LEXICON PHARMACEUTICALS, INC./DE
Form 424B2
November 24, 2014
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Filed Pursuant to Rule 424(b)(2)

Registration No. 333-198493

Prospectus supplement (To Prospectus dated September 12, 2014)

49,751,244 Shares

Common stock

We are offering up to 49,751,244 shares of our common stock to the public.

Shares of our common stock trade on The NASDAQ Global Select Market under the symbol LXRX. The last reported sale price on November 20, 2014 was $1.005 per share.

We will issue to Artal International S.C.A. (Artal), an affiliate of Invus, L.P., our largest shareholder, $150.0 million of additional shares of our common stock in a concurrent private placement at $1.005 per share, the price per share to the public in this offering.

Concurrently with this offering of common stock, we are offering to qualified institutional buyers, in an offering exempt from registration under the Securities Act of 1933, as amended, $80,000,000 aggregate principal amount of our 5.25% Convertible Senior Notes due 2021, which we refer to as the notes, or a total of $95,000,000 aggregate principal amount of notes if the initial purchasers in the concurrent notes offering exercise in full their over-allotment option. We cannot assure you that the concurrent notes offering will be completed. The offering of common stock hereby is not contingent upon the consummation of the concurrent notes offering, and the concurrent notes offering is not contingent upon the consummation of the offering of common stock hereby. See Prospectus supplement summary Private placement.

	Per share	Total
Public offering price	$ 1.005	$ 50,000,000
Underwriting discounts and commissions	$ 0.0603	$ 3,000,000
Proceeds, before expenses, to us	$ 0.9447	$ 47,000,000

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to 7,462,687 additional shares of our common stock at the public offering price less the underwriting discounts and commissions.

Investing in our common stock involves risks. See Risk factors beginning on page S-7 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about November 26, 2014.

J.P. Morgan **Goldman, Sachs & Co.**

Needham & Company **Stifel**

November 20, 2014

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Prospectus supplement

Prospectus

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About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein. We have not authorized, and the underwriters have not authorized, anyone to provide you with information that is different. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled Where you can find more information and Documents incorporated by reference in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise stated, all references in this prospectus to we, us, our, Lexicon, Lexicon Pharmaceuticals, the Company and similar designations refer to Lexicon Pharmaceuticals, Inc. and its wholly-owned 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 are registered trademarks of Lexicon Pharmaceuticals, Inc. All other trademarks or service marks appearing in this prospectus supplement are the property of their respective holders.

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Prospectus supplement summary

The following summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. This summary sets forth the material terms of this offering, but does not contain all of the information you should consider before investing in our common stock. You should read carefully this entire prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, before making an investment decision, especially the risks of investing in the common stock discussed in the section titled Risk factors in this prospectus supplement as well as the consolidated financial statements and notes to those consolidated financial statements incorporated by reference into this prospectus supplement and the accompanying prospectus. Some of the statements in this prospectus supplement constitute forward-looking statements that involve risks and uncertainties. See Special note regarding forward-looking statements. Our actual results could differ materially from those anticipated in such forward-looking statements as a result of certain factors, including those discussed in the Risk factors and other sections of this prospectus supplement. Unless the context requires otherwise, references in this prospectus supplement to Lexicon, the Company, we, us, and our refer to Lexicon Pharmaceuticals, Inc. together with its consolidated subsidiaries and references to Invus refer to Invus, L.P. and Invus C.V. Unless otherwise indicated, all information contained in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

Lexicon Pharmaceuticals, Inc.

Our business

Lexicon Pharmaceuticals is a biopharmaceutical company focused on the development of breakthrough treatments for human disease. We have advanced multiple drug candidates into clinical development. We are presently devoting most of our resources to the development of our two most advanced drug candidates:

We are developing telotristat etiprate, or LX1032, an orally-delivered small molecule drug candidate, as a treatment for carcinoid syndrome. We have completed two Phase 2 clinical trials and are presently conducting a single pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients. The Phase 3 clinical trial of telotristat etiprate is a 12-week, placebo-controlled study of approximately 120 to 130 patients with inadequately controlled carcinoid syndrome on background somatostatin analog therapy (including at least 105 patients on octreotide therapy), followed by a 36-week, open-label extension where all patients receive telotristat etiprate. Two dose levels of telotristat etiprate, 250 mg and 500 mg, three times daily (TID), are being tested along with placebo. The primary efficacy endpoint under evaluation in the Phase 3 clinical trial is the number of daily bowel movements, with secondary efficacy endpoints including changes in urinary 5-H1AA levels, flushing episodes, abdominal pain and quality of life measures. The Phase 3 program of telotristat etiprate also includes an additional companion study in carcinoid syndrome patients who do not meet the inclusion criteria for the pivotal Phase 3 clinical trial. We presently expect to complete enrollment in the single pivotal Phase 3 clinical trial in early 2015 and report top-line data from such trial in the third quarter of 2015. If supported by such data, we anticipate filing an NDA for telotristat etiprate in carcinoid syndrome in the first quarter of 2016 with potential FDA approval and commercial launch in the second half of 2016.

We are developing sotagliflozin, or LX4211, an orally-delivered small molecule drug candidate, as a treatment for type 1 and type 2 diabetes. We have completed two Phase 2 clinical trials of sotagliflozin in type 2 diabetes patients and an additional clinical trial of sotagliflozin in type 2 diabetes patients with renal impairment. We have also completed a Phase 2 clinical trial of sotagliflozin in type 1 diabetes patients. We are preparing for the

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initiation of a Phase 2 clinical trial of sotagliflozin in a younger adult type 1 diabetes population in collaboration with JDRF, from which we presently expect to report top-line data in the first quarter of 2016. We are also preparing for the initiation of Phase 3 development of sotagliflozin in type 1 diabetes in the first half of 2015. The Phase 3 development of sotagliflozin in type 1 diabetes is expected to include three Phase 3 studies, including two pivotal Phase 3 studies. Each of the pivotal Phase 3 studies are 24-week, placebo controlled studies of approximately 750 patients, which will be followed by 28-week extensions. Two dose levels of sotagliflozin, 200mg and 400mg once daily, will be tested along with placebo. The primary efficacy endpoint under evaluation will be reduction of A1C versus placebo on optimized insulin treatment at 24 weeks, with secondary endpoints including percentage of patients achieving A1C levels of less than 7%, reduction in meal-time, or bolus, insulin use and weight loss. We presently expect to report top-line data from such trials in the fourth quarter of 2016. The third Phase 3 study would be expected to enroll 1,400 patients and involve a glycemic control primary endpoint and an evaluation of safety. We also plan to conduct a dose-ranging study of sotagliflozin in patients with type 1 diabetes concurrently with our planned Phase 3 studies. We do not intend to continue development of sotagliflozin in type 2 diabetes unless we enter into a collaboration partnership.

