

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**SCHEDULE 13D**

Under the Securities Exchange Act of 1934  
(Amendment No. 3)\*

**Lexicon Pharmaceuticals, Inc.**

(Name of Issuer)

**Common Stock, par value \$0.001 per share**  
(Title of Class of Securities)

**528872104**

(CUSIP Number)

**Raymond Debbane**  
*c/o Ulys, L.L.C.*  
**750 Lexington Avenue**  
**30<sup>th</sup> Floor**  
**New York, New York 10022**  
**(212) 371-1717**

**Copies to:**

**Robert Spatt, Esq.**  
**Peter Malloy, Esq.**  
**Simpson Thacher & Bartlett LLP**  
**425 Lexington Avenue**  
**New York, NY 10017**  
**(212) 455-2000**

(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications)

**October 7, 2009**

(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

**Note:** Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7 for other parties to whom copies are to be sent.

\* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

CUSIP No. 528872104

1. Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).	
Invus, L.P. I.R.S. Identification No. 83-0359143	
2. Check the Appropriate Box if a Member of a Group (See Instructions)	
(a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3. SEC Use Only	
4. Source of Funds (See Instructions)	
OO	
5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	
6. Citizenship or Place of Organization	
Bermuda	
Number of Shares Beneficially Owned by Each Reporting Person With	7. Sole Voting Power
	51,494,038
	8. Shared Voting Power
	3,891,108
	9. Sole Dispositive Power
	51,494,038
	10. Shared Dispositive Power
	0
11. Aggregate Amount Beneficially Owned by Each Reporting Person	55,385,146
12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13. Percent of Class Represented by Amount in Row (11)	
40.3%*	
14. Type of Reporting Person (See Instructions)	
PN	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

CUSIP No. 528872104

1. Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).	
Invus Advisors, L.L.C. I.R.S. Identification No. 83-0359142	
2. Check the Appropriate Box if a Member of a Group (See Instructions)	
(a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3. SEC Use Only	
4. Source of Funds (See Instructions)	
OO	
5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	
6. Citizenship or Place of Organization	
Delaware	
Number of Shares Beneficially Owned by Each Reporting Person With	7. Sole Voting Power
	51,494,038
	8. Shared Voting Power
	3,891,108
	9. Sole Dispositive Power
	51,494,038
	10. Shared Dispositive Power
	0
11. Aggregate Amount Beneficially Owned by Each Reporting Person	55,385,146
12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13. Percent of Class Represented by Amount in Row (11)	
40.3%*	
14. Type of Reporting Person (See Instructions)	
OO	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

CUSIP No. 528872104

1. Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).	
Invus Public Equities, L.P. I.R.S. Identification No. 98-0420215	
2. Check the Appropriate Box if a Member of a Group (See Instructions)	
(a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3. SEC Use Only	
4. Source of Funds (See Instructions)	
OO	
5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	
6. Citizenship or Place of Organization	
Bermuda	
Number of Shares Beneficially Owned by Each Reporting Person With	7. Sole Voting Power
	0
	8. Shared Voting Power
	3,891,108
	9. Sole Dispositive Power
	3,891,108
	10. Shared Dispositive Power
	0
11. Aggregate Amount Beneficially Owned by Each Reporting Person	3,891,108
12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13. Percent of Class Represented by Amount in Row (11)	
2.8%*	
14. Type of Reporting Person (See Instructions)	
PN	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

CUSIP No. 528872104

1. Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).	
Invus Public Equities Advisors, LLC I.R.S. Identification No. 98-04220201	
2. Check the Appropriate Box if a Member of a Group (See Instructions)	
(a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3. SEC Use Only	
4. Source of Funds (See Instructions)	
OO	
5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	
6. Citizenship or Place of Organization	
Delaware	
Number of Shares Beneficially Owned by Each Reporting Person With	7. Sole Voting Power
	0
	8. Shared Voting Power
	3,891,108
	9. Sole Dispositive Power
	3,891,108
	10. Shared Dispositive Power
	0
11. Aggregate Amount Beneficially Owned by Each Reporting Person	3,891,108
12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13. Percent of Class Represented by Amount in Row (11)	
2.8%*	
14. Type of Reporting Person (See Instructions)	
OO	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

CUSIP No. 528872104

1.		Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).  Ulys, L.L.C. I.R.S. Identification No. 83-0359139
2.		Check the Appropriate Box if a Member of a Group (See Instructions)  (a) <input type="checkbox"/> (b) <input type="checkbox"/>
3.		SEC Use Only
4.		Source of Funds (See Instructions)  OO
5.		Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)
6.		Citizenship or Place of Organization  Delaware
Number of Shares Beneficially Owned by Each Reporting Person With	7.	Sole Voting Power  55,385,146
	8.	Shared Voting Power  0
	9.	Sole Dispositive Power  55,385,146
	10.	Shared Dispositive Power  0
11.	Aggregate Amount Beneficially Owned by Each Reporting Person  55,385,146	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13.	Percent of Class Represented by Amount in Row (11)  40.3%*	
14.	Type of Reporting Person (See Instructions)  OO	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

