

LEXICON PHARMACEUTICALS, INC./DE
Form S-3
January 28, 2011

AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON JANUARY 28, 2011
Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM S-3
REGISTRATION STATEMENT
UNDER

THE SECURITIES ACT OF 1933
Lexicon Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)
Delaware
(State or other jurisdiction of incorporation or
organization)

76-0474169
(I.R.S. Employer Identification Number)

8800 Technology Forest Place
The Woodlands, Texas 77381-1160
(281) 863-3000
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer
8800 Technology Forest Place
The Woodlands, Texas 77381-1160
(281) 863-3000
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:
David P. Oelman
Vinson & Elkins L.L.P.
2300 First City Tower
1001 Fannin
Houston, Texas 77002-6760
(713) 758-3708

Brian T. Crum
Vice President and General Counsel
Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands, Texas 77381-1160
(281) 863-3000

Approximate date of commencement of proposed sale to the public:
From time to time after this registration statement becomes effective, subject to market conditions and other factors.
If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, check the following box.
If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.
If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. Large accelerated filer Accelerated filer Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities to be Registered | Amount to be Registered (1) (3) | Proposed Maximum Aggregate Offering Price Per Unit (2) (3) | Proposed Maximum Aggregate Offering Price (3) | Amount of Registration Fee |
|--|---------------------------------|--|---|----------------------------|
| Common Stock, par value \$0.001 | | | | N/A |
| Preferred Stock, par value \$0.01 | | | | N/A |
| Debt Securities | | | | N/A |
| Warrants | | | | N/A |
| Rights | | | | N/A |
| Units | | | | N/A |
| Total | \$200,000,000 | | \$200,000,000 | \$23,220 (4) |

(1) There are being registered hereunder such indeterminate (i) number of shares of common stock and preferred stock, (ii) principal amount of debt securities, (iii) number of warrants to purchase common stock, preferred stock or debt securities, (iv) number of rights to purchase common stock, preferred stock or debt securities and (v) number of units as shall have an aggregate initial offering price not to exceed \$200,000,000. If any debt securities are issued at an original issued discount, then the offering price of such debt securities shall be in such greater principal amount as shall result in an aggregate initial offering price not to exceed \$200,000,000, less the aggregate dollar amount of all securities previously issued hereunder. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. The securities registered also include such indeterminate numbers of shares of common stock and preferred stock and amount of debt securities as may be issued upon conversion of or exchange for preferred stock or debt securities that provide for conversion or exchange, upon exercise of warrants or rights or pursuant to the antidilution provisions of any such securities. The securities registered also include, pursuant to Rule 416 under the Securities Act, such additional number of shares of common stock that may become issuable as a result of any stock split, stock dividends or similar event.

(2) The proposed maximum initial offering price per security or unit will be determined, from time to time, by the registrant in connection with the issuance by the registrant of the securities registered hereunder.

(3) The amount to be registered, proposed maximum aggregate offering price per unit and proposed maximum aggregate offering price are not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act.

(4) Calculated pursuant to Rule 457(o) under the Securities Act.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 28, 2011

\$200,000,000

Lexicon Pharmaceuticals, Inc.

Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units

We may offer common stock, preferred stock, debt securities, warrants and/or rights, either individually or in units, from time to time in one or more offerings in amounts, at prices and on terms to be determined in light of market conditions at the time of sale (including, without limitation, rights offered in a rights offering pursuant to rights held by Invus, L.P. and Invus C.V. to require us to initiate a rights offering). We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock or common stock, preferred stock or debt securities upon the exercise of warrants or rights.

Each time we sell these securities, we will provide a supplement to this prospectus that contains specific information about the offering. The supplement may also add, update or change information contained in this prospectus. You should carefully read this prospectus and any supplement before you invest.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "LXRX". The prospectus supplement will contain information, where applicable, regarding any other listing on The Nasdaq Global Select Market or any securities exchange of the securities covered by the prospectus supplement. The last reported sale price of our common stock on January 27, 2011 was \$1.82 per share.

Investing in our securities involves risks. See "Risk Factors" on page 4. Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2011.

TABLE OF CONTENTS

| | Page | | Page |
|--|-----------|--|-----------|
| <u>Lexicon Pharmaceuticals, Inc.</u> | <u>3</u> | <u>Ratio of Earnings to Fixed Charges</u> | <u>21</u> |
| <u>Risk Factors</u> | <u>4</u> | <u>Use of Proceeds</u> | <u>21</u> |
| <u>Description of Capital Stock</u> | <u>4</u> | <u>Plan of Distribution</u> | <u>21</u> |
| <u>Description of Debt Securities</u> | <u>8</u> | <u>Legal Matters</u> | <u>23</u> |
| <u>Description of Warrants</u> | <u>14</u> | <u>Experts</u> | <u>23</u> |
| <u>Description of Rights</u> | <u>16</u> | <u>Where You Can Find More Information</u> | <u>23</u> |
| <u>Description of Units</u> | <u>17</u> | <u>Documents Incorporated by Reference</u> | <u>24</u> |
| <u>Legal Ownership of Securities</u> | <u>18</u> | | |
| <u>Special Note Regarding Forward Looking Statements</u> | <u>20</u> | | |

You should rely only on the information contained in this prospectus and documents incorporated into this prospectus by reference. We have not authorized anyone to provide you with information different from that contained in this prospectus or the documents incorporated by reference herein. This prospectus may only be used where it is legal to sell these securities. The information contained in this prospectus, the documents incorporated by reference herein and any supplements to this prospectus is accurate only as of the dates of their respective covers or earlier dates as specified therein, regardless of the time of delivery of this prospectus or any supplement to this prospectus or of any sale of our common stock.