Our most advanced drug candidates, as well as compounds from a number of additional drug discovery and development programs that we have advanced into various stages of clinical and nonclinical development, originated from our own internal drug discovery efforts. These efforts were driven by a systematic, targeted biology-driven approach in which we used gene knockout technologies 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 identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery.

We are working both independently and through strategic collaborations and alliances with third parties to capitalize on our drug discovery and development programs. We seek to retain exclusive rights to the benefits of certain drug discovery and development programs by developing and commercializing drug candidates from those programs internally and to collaborate with other pharmaceutical and biotechnology companies with respect to the development and commercialization of drug candidates from other programs, particularly when the collaboration may provide us with access to expertise and resources that we do not possess internally or are complementary to our own.

Recent developments

Sotagliflozin (LX4211)

We reported top-line data in April 2014 from a Phase 2 clinical trial evaluating the safety and tolerability of sotagliflozin and its effects on glycemic parameters associated with type 1 diabetes. The Phase 2 trial enrolled 36 patients with type 1 diabetes. An initial cohort consisted of three patients treated with a 400 mg once daily dose of sotagliflozin for a period of four weeks. A subsequent cohort of 33 patients were enrolled in the randomized, double-blind, placebo-controlled portion of the study and were treated with a 400mg once daily dose of sotagliflozin or placebo for a period of four weeks. The primary efficacy endpoint under evaluation in the trial was reduction in bolus insulin use. Secondary endpoints included multiple parameters of glycemic control, basal and total insulin use and other metabolic, pharmacodynamic and pharmacokinetic parameters.

Top-line data from the study showed that treatment with sotagliflozin demonstrated statistically significant benefits in the primary and multiple secondary endpoints. Patients treated with sotagliflozin experienced a reduction in their total daily mealtime bolus insulin dose of 32% compared to 6% for patients who received

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placebo (p=0.007). We also observed a significant improvement in glycemic control, with a mean A1C reduction of 0.55% in the sotagliflozin-treated group compared to a reduction of 0.06% in the placebo-treated group (p=0.002). These observations were also accompanied by significant improvement in the time spent in a glucose range of 70-180 mg/dl, a significant reduction in time in hyperglycemic range (>180 mg/dl) and no increase in hypoglycemia. Multiple measures also indicated that patients treated with sotagliflozin experienced reduced variability in blood glucose levels. Sotagliflozin was well tolerated with no discontinuations of study medication due to adverse events.

Ipsen License and Collaboration Agreement

In October 2014, we entered into a license and collaboration agreement with Ipsen Pharma SAS, or Ipsen, pursuant to which we granted Ipsen an exclusive, royalty-bearing right and license to commercialize telotristat etiprate outside of the United States, Canada and Japan. Ipsen paid us an upfront payment of $23 million and we are eligible to receive up to approximately $30 million upon the achievement of specified regulatory and commercial launch milestones and up to 72 million upon the achievement of specified sales milestones. We are also entitled to tiered, escalating royalties ranging from low twenties to mid-thirties percentages of net sales of telotristat etiprate in the licensed territory, subject to a credit for Ipsen s payments to us for the manufacture and supply of such units of telotristat etiprate. Our receipt of these payments from Ipsen will trigger our obligation to make certain contingent payments to Symphony Icon Holdings LLC, or Holdings, pursuant to our prior arrangement with Holdings for the financing of the clinical development of telotristat etiprate. Ipsen may terminate this agreement upon a specified period of notice to us at any time.

Company information

Lexicon Pharmaceuticals 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 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. Information found on or through our website is not incorporated herein by reference and should not be considered part of this prospectus.

Concurrent convertible notes offering

Concurrently with this offering of common stock, we are offering our 5.25% Convertible Senior Notes due 2021 in aggregate principal amount of $80,000,000, or $95,000,000 if the initial purchasers in that offering exercise in full their over-allotment option, which we refer to herein as the concurrent notes offering. The concurrent notes offering is being conducted in an offering exempt from registration under the Securities Act of 1933, as amended (the Securities Act) and is being made only to qualified institutional buyers. This offering is not contingent upon the completion of the concurrent notes offering, and the concurrent notes offering is not contingent upon the completion of this offering. We cannot assure you that any of these offerings will be completed.

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Private placement

We have also entered into a stock purchase agreement with Invus and Artal (the Stock Purchase Agreement) pursuant to which Artal has agreed to purchase and we have agreed to issue to Artal on the closing date of this offering an aggregate of 149,253,731 shares of our common stock at a price of $1.005 per share, the price per share to the public in this offering, for total gross proceeds of $150.0 million.

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The offering

Common stock offered	49,751,244 shares
Common stock to be outstanding after this offering	713,839,502 shares(1)
Use of proceeds	The net proceeds of this offering are estimated to be approximately $46.8 million after deduction of underwriting discounts and commissions and estimated offering expenses (or approximately $53.9 million if the underwriters exercise in full their option to purchase additional shares). We currently intend to use the net proceeds from this offering, together with the net proceeds, if any, from the concurrent notes offering and the concurrent private placement, for the clinical development of our drug candidates and our other nonclinical research and development efforts. We may also use a portion of the net proceeds to acquire or invest in complementary products and technologies or for general corporate purposes. See Use of proceeds.
Risk factors	See Risk factors beginning on page S-7 and the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	LXRX
Concurrent convertible notes offering	Concurrently with this offering of common stock, we are offering $80,000,000 aggregate principal amount of our 5.25% Convertible Senior Notes due 2021 (or $95,000,000 aggregate principal amount if the initial purchasers in that offering exercise in full their over-allotment option). The concurrent notes offering is being conducted as an offering exempt from registration under the Securities Act and is being made only to qualified institutional buyers. This offering is not contingent upon the completion of the concurrent notes offering, and the concurrent notes offering is not contingent upon the completion of this offering. We cannot assure you that any of these offerings will be completed. See Concurrent convertible notes offering.

(1) The number of shares of our common stock to be outstanding after this offering is based on 514,834,527 shares outstanding as of November 18, 2014, and excludes:

24,313,195 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price per share of $2.16;

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3,162,232 shares of common stock issuable pursuant to outstanding restricted stock units;

13,843,239 shares of common stock available for future grant or issuance under our equity incentive plans; and

the shares of our common stock to be reserved for issuance upon conversion of the notes being offered by us in connection with the concurrent notes offering.