CUSIP No. 528872104

1.	Names of Reporting Persons. I.R.S. Identification Nos. of above persons (entities only).	
	Raymond Debbane	
2.	Check the Appropriate Box if a Member of a Group (See Instructions)	
	(a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3.	SEC Use Only	
4.	Source of Funds (See Instructions)	
	OO	
5.	Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)	
6.	Citizenship or Place of Organization	
	Panama	
Number of Shares Beneficially Owned by Each Reporting Person With	7.	Sole Voting Power
		55,385,146
	8.	Shared Voting Power
		0
	9.	Sole Dispositive Power
		55,385,146
	10.	Shared Dispositive Power
		0
11.	Aggregate Amount Beneficially Owned by Each Reporting Person	
	55,385,146	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)	
13.	Percent of Class Represented by Amount in Row (11)	
	40.3%*	
14.	Type of Reporting Person (See Instructions)	
	IN	

\* Based on 137,371,548 shares of Issuer Common Stock outstanding as of September 30, 2009, as provided by the Issuer.

This Amendment No. 3 hereby amends and supplements the statement of beneficial ownership on Schedule 13D, relating to the common stock, \$0.001 par value per share (the "Issuer Common Stock"), of Lexicon Pharmaceuticals, Inc., a Delaware corporation (the "Issuer" or "Lexicon"), initially filed on June 27, 2007, as amended by Amendment No.1 thereto filed on August 24, 2007 and Amendment No. 2 thereto filed on August 29, 2007 (as so amended, the "Statement"). All capitalized terms not otherwise defined herein have the meaning assigned to them in the Statement.

**Item 3. Source and Amount of Funds or Other Consideration**

Item 3 of the Statement is hereby amended and supplemented by inserting the following immediately after the last paragraph thereof:

On April 30, 2008, Invus, L.P. purchased 669,052 shares of Issuer Common Stock for an aggregate amount of \$1,338,104 at the purchase price of \$2.00 per share. Invus, L.P. used funds obtained from a capital call to its limited partners in respect of previously made commitments for the payment of the purchase price for such additional shares of Issuer Common Stock.

**Item 4. Purpose of Transaction**

Item 4 of the Statement is hereby amended and supplemented by inserting the following at the end of the first paragraph thereof:

Any reference in the Statement or any other document to the Securities Purchase Agreement, Warrant Agreement, Registration Rights Agreement or Stockholders' Agreement is deemed to refer to the Securities Purchase Agreement, Warrant Agreement, Registration Rights Agreement or Stockholders' Agreement, as applicable, as such may be amended or supplemented from time to time.

Item 4 of the Statement is hereby amended and supplemented by inserting the following immediately after the third paragraph thereof:

On October 7, 2009, the Issuer announced an intention to conduct a public offering of Issuer Common Stock. Pursuant to the terms of the Stockholders' Agreement, Invus, L.P. has the right to purchase its pro rata amount of the shares offered in this offering at the offering price. Invus, L.P. has not yet made a final decision whether it will purchase its pro rata amount, or any, of the shares of Issuer Common Stock to be offered by the Issuer. Invus, L.P. has not been assured by the Issuer that the offering will be consummated.

On October 7, 2009, Invus, L.P. and Lexicon entered into an Amendment to Securities Purchase Agreement (the "SPA Amendment"), pursuant to which, among other things, Invus, L.P. and Lexicon agreed to amend certain provisions of the Securities Purchase Agreement, which would become effective if Invus, L.P. grants its written consent to Lexicon's proposed public offering of Issuer Common Stock. The SPA Amendment is summarized in Item 6 below and is filed as an exhibit to the Statement. The SPA Amendment, and the description thereof included in Item 6 below, are incorporated by reference into this Item 4.



On October 7, 2009, Invus Public Equities, L.P. and Invus, L.P. entered into a voting agreement (the "Voting Agreement"), pursuant to which, among other things, Invus Public Equities, L.P. granted to Invus, L.P. a proxy card and agreed to vote its shares of Issuer Common Stock and other voting securities of Lexicon at the sole direction of Invus, L.P. The Voting Agreement is summarized in Item 6 below and is filed as an exhibit to the Statement. The Voting Agreement, and the description thereof included in Item 6 below, are incorporated by reference into this Item 4.

**Item 5. Interest in Securities of the Issuer**

Item 5 of the Statement is hereby amended and supplemented by replacing the second paragraph of clause (a) thereof with the following:

As of October 7, 2009, Invus, L.P. was the record owner of 51,494,038 shares of Issuer Common Stock and the beneficial owner of 55,385,146 shares of Issuer Common Stock, representing approximately 37.5% and approximately 40.3% of the outstanding shares of Issuer Common Stock, respectively.

Item 5 is hereby amended and supplemented by inserting the following immediately after the last paragraph of clause (a) thereof:

Except for Messrs. Amouyal, Debbane and Sobecki, none of the individuals listed in Schedule I beneficially owns any shares of Issuer Common Stock issuable pursuant to options that are exercisable within 60 days of October 7, 2009. Each of Messrs. Amouyal, Debbane and Sobecki beneficially owns 29,333 shares of Issuer Common Stock issuable pursuant to options that are exercisable within 60 days of October 7, 2009, in each case representing less than 1% of the number of outstanding shares of Issuer Common Stock.

