

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

SCHEDULE 13D

Under the Securities Exchange Act of 1934
(Amendment No. 4)*

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
30th 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 14, 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)

(b)

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

7. Sole Voting Power

66,949,183

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person
With

8. Shared Voting Power

3,891,108

9. Sole Dispositive Power

66,949,183

10. Shared Dispositive Power

0

11. Aggregate Amount Beneficially Owned by Each Reporting Person

70,840,291

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 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 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)

(b)

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

7. Sole Voting Power

66,949,183

Number of
Shares
Bene-
ficially
Owned by
Each
Reporting
Person
With

8. Shared Voting Power

3,891,108

9. Sole Dispositive Power

66,949,183

10. Shared Dispositive Power

0

11. Aggregate Amount Beneficially Owned by Each Reporting Person
70,840,291

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 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 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)

(b)

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

7. Sole Voting Power

0

Number of
Shares
Beneficially

8. Shared Voting Power

3,891,108

Owned by
Each

9. Sole Dispositive Power

3,891,108

Reporting
Person
With

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)
2.2%*

14. Type of Reporting Person (See Instructions)

PN

* Based on 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 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)

(b)

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

7. Sole Voting Power

0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person
With

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)
2.2%*

14. Type of Reporting Person (See Instructions)
OO

* Based on 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 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)

(b)

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

7. Sole Voting Power

70,840,291

Number of
Shares
Bene-
ficially
Owned by
Each
Reporting
Person
With

8. Shared Voting Power

0

9. Sole Dispositive Power

70,840,291

10. Shared Dispositive Power

0

11. Aggregate Amount Beneficially Owned by Each Reporting Person
70,840,291

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 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 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)

(b)

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

7. Sole Voting Power

70,840,291

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person
With

8. Shared Voting Power

0

9. Sole Dispositive Power

70,840,291

10. Shared Dispositive Power

0

11. Aggregate Amount Beneficially Owned by Each Reporting Person

70,840,291

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 175,704,880 shares of Issuer Common Stock outstanding as of October 15, 2009, as provided by the Issuer.

This Amendment No. 4 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, Amendment No. 2 thereto filed on August 29, 2007 and Amendment No. 3 thereto filed on October 8, 2009 (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 new paragraphs immediately after the last paragraph thereof:

On October 14, 2009, Invus, L.P. purchased 13,439,257 shares of Issuer Common Stock for an aggregate amount of \$20,158,885.50 at a purchase price of \$1.50 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.

On October 15, 2009, Invus, L.P. purchased 2,015,888 shares of Issuer Common Stock for an aggregate amount of \$3,023,832.00 at a purchase price of \$1.50 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 replacing the fourth paragraph thereof with the following new paragraph:

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. would have the right to purchase its pro rata amount of the shares offered in this offering at the offering price.

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

On October 8, 2009, Lexicon entered into an underwriting agreement with the underwriters named therein for the public offering, issuance and sale of 19,894,076 shares of Issuer Common Stock, plus an additional 2,984,111 shares of Issuer Common Stock to cover over-allotments, if any (the "2009 Issuer Public Offering").

On October 8, 2009, Invus, L.P. and Lexicon entered into a Purchase Agreement (the "2009 Purchase Agreement"), pursuant to which, among other things, Invus, L.P. agreed to

purchase, and Lexicon agreed to issue and sell, shares of Issuer Common Stock, subject to the satisfaction of certain customary closing conditions. Such purchase represents the exercise by Invus, L.P. of its preemptive rights under the Stockholders' Agreement in connection with the 2009 Issuer Public Offering. The 2009 Purchase Agreement, and the description thereof included in Item 6 below, are incorporated by reference into this Item 4.

On October 14, 2009, Lexicon completed the 2009 Issuer Public Offering by issuing and selling 22,878,187 shares of Issuer Common Stock, including 2,984,111 shares of Issuer Common Stock upon exercise of the underwriters' over-allotment option, under the underwriting agreement relating to the 2009 Issuer Public Offering. Also on October 14, 2009, pursuant to the 2009 Purchase Agreement, Invus, L.P. purchased 13,439,257 shares of Issuer Common Stock at the public offering price of \$1.50 per share.

On October 14, 2009, Invus, L.P. and Lexicon entered into a Purchase Agreement Supplement (the "Purchase Agreement Supplement"), pursuant to which, among other things, Invus, L.P. agreed to purchase, and Lexicon agreed to issue and sell, 2,015,888 additional shares of Issuer Common Stock at the public offering price of \$1.50 per share. Such purchase represents the exercise by Invus, L.P. of its preemptive rights under the Stockholders' Agreement in connection with the underwriters' exercise of their over-allotment option in the 2009 Issuer Public Offering. This purchase closed on October 15, 2009. The Purchase Agreement Supplement, 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 first and second paragraphs of clause (a) thereof with the following new paragraphs:

As of October 15, 2009, Invus Public Equities, L.P. was the record and beneficial owner of 3,891,108 shares of Issuer Common Stock, representing approximately 2.2% of the outstanding shares of Issuer Common Stock. Invus Public Equities Advisors, L.L.C., as the general partner of Invus Public Equities, L.P., controls Invus Public Equities, L.P. and accordingly may be deemed to beneficially own the shares of Issuer Common Stock held by Invus Public Equities, L.P. Invus Public Equities Advisors, L.L.C. disclaims such beneficial ownership, except to the extent of its pecuniary interest in such shares.