Unless we specifically state otherwise, all information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to 7,462,687 additional shares of our common stock or by the initial purchasers in the concurrent notes offering of their over-allotment option.

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Risk factors

An investment in our common stock involves risks. You should carefully consider the following risk factors, together with all of the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus in evaluating an investment in our common stock including the information in our Annual Report on Form 10-K for the year ended December 31, 2013 and our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014. If any of the following risks were to occur, our business, financial condition or results of operations could be materially adversely affected. In that case, the trading price of our common stock could decline and you could lose all or part of your investment.

Risks related to our need for additional financing and our financial results

We will need additional capital in the future and, if it is unavailable, we will be forced to significantly curtail or cease our operations. If it is not available on reasonable terms, we will be forced to obtain funds, if at all, by entering into financing agreements on unattractive terms.

As of September 30, 2014, we had $57.9 million in cash, cash equivalents and investments. We anticipate that the proceeds from this offering, the concurrent notes offering and the concurrent private placement, our existing capital resources and the cash and revenues we expect to derive from collaborations and other sources will enable us to fund our currently planned operations for at least the next 12 months. However, we caution you that we may not consummate either the concurrent notes offering or the concurrent private placement and we may generate less cash and revenues or incur expenses more rapidly than we currently anticipate. Our currently planned operations for the next twelve months consist of (i) the completion of our single pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients and, if successful, continued preparations for the commercialization of telotristat etiprate, (ii) a companion Phase 3 clinical trial of telotristat etiprate to study safety and 5-hydroxyindoleacetic acid in a separate patient population, with a targeted enrollment of approximately 60 patients, (iii) a Phase 2 clinical trial of sotagliflozin in a younger adult type 1 diabetes population and (iv) three concurrent Phase 3 clinical trials for sotagliflozin in type 1 diabetes, which we expect to enroll an aggregate of 2,900 patients, and a dose ranging study of sotagliflozin. In addition, we cannot be certain as to what type and how many clinical trials the FDA, or equivalent foreign regulatory agencies, will require us to conduct in order to gain approval to market either telotristat etiprate or sotagliflozin.

Although difficult to accurately predict, the amount of our future capital requirements will be substantial and will depend on many factors, including:

- the timing and progress of our single pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients, including completing enrollment in the trial and our ability to obtain priority review on any potential NDA submission;
- if approved, our ability to commercialize telotristat etiprate on the timeline anticipated;
- the amount and timing of payments, if any, under existing and any future collaboration agreements;
- the amount and timing of our nonclinical development expenditures;
- the timing and progress of the clinical development of telotristat etiprate and sotagliflozin, including the timing of any required regulatory actions, the outcome of our anticipated discussions with regulators and the outcome of our sotagliflozin dose ranging study, which we are planning to conduct concurrently with our two pivotal Phase 3 efficacy trials;
- future results from clinical trials of our drug candidates;

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the cost and timing of regulatory approvals and commercialization of drug candidates that we successfully develop;

market acceptance of products that we successfully develop and commercially launch;

the effect of competing programs and products, and of technological and market developments;

the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and

the cost and timing of establishing or contracting for sales, marketing and distribution capabilities of any approved drug candidate.

Our capital requirements have and will continue to increase substantially as our drug candidates progress into more advanced stage clinical development. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary products and technologies. For all of these reasons, our future capital requirements cannot easily be quantified.

If our capital resources are insufficient to meet future capital requirements, we will need to raise additional funds to continue our currently planned operations. If we raise additional capital by issuing equity securities, our then-existing stockholders will experience dilution and the terms of any new equity securities may have preferences over our common stock. We cannot be certain that additional financing, whether debt or equity, will be available in amounts or on terms acceptable to us, if at all. We may be unable to raise sufficient additional capital on reasonable terms, and if so, we will be forced to significantly curtail or cease our operations or obtain funds, if at all, by entering into financing agreements on unattractive terms.

We have a history of net losses, and we expect to continue to incur net losses and may not achieve or maintain profitability.

We have incurred net losses since our inception, including net losses of $97.4 million for the nine months ended September 30, 2014, $104.1 million for the year ended December 31, 2013, $110.2 million for the year ended December 31, 2012 and $116.2 million for the year ended December 31, 2011. As of September 30, 2014, we had an accumulated deficit of $1.1 billion. We are unsure when we will become profitable, if ever. The size of our net losses will depend, in part, on the rate of decline or growth in our revenues and on the level of our expenses. We expect net losses to increase significantly over the next several years as we expect to make significant investments in the development and commercialization of telotristat etiprate and sotagliflozin.

We have derived substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses. Future revenues from our existing collaborations are uncertain because they depend, to a large degree, on the achievement of milestones and payment of royalties we earn from any future products developed under the collaborations. As a result, we depend, in part, on securing new collaboration agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators, and to negotiate agreements that we believe are in our long-term best interests. We may determine, as we have with certain of our clinical drug candidates, including telotristat etiprate (in the United States, Canada and Japan) and sotagliflozin, that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues and increase our expenses. Given the current stage of our operations, we do not currently derive any revenues from sales of pharmaceutical products.

A large portion of our expenses is fixed, including expenses related to facilities and equipment. In addition, we expect to spend significant amounts to fund our nonclinical and clinical development activities, including the conduct of ongoing and planned clinical trials for telotristat etiprate and sotagliflozin. If successful, we will also

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be required to incur substantial expenditures in preparation for and to conduct commercialization activities with respect to telotristat etiprate and sotagliflozin. As a result, we will need to generate substantial additional revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our operating results have been and likely will continue to fluctuate, and we believe that period-to-period comparisons of our operating results are not a good indication of our future performance.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including:

- our ability to establish new collaborations and technology licenses, and the timing of such arrangements;
- the success rate of our discovery and development efforts leading to opportunities for new collaborations and licenses, as well as milestone payments and royalties;
- the timing and willingness of our collaborators to commercialize pharmaceutical products that would result in milestone payments and royalties; and
- general and industry-specific economic conditions, which may affect our and our collaborators research and development expenditures.

Because of these and other factors, including the risks and uncertainties described in this section, our operating results have fluctuated in the past and are likely to do so in the future. Due to the likelihood of fluctuations in our revenues and expenses, we believe that period-to-period comparisons of our operating results are not a good indication of our future performance.

The concurrent notes offering will result in substantial indebtedness that may limit cash flow available to invest in the ongoing needs of our business.