**Item 6. Contracts, Arrangements or Understandings with Respect to Securities of the Issuer**

Item 6 is hereby amended and supplemented by inserting the following immediately after the last paragraph thereof:

**e. Amendment to Securities Purchase Agreement**

On October 7, 2009, Invus, L.P. and Lexicon entered into the SPA Amendment, pursuant to which, among other things, Invus, L.P. and Lexicon agreed to amend certain provisions of the Securities Purchase Agreement. The following is a summary of selected provisions of the SPA Amendment. While the Invus Parties believe this description covers the material terms of the SPA Amendment, it is qualified in its entirety by reference to the SPA Amendment, a copy of which is included as Exhibit 7 to the Statement and is incorporated herein by reference.

***Rights Offering Oversubscription Allocation***

The definition of “Oversubscription Pro Rata Number” was changed to provide that holders exercising oversubscription rights in full in any Rights Offering will be allocated, on a pro rata basis based on the number of shares allocated to such holders pursuant to their oversubscription rights, shares not subscribed for by other holders that exercise less than their entire respective oversubscription rights.

***Rights Offerings***

For each of the Rights Offerings, the SPA Amendment (i) extends to one year (subject to extension in certain circumstances) the period during which Invus, L.P. may require Lexicon to conduct a Rights Offering, (ii) amends the date on which Invus, L.P.’s right to require Lexicon to conduct the Second Rights Offering begins to the date that is 90 days after Invus, L.P. exercises its right to require Lexicon to conduct the First Rights Offering or, if Invus does not exercise such right, the expiration of the period (as it may be extended in certain circumstances) in which Invus, L.P. may require Lexicon to conduct the First Rights Offering and (iii) eliminates Invus, L.P.’s obligation to purchase unsubscribed-for Rights Shares at the expiration of a Rights Offering.

***Rights Offering Notice Blackout Periods***

In connection with certain public offerings of Issuer Common Stock priced above \$4.50 per share proposed by Lexicon during the period in which Invus, L.P. may deliver any Rights Offering Notice, Invus, L.P. will have the right, for a period of 10 business days from the date of receipt of notice of such proposed offering, to require Lexicon to commence a Rights Offering, in which case Lexicon will forego the proposed public offering until the Rights Offering is completed or terminated and proceed with the Rights Offering. In the event that Invus, L.P. does not deliver a request to Lexicon to commence such Rights Offering, Lexicon will have the right to conduct such public offering, and Invus, L.P. will not deliver a Rights Offering Notice to Lexicon (i) for a period of 30 days from the date of receipt of Lexicon’s notice of such proposed offering and (ii) so long as such public offering occurs within such 30 day period, for a period of 90 days from the date of the consummation of such public offering. Lexicon may exercise its right to cause such periods to take effect only once in any 12 month period. The periods in which Invus, L.P. may require Lexicon to conduct a Rights Offering will be tolled for the period in which Invus, L.P. is not permitted to require a Rights Offering to be conducted pursuant to this provision.

***Shelf Registration***

Subject to certain restrictions, Lexicon may file a shelf registration statement that is reasonably satisfactory to Invus, L.P. covering the issuance of Rights and Rights Shares. Alternatively, if Lexicon has a shelf registration statement in effect sufficient to cover the issuance of the Rights and Rights Shares to be issued in a Rights Offering, then Lexicon may, subject to certain restrictions, use such shelf registration statement for purposes of such Rights Offering.

***Effectiveness***

The SPA Amendment is effective only upon delivery by Invus, L.P. to Lexicon of Invus, L.P.'s consent to the proposed public offering of Issuer Common Stock substantially in the form of Exhibit A to the SPA Amendment. If the underwriting agreement relating to such offering is not executed on or before October 13, 2009, the SPA Amendment and Invus L.P.'s consent to such offering (if delivered) will terminate.

**f. Voting Agreement**

On October 7, 2009, Invus Public Equities, L.P. and Invus, L.P. entered into the Voting Agreement, pursuant to which Invus Public Equities, L.P. agreed to vote its shares of Issuer Common Stock and other voting securities of Lexicon at the sole direction of Invus, L.P. As security for its agreement to vote its shares of common stock and other voting securities of Lexicon at the sole direction of Invus, L.P., Invus Public Equities, L.P. appointed Invus, L.P. and its designees as its proxy with respect to all such shares and other voting securities of Lexicon. A copy of the Voting Agreement is included as Exhibit 8 to the Statement and is incorporated herein by reference.

**Item 7. Material to be Filed as Exhibits**

Item 7 is hereby amended and supplemented by inserting the following at the end thereof:

7. Amendment to Securities Purchase Agreement, dated as of October 7, 2009.
8. Voting Agreement, dated as of October 7, 2009.

**SCHEDULE I**

Schedule I is hereby amended by inserting Evren Bilimer, a citizen of Turkey, as a Managing Director of Invus Advisors, L.L.C. Mr. Bilimer's present principal occupation or employment is as a Managing Director of The Invus Group, LLC.

Schedule I is hereby amended by changing the description of the citizenship of Jonas Fajgenbaum to read "citizen of the United States."

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.

