible into or exercisable for shares of our capital stock) having rights, preferences or privileges senior to or on parity with our common stock, (b) any amendment to our certificate of incorporation or bylaws, or amendment to the certificate of incorporation or bylaws of any of our subsidiaries, in a manner adversely affecting Invus' rights under the securities purchase agreement and the related agreements, (c) the repurchase, retirement, redemption or other acquisition of our or our subsidiaries' capital stock (or securities convertible into or exercisable for shares of our or our subsidiaries' capital stock), (d) any increase in the size of our board of directors to more than 12 members and (e) the adoption or proposed adoption of any stockholders' rights plan, "poison pill" or other similar plan or agreement, unless Invus is exempt from the provisions of such plan or agreement.

The provisions of the stockholders' agreement relating to minority protections will terminate on the earlier to occur of August 28, 2017 and the date on which Invus and its affiliates hold less than 15% of the total number of outstanding shares of our common stock.

Registration Rights. Concurrently with the execution of the securities purchase agreement, we entered into a registration rights agreement with Invus, pursuant to which Invus has certain demand and piggyback registration rights with respect to shares of our common stock acquired by Invus under the securities purchase agreement.

STOCKHOLDER PROPOSALS FOR THE 2010 ANNUAL MEETING OF STOCKHOLDERS

In order for a stockholder proposal to be considered for inclusion in our proxy statement for next year's annual meeting, we must receive the written proposal at our principal executive offices no later than November 13, 2009. Any such proposal must also comply with Securities and Exchange Commission regulations regarding the inclusion of stockholder proposals in company-sponsored proxy materials. Similarly, in order for any stockholder proposal to be otherwise raised during next year's annual meeting, we must receive written notice of the proposal, containing the information required by our bylaws, at our principal executive offices no later than November 13, 2009. You may contact the corporate secretary at our principal executive offices for a copy of the relevant bylaw provisions for making stockholder proposals.

WHERE YOU CAN FIND MORE INFORMATION

You may obtain, without charge, a copy of our annual report on Form 10-K, including the financial statements and exhibits thereto, by written request to Corporate Communications, Lexicon Pharmaceuticals, Inc., 8800 Technology Forest Place, The Woodlands, Texas 77381.

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any reports, statements or other information we file at the SEC's public reference room at 100 F Street, N.E., Washington, D.C., 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from commercial document retrieval services and the web site maintained by the SEC at www.sec.gov.

FORWARD-LOOKING STATEMENTS

This proxy statement contains statements that do not directly or exclusively relate to historical facts. Such statements are “forward-looking statements.” You can typically identify forward-looking statements by the use of forward-looking words, such as “may,” “will,” “could,” “project,” “believe,” “anticipate,” “expect,” “estimate,” “potential,” “plan,” “forecast,” and other similar words. Forward-looking statements in this proxy statement include statements regarding the amendment to our certificate of incorporation and our expectations and plans with respect to the additional authorized shares of our common stock.

The forward-looking statements in this proxy statement reflect our intentions, plans, expectations, assumptions and beliefs about future events and are subject to risks, uncertainties and other factors, many of which are outside our control. Important factors could cause actual results to differ materially from the expectations expressed or implied in the forward-looking statements contained herein. Except as required by law, we undertake no obligation to update or revise our forward-looking statements, whether as a result of new information, future events or otherwise.

By order of the board of directors,

Jeffrey L. Wade
Secretary

June , 2009
The Woodlands, Texas

**FORM OF
THIRD CERTIFICATE OF AMENDMENT
TO
RESTATED CERTIFICATE OF INCORPORATION
OF
LEXICON PHARMACEUTICALS, INC.**

LEXICON PHARMACEUTICALS, INC. (the "Corporation"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware ("DGCL"), hereby certifies as follows pursuant to Section 242 of the DGCL:

FIRST: That at a meeting of the Board of Directors of the Corporation, resolutions were duly adopted setting forth a proposed amendment of the Corporation's Restated Certificate of Incorporation, as amended, declaring such amendment to be advisable and calling a meeting of the Corporation's stockholders for consideration thereof. The resolution setting forth the proposed amendment is as follows:

RESOLVED that, subject to the approval of the stockholders of the Corporation, the Corporation's restated certificate of incorporation, as amended, be further amended by changing Section 4.01(a) of Article IV thereof so that, as amended, such Section shall be and read as follows:

“(a) The total number of shares of stock that the Corporation shall have the authority to issue is 905,000,000 shares of capital stock, consisting of (i) 5,000,000 shares of preferred stock, par value \$0.01 per share (the "Preferred Stock"), and (ii) 900,000,000 shares of common stock, par value \$0.001 per share (the "Common Stock”).”