Assuming the consummation of the concurrent notes offering, we will have a significant amount of indebtedness. We will incur $80.0 million of additional indebtedness if and when we sell the notes in the concurrent notes offering, or $95.0 million of additional indebtedness if the initial purchasers in that offering exercise in full their over-allotment option. We could in the future incur additional indebtedness beyond such amounts. We will not be restricted under the terms of the indenture governing the notes offered in the concurrent notes offering from incurring additional debt. Our substantial debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a substantial portion of cash flow from operations to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- obligating us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and marketable securities and funds from external sources. However, we may not have sufficient funds or may

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be unable to arrange for additional financing to pay the amounts due under our existing debt. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under our existing debt instruments could result in an event of default under those instruments. In the event of an acceleration of amounts due under our debt instruments as a result of an event of default, including upon the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, properties, assets or condition or a failure to pay any amount due, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness. In addition, the covenants under our existing debt instruments and the pledge of our assets as collateral limit our ability to obtain additional debt financing.

We may not have the ability to raise the funds necessary to repurchase the notes sold in the concurrent notes offering upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the notes.

Holders of any notes we sell in the concurrent notes offering will have the right to require us to repurchase their notes upon the occurrence of a fundamental change at a repurchase price equal to 100% of their principal amount, plus accrued and unpaid interest, if any. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of notes surrendered therefor. In addition, our ability to repurchase the notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase notes at a time when the repurchase is required by the indenture pursuant to which the concurrent notes will be issued would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the notes.

Risks related to development of our drug candidates

We have not proven our ability to successfully develop and commercialize our drug candidates.

Our success will depend upon our ability, on our own or through collaborations, to successfully develop and select an appropriate commercialization strategy for our drug candidates. We have not proven our ability to develop or commercialize drug candidates based on our drug target discoveries, and we do not know that any pharmaceutical products based on our drug target discoveries can be successfully developed or commercialized. Our strategy was historically focused principally on the discovery and development of drug candidates for targets that have not been clinically validated in humans by drugs or drug candidates generated by others. As a result, our drug candidates are subject to uncertainties as to the effects of modulating the human drug target as well as to those relating to the characteristics and activity of the particular compound.

Clinical testing of our drug candidates in humans is an inherently risky and time-consuming process that may fail to demonstrate safety and efficacy, which could result in the delay, limitation or prevention of regulatory approval.

In order to obtain regulatory approvals for the commercial sale of any products that we may develop, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of our drug candidates. We or our collaborators may not be able to obtain authority from the FDA, or other equivalent foreign regulatory agencies to initiate or complete any clinical trials. In addition, we have limited internal resources for making regulatory filings and interacting with regulatory authorities.

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Clinical trials are inherently risky and the results from nonclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger-scale, advanced stage clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving positive results in earlier trials. Although the results of our Phase 2 proof-of-concept study of sotagliflozin in type 1 diabetes patients were positive, we cannot assure you that the planned Phase 3 clinical trials of sotagliflozin will achieve positive results. A number of factors could contribute to a lack of positive results in such Phase 3 clinical trials, including a primary endpoint in such planned Phase 3 clinical trials, which has not previously been utilized for such purpose. Negative or inconclusive results from a nonclinical study or a clinical trial could cause us, one of our collaborators or the FDA to terminate a nonclinical study or clinical trial or require that we repeat or modify it. For example, concurrently with our planned Phase 3 clinical trials in our type 1 diabetes program, we plan to conduct a dose-ranging study of sotagliflozin in patients with type 1 diabetes as required by the FDA. If the results of the dose-ranging study are inconsistent with the design of our Phase 3 trials of sotaglifozin, such as suggesting that there is an effective dose of sotagliflozin in patients with type 1 diabetes lower than the doses we are studying in our Phase 3 clinical trials of sotagliflozin, we may be required to modify those Phase 3 clinical trials which could significantly delay the completion of the trials. Furthermore, we, one of our collaborators or a regulatory agency with jurisdiction over the trials may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

Any nonclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Nonclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. For example, the FDA suggested we study sotaglifozin in both type 1 and type 2 diabetes concurrently rather than only in type 1 diabetes. This could influence the way in which the FDA interprets the results of our trials of sotaglifozin. The FDA or institutional review boards at the medical institutions and healthcare facilities where we sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. Clinical trials must be conducted in accordance with the FDA s current Good Clinical Practices. The FDA and these institutional review boards have authority to oversee our clinical trials, and the FDA may require large numbers of subjects or patients. In addition, we must manufacture, or contract for the manufacture of, the drug candidates that we use in our clinical trials under the FDA s current Good Manufacturing Practices.

The rate of completion of clinical trials is dependent, in part, upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the nature of the study, the existence of competitive clinical trials and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development, which in turn could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or potential products.

We or our collaborators may not be able to successfully complete any clinical trial of a potential product within any specified time period. In some cases, we or our collaborators may not be able to complete the trial at all. Moreover, clinical trials may not show our potential products to be both safe and effective. Thus, the FDA and other regulatory authorities may not approve any products that we develop for any indication or may limit the approved indications or impose other conditions.

Risks related to regulatory approval of our drug candidates

Our drug candidates are subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our ability to commercialize products.

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Our drug candidates, including telotristat etiprate and sotagliflozin, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a drug candidate would prevent us from commercializing that drug candidate. We have not received regulatory approval to market any of our drug candidates in any jurisdiction and have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the drug candidates involved. Before a new drug application can be filed with the FDA, the drug candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. Furthermore, prior to approving a new drug, the FDA typically requires that the efficacy of the drug be demonstrated in two double-blind, controlled studies. In light of the unmet medical need in carcinoid syndrome, the results of our Phase 2 clinical trials of telotristat etiprate and our interactions with the FDA regarding those results, we believe a single Phase 3 clinical trial of telotristat etiprate will be sufficient. However, the FDA has indicated that the trial must demonstrate statistically robust evidence of important clinical benefit and an acceptable safety profile in order to warrant consideration for marketing approval. If the FDA determines that our Phase 3 results do not have statistically robust results or clinically meaningful benefit, or if the FDA requires us to conduct additional Phase 3 clinical trials of telotristat etiprate prior to seeking marketing approval, we will incur significant additional development costs and commercialization of telotristat etiprate may be prevented or delayed. The regulatory process also requires nonclinical testing, and data obtained from nonclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. For example, we will need to complete certain nonclinical studies on a pre-approval basis in connection with our diabetes program, including carcinogencity and toxicology. In our carcinoid syndrome program, we will need to conduct carcinogenicity studies on a post-approval basis and drug interaction studies on a pre-approval basis. Negative results in any of these nonclinical studies could delay or prevent approval of our product candidates. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our drug candidates may cause delays in the approval or rejection of an application. For example, the FDA may expand to Phase 3 programs for type 1 diabetes its current requirement that Phase 3 programs for type 2 diabetes include studies designed to measure cardiovascular outcomes. The FDA has asked that we submit a cardiovascular risk assesment of sotagliflozin. If the risk assesment suggests a higher than acceptable cardiovascular risk or if the FDA requests that we submit cardiovascular outcome data for sotagliflozin, it could significantly delay or prevent approval. Even if the FDA or a comparable authority in another country approves a drug candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

If our potential products receive regulatory approval, we or our collaborators will remain subject to extensive and rigorous ongoing regulation.