**INVUS, L.P.**

By: INVUS ADVISORS, L.L.C.,  
its general partner

By: /s/ RAYMOND DEBBANE  
Name: Raymond Debbane  
Title: President

**INVUS PUBLIC EQUITIES, L.P.**

By: INVUS PUBLIC EQUITIES ADVISORS, LLC,  
its general partner

By: /s/ RAYMOND DEBBANE  
Name: Raymond Debbane  
Title: President

**INVUS ADVISORS, L.L.C.**

By: /s/ RAYMOND DEBBANE  
Name: Raymond Debbane  
Title: President

**INVUS PUBLIC EQUITIES ADVISORS, LLC**

By: /s/ RAYMOND DEBBANE  
Name: Raymond Debbane  
Title: President

**ULYS, L.L.C.**

By: /s/ RAYMOND DEBBANE  
Name: Raymond Debbane  
Title: President

**RAYMOND DEBBANE**

/s/ RAYMOND DEBBANE

Dated: October 7, 2009

**AMENDMENT TO  
SECURITIES PURCHASE AGREEMENT**

This Amendment to Securities Purchase Agreement (this "Amendment") is entered into as of October 7, 2009 by and between Invus, L.P., a Bermuda limited partnership (the "Investor"), and Lexicon Pharmaceuticals, Inc., a Delaware corporation (the "Company"). Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Securities Purchase Agreement (as defined below).

W I T N E S S E T H :

WHEREAS, the Investor and the Company entered into that certain Securities Purchase Agreement, dated as of June 17, 2007 (the "Securities Purchase Agreement"), and that certain Stockholders' Agreement, made as of June 17, 2007 (the "Stockholders' Agreement");

WHEREAS, the Company desires to issue and sell shares of Company Common Stock in an underwritten offering registered under the Securities Act (the "Offering"), which Offering requires the consent of the Investor under the Securities Purchase Agreement; and

WHEREAS, in connection with the Offering, the Investor and the Company desire to amend the Securities Purchase Agreement as set forth below to (a) modify the definition of Second Rights Offering Trigger Date, (b) extend the period during which the Investor may deliver the First Rights Offering Notice and Second Rights Offering Notice from ninety (90) days to one (1) year after the First Rights Offering Trigger Date and Second Rights Offering Trigger Date, respectively, (c) eliminate the Investor's obligation to purchase unsubscribed Rights Shares at the expiration of a Rights Offering, and (d) make certain other amendments to the terms thereof.

NOW, THEREFORE, intending to be legally bound hereby, the parties hereto hereby agree as follows:

**Section 1. Amendment to Section 1.01 of the Securities Purchase Agreement**

The definition of "Oversubscription Pro Rata Number" in Section 1.01 of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

"Oversubscription Pro Rata Number" shall mean, for each holder of a Right exercising Rights Offering Oversubscription rights, a fraction the numerator of which is the total number of shares of Company Common Stock owned by such holder and the denominator of which is the total number of outstanding shares of Company Common Stock held by all holders of Rights who have validly exercised Rights Offering Oversubscription rights in the relevant Rights Offering (it being understood that no shares shall be deemed owned by more than one holder for purposes hereof); *provided* that, to the extent any holders validly exercising Rights Offering Oversubscription rights exercise such rights with respect to less than their entire respective Oversubscription Pro Rata Numbers of Oversubscription Shares (with the unsubscribed-for Oversubscription Shares

being referred to as “Excess Oversubscription Shares”), the Oversubscription Pro Rata Numbers of all other holders validly exercising Rights Offering Oversubscription rights in full shall be increased proportionately up to the maximum number of Oversubscription Shares such holders elect to purchase (it being the intent of this provision that the Oversubscription Pro Rata Numbers be established such that any such Excess Oversubscription Shares be allocated among holders exercising Rights Offering Oversubscription rights in full on a pro rata basis based on the number of Oversubscription Shares allocated to such holders, up to the total number of Excess Oversubscription Shares such holders elect to purchase); *provided further*, with the written consent of both the Investor and the Company, the determination of the Oversubscription Pro Rata Number may be based on another customary proration method.

Section 1.01 of the Securities Purchase Agreement is hereby amended by adding the following definition of “Oversubscription Shares” immediately after the definition of “Oversubscription Pro Rata Number” therein as follows:

“Oversubscription Shares” shall mean First Rights Offering Oversubscription Shares in the First Rights Offering or Second Rights Offering Oversubscription Shares in the Second Rights Offering, as applicable.

The definition of “Second Rights Offering Trigger Date” in Section 1.01 of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

“Second Rights Offering Trigger Date” means the date that is (i) ninety (90) days after the delivery of the First Rights Offering Notice or (ii) if such notice is not delivered, the date of the expiration of the period (as it may be extended by any Rights Offering Notice Blackout Period) in which the Investor may give notice to require the Company to conduct the First Rights Offering pursuant to Section 3.01(a).