As of October 15, 2009, Invus, L.P. was the record owner of 66,949,183 shares of Issuer Common Stock and the beneficial owner of 70,840,291 shares of Issuer Common Stock, representing approximately 38.1% and approximately 40.3% of the outstanding shares of Issuer Common Stock, respectively.

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

Except for Messrs. Amouyal, Debbane, Guimaraes and Sobeki, none of the individuals listed in Schedule I beneficially owns any shares of Issuer Common Stock. Each of Messrs. Amouyal and Debbane beneficially owns 29,333 shares of Issuer Common Stock issuable pursuant to options that are exercisable within 60 days of October 15, 2009. Mr. Guimaraes

beneficially owns 5,000 shares of Issuer Common Stock. Mr. Sobecki beneficially owns 30,333 shares of Issuer Common Stock, including 29,333 shares of Issuer Common Stock issuable pursuant to options that are exercisable within 60 days of October 15, 2009. For each of Messrs. Amouyal, Debbane, Guimaraes and Sobecki, shares of Issuer Common Stock beneficially owned by them represent less than 1% of the number of outstanding shares of Issuer Common Stock.

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

Item 6 is hereby amended and supplemented by inserting the following at the end of the last paragraph thereof:

While the Invus Parties believe the above description covers the material terms of the Voting Agreement, it is qualified in its entirety by reference to the Voting Agreement.

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

g. 2009 Purchase Agreement

On October 8, 2009, Invus, L.P. and Lexicon entered into the 2009 Purchase Agreement, pursuant to which, among other things, Invus, L.P. agreed to purchase 13,439,257 shares of Issuer Common Stock for an aggregate amount of \$20,158,885.50 at a purchase price of \$1.50 per share. Such purchase represents the exercise by Invus, L.P. of its preemptive rights under the Stockholders' Agreement in connection with the 2009 Issuer Public Offering. Under the 2009 Purchase Agreement, Lexicon made certain representations and warranties to Invus, L.P. and agreed to certain covenants. While the Invus Parties believe the above description covers the material terms of the 2009 Purchase Agreement, it is qualified in its entirety by reference to the 2009 Purchase Agreement, a copy of which is included as Exhibit 9 to the Statement and is incorporated herein by reference.

h. Purchase Agreement Supplement

On October 14, 2009, Invus, L.P. and Lexicon entered into the Purchase Agreement Supplement pursuant to which, among other things, Invus, L.P. agreed to purchase 2,015,888 shares of Issuer Common Stock for an aggregate amount of \$3,023,832.00 at a purchase price of \$1.50 per share. Such purchase represents the exercise by Invus, L.P. of its preemptive rights under the Stockholders' Agreement in connection with the 2009 Issuer Public Offering. The Purchase Agreement Supplement supplements and is a part of the Purchase Agreement pursuant to which Lexicon made certain representations and warranties to Invus, L.P. and agreed to certain covenants. While the Invus Parties believe the above description covers the material terms of the Purchase Agreement Supplement, it is qualified in its entirety by reference to the Purchase Agreement Supplement, a copy of which is included as Exhibit 10 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:

9. Purchase Agreement, dated as of October 8, 2009.

10. Purchase Agreement Supplement, dated as of October 14, 2009.

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 15, 2009

PURCHASE AGREEMENT

October 8, 2009

Invus, L.P.
c/o The Invus Group, L.L.C.
750 Lexington Avenue (30th 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 (a) that certain Stockholders' Agreement, dated as of June 17, 2007 (as amended, the "Stockholders' Agreement"), by and between Invus, L.P. (the "Investor") and Lexicon Pharmaceuticals, Inc. (the "Company"), (b) the Amendment to Securities Purchase Agreement, dated as of October 7, 2009 (the "Amendment"), amending that certain Securities Purchase Agreement, dated as of June 17, 2007, by and between the Investor and the Company (the "Securities Purchase Agreement"), and (c) that certain Underwriting Agreement being entered into by the Company with the representatives of the underwriters concurrently with this Purchase Agreement (the "Underwriting Agreement") providing for the issuance by the Company to the underwriters of 19,894,076 shares of Company Common Stock (the "Firm Shares"), without giving effect to any exercise of the underwriters' over-allotment option, for sale in a public offering at a price to the public of \$1.50 per share (the "Price to Public"). Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Stockholders' Agreement.