If we or our collaborators obtain initial regulatory approvals from the FDA or foreign regulatory authorities for any products that we may develop, we or our collaborators will be subject to extensive and rigorous ongoing domestic and foreign government regulation of, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of our products and drug candidates. The failure to comply with these requirements or the identification of safety problems during commercial marketing could lead

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to the need for product marketing restrictions, product withdrawal or recall or other voluntary or regulatory action, which could delay further marketing until the product is brought into compliance. The failure to comply with these requirements may also subject us or our collaborators to stringent penalties.

Risks related to commercialization of products

The commercial success of any products that we may develop will depend upon the degree of market acceptance of our products among physicians, patients, health care payors, private health insurers and the medical community.

Even if approved by the relevant regulatory authority, our ability to commercialize any products that we may develop will be highly dependent upon the extent to which these products gain market acceptance among physicians, patients, health care payors, such as Medicare and Medicaid, private health insurers, including managed care organizations and group purchasing organizations, and the medical community. If these products do not achieve an adequate level of acceptance, we may not generate adequate product revenues, if at all, and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of our products in comparison to competing products;
- the existence of any significant side effects, as well as their severity in comparison to any competing products;
- potential advantages over alternative treatments;
- the ability to offer our products for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our drug candidates, we may be unable to generate product revenues.

We have no experience as a company in the sales, marketing and distribution of pharmaceutical products and do not currently have a sales and marketing organization. Developing a sales and marketing force would be expensive and time-consuming, could delay any product launch, and we may never be able to develop this capacity. To the extent that we enter into arrangements with third parties to provide sales, marketing and distribution services, our product revenues are likely to be lower than if we market and sell any products that we develop ourselves. If we are unable to establish adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenues.

If we are unable to obtain adequate coverage and reimbursement from third-party payors for any products that we may develop, our revenues and prospects for profitability will suffer.

Our ability to commercialize any products that we may develop will be highly dependent on the extent to which coverage and reimbursement for our products will be available from third-party payors, including governmental payors, such as Medicare and Medicaid, and private health insurers, including managed care organizations and group purchasing organizations. Many patients will not be capable of paying themselves for some or all of the products that we may develop and will rely on third-party payors to pay for, or subsidize, their medical needs. If third-party payors do not provide coverage or reimbursement for any products that we

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may develop, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for our products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

Another factor that may negatively affect the pricing of drugs is any action regarding drug reimportation into the United States. For example, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 gives discretion to the Secretary of Health and Human Services to allow drug reimportation into the United States under some circumstances from foreign countries, including countries where drugs are sold at a lower price than in the United States. Proponents of drug reimportation may attempt to pass additional legislation, which would allow direct reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, it could decrease the price we receive for any products that we may develop, thereby negatively affecting our revenues and prospects for profitability.

In addition, in some foreign countries, particularly the countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, price negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement and/or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our drug candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of our drug candidates. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we may develop. Cost-control initiatives could decrease prices we might establish for products that we may develop, which would result in lower product revenues to us.

Current and future healthcare laws and regulations may negatively affect our revenues and prospects for profitability.

A primary trend in the United States and some foreign countries is toward reform and cost containment in the health care industry. The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals that may have the effect of reducing the prices that we are able to charge for products we develop. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, substantially modifies the framework by which healthcare is financed by both governmental and private insurers in the United States. A number of provisions contained in the PPACA have the potential to significantly affect the pharmaceutical industry, including:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain governmental health programs;
- expansion of eligibility criteria and increases in the rebates manufacturers must pay under certain Medicaid programs;
- a new Medicare Part D coverage program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during any coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- certain reporting requirements relating to financial arrangements with, and drug samples provided to, physicians.

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The PPACA and other healthcare reform measures which may be adopted in the future in the United States and foreign jurisdictions may result in more rigorous coverage criteria and significant downward pressure on the prices drug manufacturers may charge. As a result, our revenues and prospects for profitability could be significantly harmed.

Our competitors may develop products that make our products obsolete.

The biotechnology industry is highly fragmented and is characterized by rapid technological change. We face, and will continue to face, intense competition from biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research and development activities similar to ours. In addition, significant delays in the development of our drug candidates could allow our competitors to bring products to market before us, which would impair our ability to commercialize our drug candidates. Any products that we develop will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop products that would render our products, and those of our collaborators, obsolete and noncompetitive. For example, drug candidates are currently being developed by other pharmaceutical companies for the treatment of type 2 diabetes that act through SGLT2, one of the targets of sotagliflozin, which are in more advanced stages of development than sotagliflozin or have been approved for commercial sale by the FDA or other regulatory agencies. In addition, there may be drug candidates of which we are not aware at an earlier stage of development that may compete with our drug candidates.

We may not be able to manufacture our drug candidates in commercial quantities, which would prevent us from commercializing our drug candidates.

To date, our drug candidates have been manufactured in small quantities for nonclinical and clinical trials. If any of these drug candidates are approved by the FDA or other regulatory agencies for commercial sale, we will need to manufacture them in larger quantities. We may not be able to successfully increase the manufacturing capacity, whether in collaboration with third-party manufacturers or on our own, for any of our drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for a drug candidate, the regulatory approval or commercial launch of that drug candidate may be delayed or there may be a shortage in supply. Our drug candidates require precise, high-quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

Risks related to our relationships with third parties

We are dependent in many ways upon our collaborations with major pharmaceutical companies, including Ipsen. If we are unable to establish new collaborations, if milestones are not achieved under our collaborations or if our collaborators efforts fail to yield pharmaceutical products on a timely basis, our opportunities to generate revenues and earn royalties will be reduced.

We have derived a substantial majority of our revenues to date from collaborative drug discovery and development alliances with a limited number of major pharmaceutical companies, including Ipsen. In addition,

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we currently intend to seek a collaboration partner for Phase 3 development of sotagliflozin in type 2 diabetes and we cannot be certain that we will be successful in establishing such a collaborative alliance on terms acceptable to us, if at all.