In this prospectus, “Lexicon,” “Lexicon Pharmaceuticals,” “we,” “us” and “our” refer to Lexicon Pharmaceuticals, Inc. and its subsidiaries. We own or have rights to trademarks or trade names that we use in connection with the operation of our business. The Lexicon name and logo, LexVision® and OmniBank® are registered trademarks and Genome5000™ is a trademark of Lexicon Pharmaceuticals, Inc.

LEXICON PHARMACEUTICALS, INC.

Lexicon Pharmaceuticals, Inc. is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We have used our proprietary gene knockout technology and an integrated platform of advanced medical technologies to systematically study the physiological and behavioral functions of almost 5,000 genes in mice and assessed the utility of the proteins encoded by the corresponding human genes as potential drug targets. We have identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential new drugs, focusing in the core therapeutic areas of immunology, metabolism, cardiology and ophthalmology.

We have four drug candidates for which we have completed or are presently conducting Phase 2 clinical trials:

- LX4211, an orally-delivered small molecule compound that we are developing as a potential treatment for type 2 diabetes;
- LX1031, an orally-delivered small molecule compound that we are developing as a potential treatment for irritable bowel syndrome and other gastrointestinal disorders;
- LX2931, an orally-delivered small molecule compound that we are developing as a potential treatment for rheumatoid arthritis and other autoimmune diseases; and
- LX1032, an orally-delivered small molecule compound that we are developing as a potential treatment for the symptoms associated with carcinoid syndrome.

We have filed an investigational new drug application, or IND, for LX1033, an orally-delivered small molecule compound that we are developing as a potential treatment for irritable bowel syndrome and other gastrointestinal disorders, and we have advanced three other drug candidates into preclinical development: LX7101, a topically-delivered small molecule compound that we are developing as a potential treatment for glaucoma; LX5061, an orally-delivered small molecule compound that we are developing as a potential treatment for osteoporosis; and LX2311, an orally-delivered small molecule compound that we are developing as a potential treatment for autoimmune diseases. We have small molecule compounds from a number of additional drug discovery programs in various stages of preclinical research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline.

We are working both independently and through strategic collaborations and alliances to capitalize on our technology, drug target discoveries and drug discovery and development programs. Consistent with this approach, we seek to retain exclusive rights to the benefits of certain of our small molecule drug programs by developing drug candidates from those programs internally and to collaborate with third parties with respect to the discovery, development and commercialization of small molecule and biotherapeutic drug candidates for other targets, particularly when the collaboration provides us with access to expertise and resources that we do not possess internally or are complementary to our own. We have established drug discovery and development collaborations with a number of leading pharmaceutical and biotechnology companies which have enabled us to generate near-term cash while offering us the potential to retain economic participation in products our collaborators develop through the collaboration. In addition, we have established collaborations and license agreements with other leading pharmaceutical and biotechnology companies, research institutes and academic institutions under which we received fees and, in some cases, are eligible to receive milestone and royalty payments, in return for granting access to some of our technologies and discoveries.

Lexicon Pharmaceuticals, Inc. was incorporated in Delaware in July 1995, and commenced operations in September 1995. Our corporate headquarters are located at 8800 Technology Forest Place, The Woodlands, Texas 77381, and our telephone number is (281) 863-3000. Our common stock is listed on The Nasdaq Global Select Market under the symbol "LXRX."

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, or Exchange Act, are made available free of charge on our corporate website located at www.lexpharma.com as soon as

reasonably practicable after the filing of those reports with the Securities and Exchange Commission, or SEC. Information found on our website is not incorporated by reference into this prospectus and should not be considered part of this document.

RISK FACTORS

You should carefully consider the risk factors and all other information contained in this prospectus and any prospectus supplement and incorporated herein by reference before purchasing our securities. Investing in our securities involves a high degree of risk.

For a discussion of these risks, please see:

- Our most recent annual report on Form 10-K, and
- Our other filings with the SEC that are incorporated by reference into this prospectus.

For more information about our SEC filings, please see “Where You Can Find More Information” on page 23 and “Documents Incorporated By Reference” on page 24 of this prospectus. See also “Special Note Regarding Forward-Looking Statements” on page 20 of this prospectus.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 900 million shares of common stock, \$0.001 par value, and five million shares of preferred stock, \$0.01 par value. As of December 31, 2010, there were 337,407,756 shares of our common stock issued and outstanding, 157,833 shares of our common stock issued and held in treasury and no shares of preferred stock outstanding.