SECOND: That thereafter, pursuant to a resolution of its Board of Directors, a special meeting of the Corporation's stockholders was duly called and held upon notice in accordance with the provisions of Section 222 of the DGCL, at which meeting the necessary number of shares as required by applicable law were voted in favor of such amendment.

THIRD: That such amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL.

IN WITNESS WHEREOF, the Corporation has caused this Third Certificate of Amendment to be signed by Jeffrey L. Wade, its Executive Vice President and General Counsel, this ____ day of July, 2009.

LEXICON PHARMACEUTICALS, INC.

By: _____
Jeffrey L. Wade
Secretary

LEXICON PHARMACEUTICALS, INC.
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TX 77381-4287

VOTE BY INTERNET - www.proxyvote.com

Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

ELECTRONIC DELIVERY OF FUTURE STOCKHOLDER COMMUNICATIONS

If you would like to reduce the costs incurred by Lexicon Pharmaceuticals, Inc. in mailing proxy materials, you can consent to receiving all future proxy statements, proxy cards and annual reports electronically via e-mail or the internet. To sign up for electronic delivery, please follow the instructions above to vote using the internet and, when prompted, indicate that you agree to receive or access stockholder communications electronically in future years.

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Lexicon Pharmaceuticals, Inc. c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS

LEXP1

KEEP THIS PORTION FOR YOUR RECORDS
DETACH AND RETURN THIS PORTION ONLY

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED

LEXICON PHARMACEUTICALS, INC.

**THE BOARD OF DIRECTORS RECOMMENDS A
VOTE "FOR" ITEM 1**

Vote on Proposals

- | | | | |
|--|------------|----------------|----------------|
| | For | Against | Abstain |
| 1. Approval of an amendment to the Company's certificate of incorporation increasing the number of authorized shares of the Company's common stock from 300,000,000 to 900,000,000 | o | o | o |
| 2. In their discretion, upon such other matters that may properly come before the meeting or any adjournment or adjournments thereof. | | | |

The shares represented by this proxy, when properly executed, will be voted in the matter directed herein by the undersigned Stockholder(s). **If no direction is made, this proxy will be voted FOR item 1.** If any other matters properly come before the meeting, or if cumulative voting is required, the person named in this proxy will vote in their discretion.

Please sign your name exactly as it appears hereon. When signing as attorney, executor, administrator, trustee or guardian, please add your title as such. When signing as joint tenants, all parties in the joint tenancy must sign. If a signer is a corporation, please sign in full corporate name by duly authorized officer.

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Signature [PLEASE SIGN WITHIN BOX]

Date

--	--

Signature (Joint Owners)

Date

Important Notice Regarding the Availability of Proxy Materials for the Special Meeting:
The Notice and Proxy Statement are available at www.proxyvote.com.

LEXPH2

LEXICON PHARMACEUTICALS, INC.

THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS

SPECIAL MEETING OF STOCKHOLDERS
July 15, 2009

The stockholder(s) hereby appoint(s) Arthur T. Sands, M.D., Ph.D. and Jeffrey L. Wade, or either of them, as proxies, each with the power to appoint his substitute, and hereby authorize(s) them to represent and to vote, as designated on the reverse side of this ballot, all of the shares of Common Stock of Lexicon Pharmaceuticals, Inc. that the stockholder(s) is/are entitled to vote at the Special Meeting of Stockholders to be held at 1:30 p.m., local time, on July 15, 2009 at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas, and any adjournment or postponement thereof.

THIS PROXY, WHEN PROPERLY EXECUTED, WILL BE VOTED AS DIRECTED BY THE STOCKHOLDER(S). IF NO SUCH DIRECTIONS ARE MADE, THIS PROXY WILL BE VOTED FOR THE PROPOSAL.

PLEASE MARK, SIGN, DATE AND RETURN THIS PROXY CARD PROMPTLY USING THE ENCLOSED REPLY

CONTINUED AND TO BE SIGNED ON REVERSE SIDE