## **Section 2. Amendments to Section 3.01 of the Securities Purchase Agreement**

The first sentence of Section 3.01(a) of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

Subject to Section 3.03(e), for a period of one (1) year following the First Rights Offering Trigger Date, the Investor shall have the right, but not the obligation, exercisable by a written notice (the “First Rights Offering Notice”) to the Company in accordance with Section 10.02, to require the Company to make a pro rata offering (the “First Rights Offering”) to all holders of Company Common Stock (including the Investor and its affiliates) of non-transferable subscription rights (the “First Rights”) entitling the holders thereof to purchase shares of Company Common Stock, on the terms set forth herein, (i) in an aggregate amount equal to the First Rights Offering Amount, and (ii) at a price per share (the “First Rights Offering Price”) to be designated by the Investor at any time on or after delivery of the First Rights Offering Notice and before the establishment

of the record date for the distribution of the First Rights to the Company's stockholders (provided that the establishment of such record date shall not be prior to the time the First Rights Offering Registration Statement shall have been declared effective by the SEC) by written notice (the "First Rights Offering Pricing Notice") to the Company in accordance with Section 10.02; *provided* that the First Rights Offering Price shall be any price (A) at or above the lower of \$4.50 (as adjusted for any stock splits, reverse splits, stock dividends, combinations or similar transactions occurring after the date hereof and prior to the First Rights Offering) and the average of the volume weighted average trading prices of the Company Common Stock on the Nasdaq Stock Market for the ten (10) full trading days immediately prior to the date of the First Rights Offering Pricing Notice (the "First Rights Offering Market Price") and (B) at or below the higher of \$4.50 (as adjusted for any stock splits, reverse splits, stock dividends, combinations or similar transactions occurring after the date hereof and prior to the First Rights Offering) and the First Rights Offering Market Price.

Section 3.01(b) of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

(b) In connection with the First Rights Offering, upon the terms and subject to the conditions of this Agreement, the Investor shall be required to subscribe for and purchase a number of First Rights Shares that is not less than its Pro Rata Number of First Rights Shares.

### **Section 3. Amendments to Section 3.02 of the Securities Purchase Agreement**

The first sentence of Section 3.02(a) of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

Subject to Section 3.03(e), for a period of one (1) year following the Second Rights Offering Trigger Date, the Investor shall have the right, but not the obligation, exercisable by written notice (the "Second Rights Offering Notice" and, together with the First Rights Offering notice, the "Rights Offering Notices") to the Company in accordance with Section 10.02, to require the Company to make a pro rata offering (the "Second Rights Offering" and, together with the First Rights Offering, the "Rights Offerings") to all holders of Company Common Stock (including the Investor and its affiliates) of non-transferable subscription rights (the "Second Rights" and, together with the First Rights, the "Rights") entitling the holders thereof to purchase shares of Company Common Stock, on the terms set forth herein, (i) in an aggregate amount equal to the Second Rights Offering Amount, and (ii) at a price per share (the "Second Rights Offering Price") to be designated by the Investor at any time on or after delivery of the Second Rights Offering Notice and before the establishment of the record date for the distribution of the Second Rights to the Company's stockholders (provided that the establishment of such record date shall not be prior to the time the Second Rights Offering Registration Statement shall have been declared effective by the SEC) by written notice (the "Second Rights Offering Pricing Notice") to the

Company in accordance with Section 10.02; *provided* that the Second Rights Offering Price shall be any price (A) at or above the lower of \$4.50 (as adjusted for any stock splits, reverse splits, stock dividends, combinations or similar transactions occurring after the date hereof and prior to the Second Rights Offering) and the average of the volume weighted average trading prices of the Company Common Stock on the Nasdaq Stock Market for the ten (10) full trading days immediately prior to the date of the Second Rights Offering Pricing Notice (the "Second Rights Offering Market Price") and (B) at or below the higher of \$4.50 (as adjusted for any stock splits, reverse splits, stock dividends, combinations or similar transactions occurring after the date hereof and prior to the Second Rights Offering) and the Second Rights Offering Market Price.

Section 3.02(b) of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

(b) In connection with the Second Rights Offering, upon the terms and subject to the conditions of this Agreement, the Investor shall be required to subscribe for and purchase a number of Second Rights Shares that is not less than its Pro Rata Number of Second Rights Shares.

#### **Section 4. Amendment to Section 3.03 of the Securities Purchase Agreement**

Section 3.03 of the Securities Purchase Agreement is hereby amended by adding new Section 3.03(e) at the end thereof as follows:

(e) In the event that the Company delivers a bona fide Notice of Issuance in connection with a Marketed Offering (in each case, as such terms are defined and contemplated by Section 4.02 of the Stockholders' Agreement) to the Investor during the period in which the Investor may deliver any Rights Offering Notice under Section 3.01(a) or Section 3.02(a), the Investor shall have the right, for a period of ten (10) business days from the date of receipt of such Notice of Issuance, to deliver a Rights Offering Notice to the Company, in which case the Company shall retract the Notice of Issuance, proceed with the Rights Offering contemplated by the Investor's notice, and forego the Marketed Offering contemplated thereby until such Rights Offering is completed or, with the consent of the Investor, terminated. In the event that the Investor does not deliver such Rights Offering Notice to the Company upon the expiration of such ten (10) business day period, the Company shall have the right to conduct the Marketed Offering contemplated by the Notice of Issuance, and the Investor shall not deliver a Rights Offering Notice to the Company (i) for a period of thirty (30) days from the date of delivery by the Company of the Notice of Issuance (the "Initial Rights Offering Notice Blackout Period") and (ii) so long as the offering of New Securities (as defined in the Stockholders' Agreement) described in such Notice of Issuance occurs within the Initial Rights Offering Notice Blackout Period, and only if requested in writing by the underwriters for the Marketed Offering contemplated by such Notice of Issuance, for a period of ninety (90)