The following summary description of our capital stock is based on the provisions of our restated certificate of incorporation, as amended, restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our restated certificate of incorporation, as amended, restated bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our restated certificate of incorporation, as amended, and restated bylaws, see “Where You Can Find More Information” on page 23 of this prospectus.

Common Stock

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. Upon the liquidation, dissolution or winding up of Lexicon, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are, and all shares of common stock that may be issued under this prospectus will be, fully paid and non-assessable.

Preferred Stock

Pursuant to our restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to five million shares of preferred stock, in one or more series. Our board of directors is authorized to fix or alter from time to time the designation, powers, preferences and rights of the shares of each series of preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms. Our board of directors may also establish from time to time the number of shares constituting any series of preferred stock, and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of any series then outstanding.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designation relating to that series. We will incorporate by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report filed under the Exchange Act, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

- the title and stated value;

- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

The Delaware General Corporation Law provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock.

This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Arrangements with Invus, L.P. and Its Affiliates

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment of approximately \$205.5 million to purchase 50,824,986 shares of our common stock in August 2007. Under the securities purchase agreement, as amended and supplemented, and after accounting for the \$181.5 million in net proceeds from our public offering and concurrent private placement of common stock in March 2010, Invus, L.P. and its affiliate Invus C.V., which we collectively refer to as Invus, have the right to require us to initiate a pro rata rights offering 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 approximately \$163.0 million, less the proceeds of any “qualified offerings” that we may complete before February 28, 2011 involving the sale of our common stock at prices above \$4.50 per share. We have not completed any such qualified offering. Invus may exercise its right to require us to conduct such a rights offering by giving us notice within a period of one year beginning on February 28, 2011, which will be extended by the number of days during such period that Invus is not permitted under the securities purchase agreement to initiate the rights offering as a result of any “blackout period” in connection with certain public offerings of our common stock. If Invus elects to exercise its right to require us to initiate a rights offering, Invus would be required to purchase its pro rata portion of the offering.

Under the securities purchase agreement, until the later of the completion of the rights offering or the expiration of

the period during which Invus may require us to initiate the rights offering, we have agreed not to issue any of our common stock for a per share price of less than \$4.50 without the prior written consent of Invus, except pursuant to an employee or director stock option, incentive compensation or similar plan or to persons involved in the pharmaceutical industry in connection with simultaneous strategic transactions involving such persons in the ordinary course. In addition, if we notify Invus of a proposed public offering for an offering above \$4.50 per share during the period in which Invus may require us to initiate the rights offering, Invus will have a period of 10 business days in which to exercise its right to require us to conduct the rights offering, in which case we would be required to forego the proposed public offering and proceed with the rights offering.

Board of Directors. Concurrently with the execution of the securities purchase agreement, we entered into a stockholders' agreement with Invus, L.P. 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, 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 over-allotment (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 offering 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

6

- 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

7

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, L.P., pursuant to which Invus, L.P. and its affiliates have certain demand and piggyback registration rights with respect to shares of our common stock held by them. Invus, L.P. and its affiliates which hold our common stock have waived these registration rights with respect to any offerings of our securities pursuant to this prospectus.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly-held Delaware corporation such as Lexicon from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of our voting stock.

Charter Documents. Our restated certificate of incorporation, as amended, requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by a consent in writing. Additionally, our restated certificate of incorporation, as amended:

- does not provide for the use of cumulative voting in the election of directors;
- provides for a board of directors, classified into three classes of directors;
- provides that the authorized number of directors may be changed only by resolution of our board of directors; and
- provides for the authority of our board of directors to issue up to five million shares of "blank check" preferred stock and to determine the price, powers, preferences and rights of these shares, without stockholder approval.

Our restated bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us not less than 120 days nor more than 150 days in advance of the first anniversary of the date of our proxy statement relating to the previous year's annual meeting of stockholders. The authorized number of directors is fixed in accordance with our restated certificate of incorporation, as amended. Our board of directors currently consists of nine members, divided into three classes. As a result, a portion of the board of directors will be elected each year. The board of directors may appoint new directors to fill vacancies or newly created directorships. Our restated bylaws also limit who may call a special meeting of stockholders.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is BNY Mellon Shareowner Services. The transfer agent for any series of preferred stock will be named and described in the prospectus supplement for that series.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus and the related indenture. While the terms summarized below will apply generally to any debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any debt securities offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall

fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may offer debt securities in the form of either senior debt securities or subordinated debt securities. Unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness.

The debt securities will be issued under an indenture between us and a trustee. The following summary of the general features of the debt securities to be governed by the indenture is subject to, and qualified in its entirety by reference to, the provisions of the indenture applicable to a particular series of debt securities. We have filed a form of indenture as an exhibit to the registration statement which includes this prospectus. Capitalized terms used in the summary have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors, or a committee thereof, and set forth or determined in the manner provided in an officer's certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series, including any pricing supplement.