Future revenues from our existing drug discovery and development alliances depend upon the achievement of milestones and payment of royalties we earn from any future products developed under the collaborations. If our relationship terminates with any of our collaborators, our reputation in the business and scientific community may suffer and revenues will be negatively impacted to the extent such losses are not offset by additional collaboration agreements. If milestones are not achieved under our collaborations or our collaborators are unable to successfully develop products from which royalties are payable, we will not earn the revenues contemplated by those drug discovery and development collaborations. In addition, some of our alliances are exclusive and preclude us from entering into additional collaborative arrangements with other parties in the field of exclusivity.

We have limited or no control over the resources that any collaborator may devote to the development and commercialization of products under our alliances. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct discovery, development or commercialization activities successfully or in a timely manner. Further, our collaborators may elect not to develop pharmaceutical products arising out of our collaborative arrangements or may not devote sufficient resources to the development, approval, manufacture, marketing or sale of these products. If any of these events occurs, we may not be able to develop or commercialize potential pharmaceutical products.

Conflicts with our collaborators could jeopardize the success of our collaborative agreements and harm our product development efforts.

We may pursue opportunities in specific disease and therapeutic modality fields that could result in conflicts with our collaborators, if any of our collaborators takes the position that our internal activities overlap with those activities that are exclusive to our collaboration. Moreover, disagreements could arise with our collaborators over rights to our intellectual property or our rights to share in any of the future revenues of compounds or therapeutic approaches developed by our collaborators. Any conflict with or among our collaborators could result in the termination of our collaborative agreements, delay collaborative research or development activities, impair our ability to renew or obtain future collaborative agreements or lead to costly and time consuming litigation. Conflicts with our collaborators could also have a negative impact on our relationship with existing collaborators, materially impairing our business and revenues. Some of our collaborators are also potential competitors or may become competitors in the future. Our collaborators could develop competing products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Any of these events could harm our product development efforts.

We rely on third parties to carry out drug development activities.

We rely on clinical research organizations and other third party contractors to carry out many of our drug development activities, including the performance of nonclinical laboratory and animal tests under the FDA s current Good Laboratory Practices regulations and the conduct of clinical trials of our drug candidates in accordance with protocols we establish. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, our drug development activities may be delayed, suspended or terminated. Such a failure by these third parties could significantly impair our ability to develop and commercialize the affected drug candidates.

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We lack the capability to manufacture materials for nonclinical studies, clinical trials or commercial sales and rely on third parties to manufacture our drug candidates, which may harm or delay our product development and commercialization efforts.

We currently do not have the manufacturing capabilities or experience necessary to produce materials for nonclinical studies, clinical trials or commercial sales and intend in the future to continue to rely on collaborators and third-party contractors to produce such materials. We will rely on selected manufacturers to deliver materials on a timely basis and to comply with applicable regulatory requirements, including the current Good Manufacturing Practices of the FDA, which relate to manufacturing and quality control activities. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. In addition, there are a limited number of manufacturers that operate under the FDA s current Good Manufacturing Practices and that are capable of producing such materials, and we may experience difficulty finding manufacturers with adequate capacity for our needs. If we are unable to contract for the production of sufficient quantity and quality of materials on acceptable terms, our product development and commercialization efforts may be delayed. Moreover, noncompliance with the FDA s current Good Manufacturing Practices can result in, among other things, fines, injunctions, civil and criminal penalties, product recalls or seizures, suspension of production, failure to obtain marketing approval and withdrawal, suspension or revocation of marketing approvals.

Risks related to our intellectual property

If we are unable to adequately protect our intellectual property, third parties may be able to use our products and technologies, which could adversely affect our ability to compete in the market.

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our products and technologies. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our products and technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our products and technologies as and when we deem appropriate. Pending patent applications do not provide protection against competitors because they are not enforceable until they issue as patents. Further, the disclosures contained in our current and future patent applications may not be sufficient to meet statutory requirements for patentability. Once issued, patents still may not provide commercially meaningful protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from developing competing products and technologies. Furthermore, others may independently develop similar or alternative products or technologies or design around our patents. If anyone infringes upon our or our collaborators patent rights, enforcing these rights may be difficult, costly and time-consuming and, as a result, it may not be cost-effective or otherwise expedient to pursue litigation to enforce those patent rights. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for these inventions.

Because patent applications can take many years to issue, there may be currently pending applications which may later result in issued patents that cover the production, manufacture, commercialization or use of our drug targets or drug candidates. If any such patents are issued to other entities, we will be unable to obtain patent protection for the same or similar discoveries that we make relating to our drug targets or drug candidates. Moreover, we may be blocked from using our drug targets or drug candidates or developing or commercializing our drug candidates, or may be required to obtain a license that may not be available on reasonable terms, if at

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all. Further, others may discover uses for our drug targets and drug candidates other than those covered in our issued or pending patents, and these other uses may be separately patentable. Even if we have a patent claim on a particular technology or product, the holder of a patent covering the use of that technology or product could exclude us from selling a product that is based on the same use of that product.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, if the patent owner has failed to work the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our drug candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement.

We rely on trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

We may be involved in patent litigation and other disputes regarding intellectual property rights and may require licenses from third parties for our planned nonclinical and clinical development and commercialization activities. We may not prevail in any such litigation or other dispute or be able to obtain required licenses.

Our nonclinical and clinical development efforts as well as our potential products and those of our collaborators may give rise to claims that they infringe the patents of others. We are aware that other companies and institutions are developing products acting through the same drug targets through which some of our drug candidates currently in clinical development act, have conducted research on many of the same targets that we have identified and have filed patent applications potentially covering drug targets that we have identified and certain therapeutic products addressing such targets. In some cases, patents have issued from these applications. In addition, many companies and institutions have well-established patent portfolios directed to common techniques, methods and means of developing, producing and manufacturing pharmaceutical products. These or other companies or institutions could bring legal actions against us or our collaborators for damages or to stop us or our collaborators from engaging in certain nonclinical or clinical development activities or from manufacturing and marketing therapeutic products that allegedly infringe their patent rights. If any of these actions are successful, in addition to our potential liability for damages, these entities would likely require us or our collaborators to obtain a license in order to continue engaging in the infringing activities or to manufacture or market the infringing therapeutic products or may force us to terminate such activities or manufacturing and marketing efforts.