days from the date of issuance of the New Securities contemplated by such Notice of Issuance (such period, together with the Initial Rights Offering Notice Blackout Period, the “Rights Offering Notice Blackout Periods”). Notwithstanding anything to the contrary in the foregoing, the Company may exercise its right to cause Rights Offering Notice Blackout Periods under this Section 3.03(e) only once in any twelve (12) month period; *provided* that, for such purposes, the Company shall not be deemed to have exercised such right if, following the Company’s delivery of a Notice of Issuance in connection with a Marketed Offering, the Investor shall have delivered a Rights Offering Notice to the Company and the Company shall have retracted such Notice of Issuance in accordance with this Section 3.03(e); and *provided, further*, that nothing in this Section 3.03(e) shall prohibit the Company from conducting a Marketed Offering without exercising its right to cause a Rights Offering Notice Blackout Period under this Section 3.03(e). The running of the period in which the Investor may deliver any Rights Offering Notice under Section 3.01(a) or Section 3.02(a), as applicable, shall be tolled while any Rights Offering Notice Blackout Period is in effect.

**Section 5. Addition of Section 3.04 of the Securities Purchase Agreement**

The Securities Purchase Agreement is hereby amended by adding new Section 3.04:

**SECTION 3.04. Shelf Registration.**

(a) So long as it would not reasonably be expected to materially delay the applicable Rights Offering, (i) the Company may, at its option, file with the SEC one or more shelf registration statements on Form S-3 (or, if Form S-3 is not then available to the Company, on such form of registration statement as is then available to effect a registration of securities), in form and substance reasonably satisfactory to the Investor, covering the issuance of Rights and Rights Shares, together with such other securities as the Company may elect (together with the prospectus relating thereto and any prospectus supplement and offering documents, a “Shelf Registration Statement”) and (ii) in the event the Company has in effect, at the time of the Investor’s delivery of a Rights Offering Notice, an effective Shelf Registration Statement sufficient to cover the issuance of the Rights and the Rights Shares to be offered in such Rights Offering, then rather than filing a Rights Offering Registration Statement pursuant to Section 3.01(c) or 3.02(c), as applicable, the Company shall be entitled to employ such Shelf Registration Statement as the relevant Rights Offering Registration Statement for purposes of such Rights Offering. Any such Shelf Registration Statement (and each amendment or supplement thereto, and each request for acceleration of effectiveness thereof) will be provided to the Investor prior to its filing with or other submission to the SEC. The Company shall not include any other securities in the prospectus supplement relating to any Rights Offering. Any such Shelf Registration Statement employed as a Rights Offering Registration Statement will comply in all material respects with the requirements of the Securities Act and the rules and regulations thereunder and other applicable Laws. The Company

promptly will correct any information included in any Shelf Registration Statement employed as a Rights Offering Registration Statement if, and to the extent that, such information becomes false or misleading in any material respect, and the Company will take all steps necessary to cause the applicable prospectus (including any applicable prospectus supplement) contained in such Shelf Registration Statement employed as a Rights Offering Registration Statement, as so corrected, to be filed with the SEC and to be disseminated to the distributees of Rights, in each case as and to the extent required by applicable federal securities laws. The Investor will be given a reasonable opportunity to review and comment upon any Shelf Registration Statement in each instance before it is filed with the SEC. In addition, the Company will provide the Investor with any written comments or other written communications that the Company receives from time to time from the SEC or its staff with respect to any Shelf Registration Statement promptly after the receipt of such comments or other communications.

(b) Notwithstanding the provisions of Section 3.01(d) or 3.02(d), as applicable, in the event the Company employs a Shelf Registration Statement as the relevant Rights Offering Registration Statement for purposes of a Rights Offering, the Company will commence such Rights Offering as soon as reasonably practicable following its receipt of the Rights Offering Notice relating thereto.

**Section 6. Amendment to Section 6.02(a) of the Securities Purchase Agreement**

Section 6.02(a) of the Securities Purchase Agreement is hereby amended and restated in its entirety to read as follows:

(a) Until (i) the completion of the Second Rights Offering as contemplated by Section 3.02 or (ii) the expiration of the period following the Second Rights Offering Trigger Date during which the Investor may exercise its right to require the Company to conduct the Second Rights Offering (as such period may be extended), if the Investor does not exercise such right within such period, the prior written consent of the Investor shall be required for the issuance by the Company of any shares of Company Common Stock for a per share price of less than \$4.50 (as adjusted for any stock splits, reverse splits, stock dividends, combinations or similar transactions occurring after the date hereof and prior to the Second Rights Offering); *provided* that the provisions of this Section 6.02 shall not apply to the issuance of Company Common Stock (A) pursuant to employee or director stock option, incentive compensation or similar plans approved by the Board or a duly authorized committee thereof or such committee, (B) to persons involved in the pharmaceutical industry in connection with simultaneous strategic transactions involving such persons in the ordinary course or (C) in connection with the exercise, on or after February 27, 2011, of the Company's option to acquire Symphony Icon, Inc. in accordance with the terms of its Purchase Option Agreement among the Company, Symphony Icon Holdings LLC and Symphony Icon, Inc., as such agreement is in effect on October 6, 2009.