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium or at a discount. We will set forth in a prospectus supplement, including any pricing supplement, relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities:

- the title of the debt securities;
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which we will pay the principal on the debt securities;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and premium and interest on, the debt securities will be payable;
- the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities;
- the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;
 - if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

- the manner in which the amounts of payment of principal of, or premium or interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
 - any addition to or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
 - any addition to or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
 - any conversion provisions, including the conversion price, the conversion period, provisions as to whether conversion will be mandatory, at the option of the holder or at our option, the events requiring an adjustment of the conversion price and provisions affecting conversion if such series of debt securities are redeemed;
 - whether the debt securities will be senior debt securities or subordinated debt securities and, if applicable, a description of the subordination terms thereof;
 - any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities; and
 - any other terms of the debt securities, which may modify, delete, supplement or add to any provision of the indenture as it applies to that series.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of, and premium and interest on, any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, as Depositary, or a nominee (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “Legal Ownership of Securities” below, book-entry securities will not be issuable in certificated form.

You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, and any premium and interest on, certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the

event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to, any person, which we refer to as a successor person, unless:

- we are the surviving corporation or the successor person (if other than Lexicon) is organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;
- immediately after giving effect to the transaction, no event of default, and no event which, after notice or lapse of time, or both, would become an event of default, shall have occurred and be continuing under the indenture; and
- certain other conditions are met.

Events of Default

Event of default means, with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of that default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of or premium on any debt security of that series when due and payable;
- default in the deposit of any sinking fund payment, when and as due in respect of any debt security of that series;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 90 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of not less than a majority in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain events of bankruptcy, insolvency or reorganization of our company; and
- any other event of default provided with respect to debt securities of that series that is described in the applicable prospectus supplement accompanying this prospectus.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under our bank credit agreements in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time. If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of, and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an event of default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the

holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

The indenture provides that the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any holder of outstanding debt securities, unless the trustee receives indemnity satisfactory to it against any loss, liability or expense. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and
- the holders of at least a majority in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding the foregoing, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, and any premium and interest on, that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

If any securities are outstanding under the indenture, the indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any default or event of default (except in payment on any debt securities of that series) with respect to debt securities of that series if it in good faith determines that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

We may modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of, or premium or interest on, any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, or any premium or interest on, any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (except for certain obligations to register the transfer or exchange of debt securities of such series, to replace stolen, lost or mutilated debt securities of such series, and to maintain paying agencies and certain provisions relating to the treatment of funds held by paying agents). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets”
- and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a default or an event of default with respect to the debt securities of that series, or covenant defeasance.

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

Covenant Defeasance and Events of Default. In the event we exercise our option to effect covenant defeasance with respect to any series of debt securities and the debt securities of that series are declared due and payable because of the occurrence of any event of default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the event of default. In such a case, we would remain liable for those payments. “Foreign Government Obligations” means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars:

- direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged which are not callable or redeemable at the option of the issuer thereof; or
- obligations of a person controlled or supervised by or acting as an agency or instrumentality of that government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government which are not callable or redeemable at the option of the issuer thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the laws of the State of New York.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below.

However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report filed under the Exchange Act.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable; in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;

- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any; or
- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

The warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

DESCRIPTION OF RIGHTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the rights that we may offer under this prospectus and the related rights agreements (including, without limitation, rights offered in a rights offering conducted pursuant to Invus' right to require us to initiate a rights offering). While the terms summarized below will apply generally to any rights that we may offer under this prospectus, we will describe the particular terms of any series of rights that we may offer in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any rights offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific rights agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report filed under the Exchange Act.

General

We may issue rights to purchase common stock, preferred stock, debt securities or other securities. These rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the rights in such offering. In connection with any offering of such rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

Each series of rights will be issued under a separate rights agreement which we will enter into with a bank or trust company, as rights agent, all as set forth in the applicable prospectus supplement. The rights agent will act solely as our agent in connection with the certificates relating to the rights and will not assume any obligation or relationship of agency or trust with any holders of rights certificates or beneficial owners of rights. We will file the rights agreement and the rights certificates relating to each series of rights with the SEC, and incorporate them by reference as an exhibit to the registration statement of which this prospectus is a part on or before the time we issue a series of rights. We will describe in the applicable prospectus supplement the terms of the series of rights, including:

- the date of determining the stockholders entitled to the rights distribution;
- the number of rights issued or to be issued to each stockholder;
- the exercise price payable for each share of common stock, preferred stock, debt securities or other securities upon the exercise of the rights;
- the number and terms of the shares of common stock, preferred stock, debt securities or other securities which may be purchased per each right;
- the extent to which the rights are transferable, if at all;
- the date on which the holder's ability to exercise the rights shall commence, and the date on which the rights shall expire;
- the extent to which the rights may include an over-subscription privilege with respect to unsubscribed securities;
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of such rights; and
- any other terms of the rights, including the terms, procedures, conditions and limitations relating to the exchange and exercise of the rights.

The description in the applicable prospectus supplement of any rights that we may offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable rights certificate, which will be filed with the SEC.