We may need to pursue litigation against others to enforce our patents and intellectual property rights and may be the subject of litigation brought by third parties to enforce their patent and intellectual property rights. In addition, we may become involved in litigation based on intellectual property indemnification undertakings that

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we have given to certain of our collaborators. Patent litigation is expensive and requires substantial amounts of management attention. The eventual outcome of any such litigation is uncertain and involves substantial risks.

We believe that there will continue to be significant litigation in our industry regarding patent and other intellectual property rights. We have expended and many of our competitors have expended and are continuing to expend significant amounts of time, money and management resources on intellectual property litigation. If we become involved in future intellectual property litigation, it could consume a substantial portion of our resources and could negatively affect our results of operations.

We have not sought patent protection outside of the United States for some of our inventions, and some of our licensed patents only provide coverage in the United States. As a result, our international competitors could be granted foreign patent protection with respect to our discoveries.

We have decided not to pursue patent protection with respect to some of our inventions outside the United States, both because we do not believe it is cost-effective and because of confidentiality concerns. Accordingly, our international competitors could develop, and receive foreign patent protection for, genes or gene sequences, uses of those genes or gene sequences, gene products and drug targets, assays for identifying potential therapeutic products, potential therapeutic products and methods of treatment for which we are seeking United States patent protection.

We may be subject to damages resulting from claims that we, our employees or independent contractors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and independent contractors were previously employed at universities, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and divert management s attention. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain drug candidates, which could severely harm our business.

Risks related to employees, advisors and facilities operations

The loss of key personnel or the inability to attract and retain additional personnel could impair our ability to expand our operations.

We are highly dependent upon the principal members of our management and scientific staff, the loss of whose services might adversely impact the achievement of our objectives. Recruiting and retaining qualified medical, clinical and scientific personnel will be critical to support activities related to advancing our nonclinical and clinical development programs, and to support our collaborative arrangements. Competition is intense for experienced medical and clinical personnel, in particular, and we may be unable to retain or recruit medical and clinical personnel with the expertise or experience necessary to allow us to pursue collaborations, develop our products or expand our operations to the extent otherwise possible. Further, all of our employees are employed at will and, therefore, may leave our employment at any time.

Our collaborations with outside scientists may be subject to restriction and change.

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our nonclinical and clinical development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their availability to us. Although these advisors and collaborators

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generally agree not to perform competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In such a circumstance, our development efforts with respect to the matters on which they were working may be significantly delayed or otherwise adversely affected. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

Security breaches may disrupt our operations and harm our operating results.

Our network security and data recovery measures may not be adequate to protect against computer viruses, break-ins, and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets could have a material adverse impact on our business, operating results and financial condition.

Risks related to environmental and product liability

We use hazardous chemicals and radioactive and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes have historically involved the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations have produced hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may face liability for any injury or contamination that results from our use or the use by third parties of these materials, and such liability may exceed our insurance coverage and our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials used by these parties. Further, we may be required to indemnify our collaborators against all damages and other liabilities arising out of our development activities or products produced in connection with these collaborations.

We may be sued for product liability.

We or our collaborators may be held liable if any product that we or our collaborators develop, or any product that is made with the use or incorporation of any of our technologies, causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Although we currently have and intend to maintain product liability insurance, this insurance may become prohibitively expensive or may not fully cover our potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of products developed by us or our collaborators. If we are sued for any injury caused by our or our collaborators products, our liability could exceed our total assets.

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Risks related to our common stock

Invus and its affiliates own a controlling interest in our outstanding common stock and may have interests which conflict with those of our other stockholders.

After this offering and the concurrent private placement, Invus and its affiliates will hold approximately 60.58% of the outstanding shares of our common stock (or 59.95% if the underwriters exercise in full their option to purchase additional shares of common stock) and are thereby able to control the election and removal of our directors and determine our corporate and management policies, including potential mergers or acquisitions, asset sales, the amendment of our articles of incorporation or bylaws and other significant corporate transactions. This concentration of ownership may delay or deter possible changes in control of our company, which may reduce the value of an investment in our common stock. The interests of Invus and its affiliates may not coincide with the interests of other holders of our common stock.

Conversion of the notes sold in the concurrent notes offering may dilute the ownership interest of our existing stockholders, including holders who had previously converted their notes, or may otherwise depress the price of our common stock.

The conversion of some or all of the notes sold in the concurrent notes offering will dilute the ownership interests of existing stockholders to the extent we deliver shares upon conversion of any of the notes. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants because the conversion of the notes could be used to satisfy short positions, or anticipated conversion of the notes into shares of our common stock could depress the price of our common stock.

Invus has additional rights under our stockholders agreement with Invus, L.P. which provides Invus with substantial influence over certain significant corporate matters.

Under our stockholders agreement with Invus, L.P., Invus has 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. Invus has designated three of the nine current members of our board of directors. While Invus has not presently exercised its director designation rights in full, it may exercise them at any time in the future in its sole discretion. To facilitate the exercise of such rights, we have agreed, upon written request from Invus, to take all necessary steps in accordance with our obligations under the stockholders agreement to (1) increase the number of directors to the number specified by Invus (which number shall be no greater than reasonably necessary for the exercise of Invus director designation rights under the stockholders agreement) and (2) cause the appointment to the newly created directorships of directors so designated by Invus pursuant to its rights under the stockholders agreement.

Invus also has the right to require proportionate representation of Invus-appointed directors on the audit, compensation and corporate governance committees of our board of directors, subject to certain restrictions. Invus-designated directors currently serve as one of the three members of each of the compensation committee and the corporate governance committee of our board of directors. No Invus-designated directors currently serve on the audit committee of our board of directors.

The provisions of the stockholders agreement relating to Invus rights to designate members of our board of directors and its audit, 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 also has the right to terminate these provisions at any time in its discretion.

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Invus has preemptive rights under the stockholders agreement to participate in future equity issuances by us, 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 overallotment (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. Artal s purchase of shares of our common stock in the concurrent private placement satisfies Invus preemptive rights with respect to the issuance of common stock pursuant to this prospectus supplement. Invus has waived its preemptive right with respect to the concurrent convertible notes offering and the issuance of common stock upon conversion of such notes.

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%.

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

The provisions of the stockholders agreement relating to those consent rights 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.

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile, and we believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following:

- adverse results or delays in clinical trials;
- announcement of FDA approval or non-approval, or delays in the FDA review process, of our or our collaborators product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators or our competitors clinical trials;
- the announcement of new products by us or our competitors;
- quarterly variations in our or our competitors results of operations;
- conflicts or litigation with our collaborators;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

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financing transactions;

developments in the biotechnology or pharmaceutical industry;

sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;

departures of key personnel or board members;

developments concerning current or future collaborations;

FDA or international regulatory actions;

third-party reimbursement policies;

acquisitions of other companies or technologies;

disposition of any of our subsidiaries, drug programs or other technologies; and

other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

These factors, as well as general economic, political and market conditions, may materially adversely affect the market price of our common stock.