**Section 7. Consent to Further Amendments; Further Assurances**

The parties hereto hereby consent to such other amendments and changes to the Securities Purchase Agreement and Ancillary Agreements as necessary to give effect to the intent of this Amendment and shall execute and deliver or cause to be executed and delivered any additional documents, certificates, consents, waivers and instruments and perform any additional acts that may be reasonably necessary or appropriate to effectuate and perform the provisions of this Amendment and those transactions contemplated herein.

**Section 8. Consent to Waiver of Investor Election Period in Sections 4.02(b) and 4.02(c) of the Stockholders' Agreement; Rights Offering Blackout**

(a) With respect to the Offering (including any related overallotment option), the Company and the Investor hereby waive any applicability to the Offering of the notice provisions contained in Sections 4.02(b) and (c) of the Stockholders' Agreement and agree that notice will be delivered as follows: the Company shall deliver a Notice of Issuance specifying the price to public and number of shares to be sold to public in the Offering on the date the underwriting agreement is expected to be signed by the Company in connection with the Offering and, upon receipt of such notice by the Investor, the Investor (i) shall exercise its rights under Section 4.02 with respect to the Offering by delivering notice of such exercise substantially concurrently with the signing by the Company of the underwriting agreement with respect thereto, and (ii) shall retain the right to make an election whether to exercise its rights under Section 4.02 with respect to any additional New Securities issued upon the exercise by the underwriters of their overallotment option in connection with such Offering by delivering notice of such exercise as promptly as practicable following the Company's notice to the Investor of the underwriters' exercise of such option. For the avoidance of doubt, with respect to the Offering, the Investor waives its right to deliver notice of its intent to participate in the Offering ten (10) business days following receipt of the Notice of Issuance related thereto.

(b) The Investor agrees not to exercise its right to cause the Company to conduct a Rights Offering during the ninety (90) day period following the delivery of the Offering Consent (as defined in Section 9 hereof). Notwithstanding the amendments to Section 3.03 of the Securities Purchase Agreement effected hereby, the periods in which the Investor may deliver any Rights Offering Notice under Section 3.01(a) and Section 3.02(a) shall not be extended by such ninety (90) day period, and shall not be deemed to be an exercise of the Company's right to cause Rights Offering Notice Blackout Periods under Section 3.03(e).

(c) The Investor expressly acknowledges and agrees that the provisions of Sections 4.02(b) and 4.02(c) of the Stockholders' Agreement relating to the free transferability of shares to be received in the Offering shall not affect its obligations under its "lock-up" agreement dated October 5, 2009 with the underwriters, which restricts the transferability of New Securities to be issued by the Company in connection with the Offering.

**Section 9. Effectiveness; Termination**

This Amendment shall become effective only upon delivery by the Investor to the Company, pursuant to Section 6.02(a) of the Securities Purchase Agreement, of the Investor's written consent to the Offering substantially in the form of Exhibit A hereto (the "Offering Consent"). Notwithstanding any such delivery, in the event that the underwriting agreement relating to the Offering is not executed on or before October 13, 2009, (i) this Amendment shall terminate and cease to have any force or effect and (ii) the Offering Consent shall be of no force or effect.

**Section 10. Ratification and Confirmation**

The Securities Purchase Agreement and Stockholders' Agreement, as hereby amended or supplemented, are hereby ratified and confirmed in all respects. This Amendment shall be interpreted and construed together with, and as a part of, the Securities Purchase Agreement or Stockholders' Agreement, as applicable. Any reference in any other document to the Securities Purchase Agreement or Stockholders' Agreement shall be deemed to refer to the Securities Purchase Agreement or Stockholders' Agreement, as applicable, as modified by this Amendment. The execution, delivery and effectiveness of this Amendment shall not constitute a modification or waiver of any provision of the Securities Purchase Agreement or Stockholders' Agreement except as expressly provided herein.

**Section 11. Governing Law**

This Amendment shall be governed by, and construed in accordance with, the laws of the State of New York. All actions and proceedings arising out of or relating to this Amendment shall be heard and determined exclusively in any New York state or federal court, in each case sitting in the Borough of Manhattan. The parties hereto hereby (a) submit to the exclusive jurisdiction of any New York state or federal court, in each case sitting in the Borough of Manhattan, for the purpose of any Action arising out of or relating to this Amendment brought by any party hereto, and (b) irrevocably waive, and agree not to assert by way of motion, defense, or otherwise, in any such Action, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the Action is brought in an inconvenient forum, that the venue of the Action is improper, or that this Amendment may not be enforced in or by any of the above-named courts.