Exercise of Rights

Each right will entitle the holder of the right to purchase for cash such amount of shares of common stock, preferred

stock, debt securities or other securities at such exercise price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the rights offered thereby. Rights may be exercised at any time up to the close of business on the expiration date for such rights set forth in the prospectus supplement. After the close of business on the expiration date, all unexercised rights will become void.

Rights may be exercised as set forth in the prospectus supplement relating to the rights offered thereby. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will forward, as soon as practicable, the shares of common stock, preferred stock, debt securities or other securities purchasable upon such exercise. We may determine to offer any unsubscribed offered securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting arrangements, as set forth in the applicable prospectus supplement.

Governing Law

The rights and rights agreements will be governed by and construed in accordance with the laws of the State of New York.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus and the related unit agreements. While the terms summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units that we may offer in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any units offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific unit agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a report filed under the Exchange Act.

General

We may issue units comprised of one or more shares of common stock, shares of preferred stock, debt securities and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for

more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Title

Lexicon, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary. See “Legal Ownership of Securities.”

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depository or its nominee. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor

chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form. A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- An investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

- An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- The depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way;
- The depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- Financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this prospectus contain certain information regarding our financial projections, plans and strategies that are forward-looking statements within the meaning of Section 27A of the Securities Act and 21E of the Exchange Act. We have attempted to identify forward-looking statements by terminology including “anticipate,” “believe,” “can,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “potential,” “predict,” “should” or “will” or the negative of these terms or other comparable terminology. These statements, which are only predictions and involve known and unknown risks, uncertainties and other important factors may include, among other things, statements which address our strategy and operating performance, events or developments that we expect or anticipate will occur in the future, such as projections of our future results of operations or of our financial condition, the status of any collaborative agreements or clinical trials, the expected timing of the completion of our ongoing and future clinical trials and the results of such trials, including top-line data, expected timing

of initiation of our planned clinical trials, expected enrollment in our ongoing and future clinical trials, and our research and development efforts and anticipated trends in our business.

We have based these forward-looking statements on our current expectations and projections about future events. However, there may be events in the future that we are not able to predict accurately or which we do not fully control that could cause actual results to differ materially from those expressed or implied in our forward-looking statements. Many important factors could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including those discussed under “Risk Factors” in this prospectus and any prospectus supplement and other sections of the documents incorporated by reference into this prospectus. Except as required by applicable law, we undertake no obligation to publicly release any revisions to the forward-looking statements or reflect events or circumstances after the date of this prospectus.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges in each of the years in the five-year period ended December 31, 2009 and in the nine-month period ended September 30, 2010. “Fixed charges” consist of interest expense and the estimated interest included in rental expense. The following table sets forth the computation of our ratio of earnings to fixed charges for the periods indicated:

| | Nine months ended September 30, | Fiscal years ended December 31, | | | | |
|--|---------------------------------------|---------------------------------|------|------|------|------|
| | | 2009 | 2008 | 2007 | 2006 | 2005 |
| Ratio of earnings to fixed charges (1) | — | — | — | — | — | — |

For the nine months ended September 30, 2010, and the fiscal years ended December 31, 2009, 2008, 2007, 2006 (1) and 2005, our earnings were insufficient to cover fixed charges by \$78.8 million, \$82.9 million, \$76.9 million, \$58.8 million, \$54.4 million and \$36.2 million, respectively.

For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments. Therefore, our ratios of earnings to combined fixed charges and preferred stock dividends for the periods indicated are identical to the ratios presented in the table above.

USE OF PROCEEDS

Except as otherwise described in the prospectus supplement relating to an offering, we intend to use the net proceeds from the sale(s) of securities offered pursuant to this prospectus and any prospectus supplement for research and development and general corporate purposes, including capital expenditures and working capital needs. We may also use some or all of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own.

The amounts that we actually expend for working capital purposes, investments or acquisitions will vary significantly depending on a number of factors, including our future revenues, the amount of cash we generate from operations and the progress of our product development efforts. Accordingly, our management will retain broad discretion in the allocation of the net proceeds from the sale(s) of the offered securities. If we elect at the time of the issuance of the securities to make different or more specific use of proceeds other than as described in this prospectus, the change in use of proceeds will be described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell securities under this prospectus from time to time in any one or more of the following ways:

- to or through underwriters;
- through brokers or dealers;
- directly to other purchasers; or
- through agents.

We may sell securities under this prospectus from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

The prospectus supplement relating to the securities will set forth the terms of the offering of such securities, including the name or names of any underwriters, brokers, dealers or agents, the name or names of any managing underwriter or underwriters, the purchase price of the securities and the net proceeds to us from such sale, any delayed delivery arrangements, any underwriting discounts and commissions and other items constituting underwriters' compensation, any public offering price, any discounts or concessions allowed or reallocated or paid to dealers, any commissions paid to agents and any securities exchange or market on which the securities may be listed.