Pursuant to Section 4.02 of the Stockholders' Agreement and Section 8 of the Amendment, on the terms and subject to the conditions set forth herein, the Investor hereby agrees to purchase from the Company the number of shares specified below (the "Invus Shares") of Company Common Stock at a price per share equal to the Price to Public, for the total purchase price specified below:

Number of Shares: 13,439,257 shares of Company Common Stock

Total Purchase Price: \$20,158,885.50

The Company hereby represents and warrants to and agrees with the Investor to all the same representations and warranties contained in Section 1 and the covenants contained in Section 6 (other than the last paragraph thereof) of the Underwriting Agreement mutatis mutandis to the same extent as if such representations and warranties and covenants were set

forth herein for the benefit of the Investor instead of the underwriters party to the Underwriting Agreement (except that references to the Underwriting Agreement therein shall be references to this Agreement and references to the Shares thereunder shall be references to the Invus Shares). The obligation of the Investor to purchase the Invus Shares from the Company, and of the Company to sell the Invus Shares to Invus, will be subject to (i) the satisfaction of the conditions set forth in the Underwriting Agreement (other than clauses (i) and (j) thereunder) and the concurrent closing of the sale of the Firm Shares under the terms set forth in the Underwriting Agreement, (ii) the delivery to the Investor of opinions of counsel to the Company by the same counsel and covering the same matters (except that references to the Underwriting Agreement therein shall be references to this Agreement and references to the Shares thereunder shall be references to the Invus Shares) as set forth in Sections 4(c), (d) and (e) and (iii) the delivery to the Investor of the officer's certificate contemplated by Section 4(b) of the Underwriting Agreement, and such obligations shall terminate in the event the Underwriting Agreement is terminated. The Company shall cause the Invus Shares to be listed on the NASDAQ Global Market.

The closing of the sale of the Invus Shares shall take place concurrently with the closing of the sale of the Firm Shares under the Underwriting Agreement, (i) with payment for the Invus Shares to be made to the Company by wire transfer of immediately available funds on the closing date and (ii) with delivery of the Invus Shares registered in the name of Invus, L.P. or its designee and free and clear of all liens (other than those under applicable law, the Stockholders Agreement and the "lock-up" agreement entered into between the Investor and the underwriters party to the Underwriting Agreement), with any transfer or stamp taxes duly paid, to the Investor.

This Agreement shall be deemed to satisfy the Company's obligations under the Stockholders' Agreement with respect to the delivery of a Notice of Issuance with respect to the Firm Shares.

This Agreement shall automatically terminate upon any termination of the Underwriting Agreement. The provisions of Sections 9.03 and 9.04 and Article X of the Securities Purchase Agreement are incorporated herein by reference and shall apply to this Agreement mutatis mutandis.

Sincerely,

INVUS, L.P.,
a Bermuda limited partnership

By: /s/ RAYMOND DEBBANE

Name: Raymond Debbane

Title: President, Invus Advisors, L.L.C., its
General Partner

Accepted and agreed to:

LEXICON PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ JAMES F. TESSMER

Name: James F. Tessmer

Title: Vice President of Finance and Accounting

PURCHASE AGREEMENT SUPPLEMENT

October 14, 2009

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

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

Re: Purchase Agreement Supplement

Ladies and Gentlemen:

Reference is made to that certain Purchase Agreement, dated as October 8, 2009 (the "Purchase Agreement"), by and between Invus, L.P. (the "Investor") and Lexicon Pharmaceuticals, Inc. (the "Company"). Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Purchase Agreement. The Company has informed the Investor that the underwriters under the Underwriting Agreement, dated as of October 8, 2009, by and between the Company and the several underwriters party thereto have exercised their over-allotment option thereunder to purchase an additional 2,984,111 shares of Company Common Stock.

Accordingly, the Investor hereby agrees to purchase from the Company the number of additional shares of Company Common Stock specified below (the "Additional Invus Shares") at a price per share equal to the Price to Public, for the total purchase price specified below:

Number of Shares: 2,015,888 shares of Company Common Stock

Total Purchase Price: \$3,023,832.00

The issuance, purchase and delivery of the Additional Invus Shares is being made on the basis of the same representations and warranties and on the same terms and subject to the same conditions, and is considered a part of, the sale of the Invus Shares. The closing of the sale of the Additional Invus Shares shall take place at a time and place to be mutually agreed to by the parties.

The Purchase Agreement is hereby amended by replacing the references therein to Sections 4(b), (c), (d) and (e) of the Underwriting Agreement with references to Sections 5(b), (c), (d) and (e) of the Underwriting Agreement, respectively.

This supplement to the Purchase Agreement shall be deemed to satisfy the Company's obligations under the Stockholders' Agreement with respect to the delivery of a Notice of Issuance with respect to the Additional Invus Shares.

This supplement shall automatically terminate upon any termination of the Purchase Agreement and shall be interpreted as a part of and in accordance with the Purchase Agreement.

[Signature Page Follows]

Sincerely,

INVUS, L.P.,
a Bermuda limited partnership

By: /s/ RAYMOND DEBBANE

Name: Raymond Debbane

Title: President, Invus Advisors, L.L.C., its
General Partner

Accepted and agreed to:

LEXICON PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ JAMES F. TESSMER

Name: James F. Tessmer

Title: Vice President of Finance and Accounting