**Section 12. Counterparts**

This Amendment may be executed and delivered (including by facsimile transmission) in one or more counterparts, and by the different parties hereto in separate counterparts, each of which when executed and delivered shall be deemed to be an original but all of which taken together shall constitute one and the same agreement.

*[Signature Page Follows]*

IN WITNESS WHEREOF, the Investor and the Company have caused this Amendment to be executed as of the date first written above by their respective officers thereunto duly authorized.

**INVESTOR:**

INVUS, L.P.,  
a Bermuda limited partnership

By: /s/ Raymond Debbane  
Name: Raymond Debbane  
Title: President, Invus Advisors, L.L.C.

**COMPANY:**

LEXICON PHARMACEUTICALS, INC.,  
a Delaware corporation

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

*[Signature Page to Amendment to Securities Purchase Agreement]*

**NOTICE OF  
CONSENT TO OFFERING**

October \_\_, 2009

Invus, L.P.  
c/o The Invus Group, L.L.C.  
750 Lexington Avenue (30<sup>th</sup> Floor)  
New York, New York 10022

Lexicon Pharmaceuticals, Inc.  
8800 Technology Forest Place  
The Woodlands, Texas 77381  
Attn: President and Chief Executive Officer

Ladies and Gentlemen:

Reference is made to that certain Securities Purchase Agreement, dated as of June 17, 2007 (as amended, the "Securities Purchase Agreement"), by and between Invus, L.P. (the "Investor") and Lexicon Pharmaceuticals, Inc. (the "Company") and to that certain Amendment to Securities Purchase Agreement, dated as of October \_\_, 2009, by and between the Investor and the Company. Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Securities Purchase Agreement.

Pursuant to Section 6.02(a) of the Securities Purchase Agreement, the Investor hereby consents to an underwritten offering by the Company of Company Common Stock on the following terms:

Issuer: Lexicon Pharmaceuticals, Inc.

Offering: \_\_\_\_\_ shares of Company Common Stock (the "Firm Shares"), and up to \_\_\_\_\_ additional shares to cover over allotments by the underwriters in such offering as provided in the underwriting agreement to be executed in connection with such offering (the "Underwriting Agreement")

Size: \$\_\_\_\_\_ at a \$\_\_\_\_\_ per share purchase price to the public.

Timing: pricing to occur on or before \_\_\_\_\_, 2009 with closing within T+3 (subject to extension as provided in the Underwriting Agreement).

Sincerely,

INVUS, L.P.,  
a Bermuda limited partnership

By: \_\_\_\_\_  
Name:  
Title:

October 7, 2009

Invus Public Equities, L.P.  
c/o The Invus Group, LLC  
750 Lexington Avenue (30<sup>th</sup> Floor)  
New York, New York 10022

Invus, L.P.  
c/o The Invus Group, LLC  
750 Lexington Avenue (30<sup>th</sup> Floor)  
New York, New York 10022

Re: Voting Agreement

Ladies and Gentlemen:

For good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Invus Public Equities, L.P. (the "Stockholder") agrees that at any stockholders' meeting of Lexicon Pharmaceuticals, Inc. (the "Company"), the Stockholder will (i) appear, in person or by proxy, or otherwise cause all shares of common stock and other voting securities of the Company (including, without limitation, any such shares and other voting securities acquired by the Stockholder on or after the date hereof) beneficially owned by the Stockholder at such time at the time of such vote to be counted as present for purposes of determining a quorum and (ii) vote, or instruct to be voted (including by written consent, if applicable), all such shares of common stock and other voting securities of the Company at the sole direction of Invus, L.P.

As security for the agreements of the parties hereto provided in this letter agreement, the Stockholder hereby grants and delivers to, and appoints, Invus, L.P. and any of its designees, and each of them individually, as the Stockholder's proxy, agent and attorney-in-fact (with full power of substitution), for and in the name, place and stead of the Stockholder, to vote (or cause to be voted) all shares of common stock and other voting securities of the Company beneficially owned by the Stockholder. This proxy shall will be irrevocable to the fullest extent permitted by law.

This letter agreement may not be amended other than by a written instrument executed by the Stockholder and Invus, L.P. This letter agreement represents the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior negotiations and understandings between the parties hereto with respect to such subject matter. This letter agreement may be executed and delivered (including by facsimile transmission) in one or more counterparts, and by the parties hereto in separate counterparts, each of which when executed and delivered shall be deemed to be an original but all of which taken together shall constitute one and the same agreement. This letter agreement is for the benefit of the parties hereto, and no other person shall have any rights hereunder.

This letter agreement shall be governed by, and construed in accordance with, the laws of the State of New York. All actions and proceedings arising out of or relating to this letter agreement shall be heard and determined exclusively in any New York state or federal court, in each case sitting in the Borough of Manhattan.

Very truly yours,

INVUS PUBLIC EQUITIES, L.P.

By: Invus Public Equities Advisors, LLC,  
its general partner

By: /s/ RAYMOND DEBBANE  
Name: **Raymond Debbane**  
Title: **President**

AGREED TO AND ACCEPTED:

INVUS, L.P.

By: Invus Advisors, L.L.C.,  
its general partner

By: /s/ RAYMOND DEBBANE  
Name: **Raymond Debbane**  
Title: **President**