If we use underwriters in the sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless we inform you otherwise in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all of the offered securities if they purchase any of them. The underwriters may change from time to time any public offering price and any discounts or concessions allowed or reallocated or paid to dealers. In connection with the sale of our securities, underwriters, brokers, dealers or agents may receive compensation from us or purchasers of securities for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters, dealers and agents that participate in the distribution of our securities may be deemed to be underwriters, and any discounts or commissions received by them from us and any profit on the resale of securities by them may be deemed to be underwriting discounts and commissions under the Securities Act. Any person who may be deemed to be an underwriter will be identified, and the compensation received from us will be described, in the prospectus supplement.

During and after an offering through underwriters, the underwriters may purchase and sell the securities in the open market. These transactions may include over-allotment and stabilizing transactions and purchases to cover syndicate short positions created in connection with the offering. The underwriters may also impose a penalty bid, whereby selling concessions allowed to syndicate members or other broker-dealers for the securities sold for their account may be reclaimed by the syndicate if those securities are repurchased by the syndicate in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the securities, which may be higher than the price that might otherwise prevail in the open market, and, if commenced, may be discontinued at any time.

If dealers or brokers acting as dealers are used in the sale of the securities, we will sell the securities to such dealers or brokers as principals. The dealers or brokers acting as dealers may then resell such securities to the public at varying prices to be determined by such dealers or brokers at the time of resale. The names of dealers or brokers acting as dealers and the terms of the transaction will be set forth in the prospectus supplement relating to such securities. We may sell the securities directly or through agents designated by us from time to time. Any agent involved in the offer or sale of the securities will be named, and any commissions that we pay to such agent will be set forth, in the prospectus supplement relating to such securities. Unless otherwise indicated in the prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

We may sell securities directly, in which case no underwriters or agents would be involved. We may sell securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities.

We may offer securities through agents in connection with a distribution to our stockholders of rights to purchase such securities (including, without limitation, rights offered in a rights offering conducted pursuant to Invus' right to require us to initiate a rights offering). The terms of any such sales will be described in the prospectus supplement relating thereto. Pursuant to any standby underwriting agreement entered into in connection with a rights offering to our

stockholders, persons acting as standby underwriters may receive a commitment fee for all securities underlying the rights that the underwriter commits to purchase on a standby basis. Additionally, prior to the expiration date with respect to any rights, any standby underwriters in a rights offering to our stockholders may offer such securities on a when-

22

issued basis, including securities to be acquired through the purchase and exercise of rights, at prices set from time to time by the standby underwriters. After the expiration date with respect to such rights, the underwriters may offer securities of the type underlying the rights, whether acquired pursuant to a standby underwriting agreement, the exercise of the rights or the purchase of such securities in the market, to the public at a price or prices to be determined by the underwriters. The standby underwriters may thus realize profits or losses independent of the underwriting discounts or commissions paid by us. If we do not enter into a standby underwriting agreement in connection with a rights offering to our stockholders, we may elect to retain a dealer-manager to manage such a rights offering for us. We also may enter into a standby arrangement with other purchasers pursuant to which such purchasers may be required to purchase any securities remaining unsubscribed for after such offering. Any such dealer-manager may offer securities of the type underlying the rights acquired or to be acquired pursuant to the purchase and exercise of rights and may thus realize profits or losses independent of any dealer-manager fee paid by us.

If Invus elects to exercise its right to require us to initiate a rights offering to our stockholders, Invus would be required to purchase its pro rata portion of the offering.

All securities we offer, other than common stock and other securities issued upon a reopening of a previous series, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

If so indicated in the prospectus supplement, we will authorize agents, underwriters, brokers or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth also the commission payable for solicitation of such contracts.

We may have agreements with the underwriters, dealers and agents to indemnify them against specific civil liabilities, including liabilities under the Securities Act, or to contribute with respect to payments which the underwriters, dealers or agents may be required to make as a result of those specific civil liabilities.

Underwriters and agents and their affiliates may be customers of, engage in transactions with, or perform services for us or our subsidiaries in the ordinary course of their businesses.

LEGAL MATTERS

The validity of the issuance of the securities offered by this prospectus has been passed upon for us by Vinson & Elkins L.L.P., Houston, Texas.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements for the year ended December 31, 2009, included in our Annual Report on Form 10-K, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC. You may read and copy the reports, proxy statements and other information that we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information about the operation of its Public Reference Room and for its prescribed rates to obtain copies of such material. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants, like us, that file electronically with the SEC. The address of the SEC's Internet site is <http://www.sec.gov>.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and other filings with the SEC are available, free of charge, through our website, as soon as reasonably practicable after those reports or filings are electronically filed with or furnished to the SEC. Information on our website or any other website is not

incorporated by reference into this prospectus or any prospectus supplement and does not constitute a part of this

23

prospectus or any prospectus supplement.

This prospectus is part of a registration statement we filed with the SEC relating to the securities we may offer. As permitted by SEC rules, this prospectus does not contain all of the information we have included in the registration statement and the accompanying exhibits and schedules we filed with the SEC. You may refer to the registration statement, exhibits and schedules for more information about us and the securities. The registration statements, exhibits and schedules are available at the SEC's public reference room or through its website.

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to “incorporate by reference” the information we have filed with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below that we have previously filed with the SEC and any future documents filed with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act subsequent to the date of this prospectus and prior to the termination of the offering of the securities covered by this prospectus:

- our annual report on Form 10-K for the year ended December 31, 2009;
- our quarterly reports on Form 10-Q for the quarterly periods ended March 31, June 30 and September 30, 2010;
- our current reports on Form 8-K dated January 8, February 15, February 16, February 17, March 19, April 29, May 17 and July 30, 2010 and both our current reports on Form 8-K dated March 15, 2010; and
- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on March 27, 2000 pursuant to Section 12 of the Securities Exchange Act of 1934, including any amendments and reports filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as so modified or superseded. You may rely on any statement contained in this prospectus or in documents incorporated or deemed to be incorporated in this prospectus, unless that statement has been subsequently modified or superseded as described above prior to the time you make your investment decision. Upon your written or oral request, we will provide you at no cost a copy of any or all of the documents incorporated by reference in this prospectus, other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into this prospectus. You may request a copy of these documents by contacting:

Investor Relations
Lexicon Pharmaceuticals, Inc.
8800 Technology Forest Place
The Woodlands, Texas 77381-1160
Telephone: (281) 863-3000

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The estimated expenses payable by the Registrant in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions) are as follows:

| | |
|-----------------------------------|-----------|
| SEC Registration Fee | \$23,220 |
| Printing Expenses | 25,000 |
| Accounting Fees and Expenses | 25,000 |
| Legal Fees and Expenses | 100,000 |
| Transfer Agent and Registrar Fees | 3,000 |
| Miscellaneous Expenses | 3,780 |
| Total | \$180,000 |

Item 15. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law (“DGCL”) provides that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. Section 145 further provides that a corporation similarly may indemnify any such person serving in any such capacity who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that he is or was a director, officer, employee or agent of the corporation or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Delaware Court of Chancery or such other court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Delaware Court of Chancery or such other court shall deem proper.

Lexicon's restated certificate of incorporation, as amended, and restated bylaws provide that indemnification shall be to the fullest extent permitted by the DGCL for all current or former directors or officers. As permitted by the DGCL, the restated certificate of incorporation provides that directors of Lexicon shall have no personal liability to Lexicon or its stockholders for monetary damages for breach of fiduciary duty as a director, except (1) for any breach of the director's duty of loyalty to Lexicon or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or knowing violation of law, (3) under Section 174 of the DGCL or (4) for any transaction from which a director derived an improper personal benefit.

Lexicon has entered into indemnification agreements with each of its officers and directors. These agreements, among other things, require Lexicon to indemnify each officer and director for all expenses, including attorneys' fees, liabilities, judgments, fines, penalties, excise taxes and settlement amounts incurred by any such person in any claim,

action, suit or proceeding, including any action by or in the right of Lexicon, arising out of the person's services as a director, officer, employee, agent or fiduciary to Lexicon, any subsidiary of Lexicon or to any other company or enterprise for which the person provides services at Lexicon's request.

At present, there is no pending litigation or proceeding involving a director or officer of Lexicon as to which indemnification is being sought nor is Lexicon aware of any threatened litigation that may result in claims for indemnification

by any officer or director.

Item 16. Exhibits.

| Exhibit No. | Description |
|-------------|--|
| *1.1 | — Form of Underwriting Agreement. |
| 3.1 | — Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein). |
| 3.2 | — First Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.2 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein). |
| 3.3 | — Second Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.3 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein). |
| 3.4 | — Third Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2009 and incorporated by reference herein). |
| 3.5 | — Amended and Restated Bylaws (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated October 24, 2007 and incorporated by reference herein). |
| 4.1 | — Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.2 | — Amendment, dated October 7, 2009, to Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 7, 2009 and incorporated by reference herein). |
| 4.3 | — Registration Rights Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.4 | — Supplement to Transaction Agreements, date March 15, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated March 15, 2010 and incorporated by reference herein). |
| 4.5 | — Stockholders' Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.6 | — Amended and Restated Purchase Option Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC and Symphony Icon, Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |
| 4.7 | — Amended and Restated Registration Rights Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |
| *4.8 | — Form of Certificate of Designation of Preferred Stock. |
| 4.9 | — Form of Indenture. |
| *4.10 | — Form of Note. |
| *4.11 | — Form of Common Stock Warrant Agreement and Warrant Certificate. |
| *4.12 | — Form of Preferred Stock Warrant Agreement and Warrant Certificate. |
| *4.13 | — Form of Debt Securities Warrant Agreement and Warrant Certificate. |
| *4.14 | — Form of Rights Agreement and Rights Certificate. |
| *4.15 | — Form of Unit Agreement. |
| 5.1 | — Opinion of Vinson & Elkins L.L.P. |
| 12.1 | — Statement of Computation of Ratio of Earnings to Fixed Charges. |

- 23.1 — Consent of Independent Registered Public Accounting Firm.
- 23.2 — Consent of Vinson & Elkins L.L.P. (contained in Exhibit 5.1).
- 24.1 — Power of Attorney (contained in signature page).
- *25.1 — Statement of Eligibility of Trustee under the Indenture.

* To be filed by amendment, as an exhibit to a report filed under the Securities Exchange Act of 1934, as amended, or as otherwise required by regulation of the Securities and Exchange Commission, and incorporated by reference herein.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

(a) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");

(ii) to reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement;

provided, however, that paragraphs (a)(i) and (a)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are incorporated by reference in this registration statement.

(b) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

The Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein and the offering of such securities at the time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final

adjudication of such issue.

The Registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act (the "Act") in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of The Woodlands, in the State of Texas, on January 28, 2011.

Lexicon Pharmaceuticals, Inc.

By: /s/ Arthur T. Sands
Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below appoints Arthur T. Sands and Jeffrey L. Wade, and each of them, any of whom may act without the joinder of the other, as his true and lawful attorneys-in-fact and agents with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement and any Registration Statement (including any amendment thereto) for this offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he might or would do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute and substitutes, may lawfully do or cause to be done by virtue hereof.

PURSUANT TO THE REQUIREMENTS OF THE SECURITIES ACT OF 1933, AS AMENDED, THIS REGISTRATION STATEMENT HAS BEEN SIGNED BELOW BY THE FOLLOWING PERSONS IN THE CAPACITIES AND ON THE DATES INDICATED BELOW.

| Signature | Title | Date |
|--|---|------------------|
| /s/ Arthur T. Sands Arthur T. Sands, M.D., Ph.D. | President, Chief Executive Officer and Director (principal executive officer) | January 28, 2011 |
| /s/ Jeffrey L. Wade Jeffrey L. Wade | Executive Vice President, Corporate Development and Chief Financial Officer (principal financial officer) | January 28, 2011 |
| /s/ James F. Tessmer James F. Tessmer | Vice President, Finance and Accounting (principal accounting officer) | January 28, 2011 |
| /s/ Samuel L. Barker Samuel L. Barker, Ph.D. | Chairman of the Board of Directors | January 28, 2011 |
| /s/ Philippe J. Amouyal Philippe J. Amouyal | Director | January 28, 2011 |
| /s/ Raymond Debbane Raymond Debbane | Director | January 28, 2011 |
| /s/ Robert J. Lefkowitz Robert J. Lefkowitz, M.D. | Director | January 28, 2011 |
| /s/ Alan S. Nies Alan S. Nies, M.D. | Director | January 28, 2011 |
| /s/ Frank P. Palantoni Frank P. Palantoni | Director | January 28, 2011 |
| /s/ Christopher J. Sobecki Christopher J. Sobecki | Director | January 28, 2011 |
| /s/ Judith L. Swain | Director | January 28, 2011 |

Judith L. Swain, M.D.

29

EXHIBIT INDEX

| Exhibit No. | Description |
|-------------|--|
| *1.1 | — Form of Underwriting Agreement. |
| 3.1 | — Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein). |
| 3.2 | — First Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.2 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein). |
| 3.3 | — Second Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.3 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein). |
| 3.4 | — Third Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2009 and incorporated by reference herein). |
| 3.5 | — Amended and Restated Bylaws (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated October 24, 2007 and incorporated by reference herein). |
| 4.1 | — Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.2 | — Amendment, dated October 7, 2009, to Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 7, 2009 and incorporated by reference herein). |
| 4.3 | — Registration Rights Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.4 | — Supplement to Transaction Agreements, date March 15, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated March 15, 2010 and incorporated by reference herein). |
| 4.5 | — Stockholders' Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.6 | — Amended and Restated Purchase Option Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC and Symphony Icon, Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |
| 4.7 | — Amended and Restated Registration Rights Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |
| *4.8 | — Form of Certificate of Designation of Preferred Stock. |
| 4.9 | — Form of Indenture. |
| *4.10 | — Form of Note. |
| *4.11 | — Form of Common Stock Warrant Agreement and Warrant Certificate. |
| *4.12 | — Form of Preferred Stock Warrant Agreement and Warrant Certificate. |
| *4.13 | — Form of Debt Securities Warrant Agreement and Warrant Certificate. |
| *4.14 | — Form of Rights Agreement and Rights Certificate. |
| *4.15 | — Form of Unit Agreement. |
| 5.1 | — Opinion of Vinson & Elkins L.L.P. |

- 12.1 — Statement of Computation of Ratio of Earnings to Fixed Charges.
- 23.1 — Consent of Independent Registered Public Accounting Firm.
- 23.2 — Consent of Vinson & Elkins L.L.P. (contained in Exhibit 5.1).
- 24.1 — Power of Attorney (contained in signature page).
- *25.1 — Statement of Eligibility of Trustee under the Indenture.

To be filed by amendment, as an exhibit to a report filed under the Securities Exchange Act of 1934, as amended, or as otherwise required by regulation of the Securities and Exchange Commission, and incorporated by reference herein.

30