In the past, following periods of volatility in the market price of a company s securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs and divert management s attention and resources, which could have a material and adverse effect on our business.

We may engage in future acquisitions, which may be expensive and time consuming and from which we may not realize anticipated benefits.

We may acquire additional businesses, technologies and products if we determine that these businesses, technologies and products complement our existing technology or otherwise serve our strategic goals. If we do undertake any transactions of this sort, the process of integrating an acquired business, technology or product may result in operating difficulties and expenditures and may not be achieved in a timely and non-disruptive manner, if at all, and may absorb significant management attention that would otherwise be available for ongoing development of our business. If we fail to integrate acquired businesses, technologies or products effectively or if key employees of an acquired business leave, the anticipated benefits of the acquisition would be jeopardized. Moreover, we may never realize the anticipated benefits of any acquisition, such as increased revenues and earnings or enhanced business synergies. Future acquisitions could result in potentially dilutive issuances of our equity securities, the incurrence of debt and contingent liabilities and amortization expenses related to intangible assets, which could materially impair our results of operations and financial condition.

Future sales of our common stock may depress our stock price.

If our stockholders sell substantial amounts of our common stock (including shares issued upon the exercise of options) in the public market, the market price of our common stock could fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. For example, following an acquisition, a significant number of shares of our common stock held by new stockholders may become freely tradable or holders of registration rights could cause us to register their shares for resale. Sales of

these shares of common stock held by existing stockholders could cause the market price of our common stock to decline.

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If we are unable to meet Nasdaq continued listing requirements, Nasdaq may take action to delist our common stock.

Our common stock trades on The Nasdaq Global Select Market, which has qualitative and quantitative listing criteria, including operating results, net assets, corporate governance, minimum trading price and minimums for public float, which is the amount of stock not held by our affiliates. If we are unable to meet Nasdaq continued listing requirements, Nasdaq may take action to delist our common stock. A delisting of our common stock could negatively impact us and our shareholders by reducing the liquidity and market price of our common stock and potentially reducing the number of investors willing to hold or acquire our common stock.

Risks related to this offering

We have broad discretion in the use of the net proceeds from this offering, the concurrent private placement and the concurrent notes offering and may not use them effectively.

As of the date of this prospectus supplement, we cannot specify with certainty the particular uses for the net proceeds we will receive from this offering, the concurrent notes offering or the concurrent private placement of shares of our common stock to Invus, if any. We will have broad discretion in the application of the net proceeds, including any of the purposes described in Use of proceeds. Any failure by us to apply these funds effectively could have a material adverse effect on our business.

Provisions contained in our charter documents and Delaware law may inhibit a takeover attempt, which could reduce or eliminate the likelihood of a change of control transaction and, therefore, the ability of our stockholders to sell their shares for a premium.

Provisions in our corporate charter and bylaws and applicable provisions of the Delaware General Corporation Law may make it more difficult for a third party to acquire control of us without the approval of our board of directors. These provisions include:

- a classified board of directors;
- limitations on the removal of directors;
- limitations on stockholder proposals at meetings of stockholders;
- the inability of stockholders to act by written consent or to call special meetings; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval.

These provisions may discourage transactions that otherwise could involve the payment of a premium over prevailing market prices of our common stock. Under certain circumstances, these provisions could reduce the market price of our common stock.

The availability of shares of our common stock for future sale could depress our stock price.

Upon completion of this offering and the concurrent private placement, we will have outstanding an aggregate of 713,839,502 shares of common stock (or 721,302,189 shares of common stock if the underwriters exercise in full their option to purchase additional shares of common stock), assuming no issuance of additional shares pursuant to the exercise of outstanding stock options or vesting of outstanding restricted stock units or the issuance of shares of common stock upon conversion of the notes to be offered and sold in the concurrent notes offering. Sales of a substantial number of shares of our common stock in the public markets following this

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offering, or the perception that such sales might occur, could have a material adverse effect on the price of our common stock or could impair our future ability to obtain capital through offerings of our equity securities.

Our executive officers, directors and Invus have agreed pursuant to lock-up agreements that, subject to certain exceptions, for a period of 90 days from the date of this prospectus supplement, they will not sell any shares of common stock without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co. See Underwriting.

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Special note regarding forward-looking statements

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus contain certain information regarding our financial projections, plans and strategies that are forward-looking statements. We have attempted to identify forward-looking statements by terminology including anticipate, believe, can, continue, could, estimate, expect, intend, may, plan, potential, predict, should or will or the negative of these terms or other comparable terminol 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, the expected timing of discussions with our regulators regarding such 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, our research and development efforts, the use of proceeds from this offering, the concurrent notes offering, the concurrent private placement, the successful completion of the concurrent notes offering, and anticipated trends in our business. Discussions containing forward-looking statements may be found in, among other places, the Prospectus Supplement Summary section of this prospectus supplement, as well as in the Business and Management s Discussion and Analysis of Financial Condition and Results of Operations sections of documents incorporated by reference herein.

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 that could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including those discussed under Risk factors beginning on page S-7 of this prospectus supplement and other sections of the documents incorporated by reference into this prospectus supplement and the accompanying 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 supplement.

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Use of proceeds

We estimate that the net proceeds from the sale of shares of common stock that we are offering will be approximately $46.8 million after deducting underwriting discounts and commissions and estimated offering expenses. If the underwriters exercise in full their option to purchase additional shares in this offering, we estimate the aggregate net proceeds to us will be approximately $53.9 million. In addition, we estimate that the net proceeds we will receive from (i) the concurrent notes offering will be approximately $77.0 million, after deducting initial purchaser discounts and estimated offering expenses payable by us and (ii) Artal s purchase of additional shares of common stock from us in a concurrent private placement will be $149.9 million after deducting estimated expenses payable by us. If the initial purchasers in the concurrent notes offering exercise their over-allotment option in full, we estimate that the net proceeds to us from the concurrent notes offering will be approximately $91.5 million, after deducting initial purchaser discounts and estimated offering expenses payable by us. This offering is not contingent upon the completion of the concurrent notes offering, and the concurrent notes offering is not contingent upon the completion of this offering. We cannot assure you that any of these offerings will be completed.

We currently intend to use the net proceeds from this offering, together with the net proceeds, if any, from the concurrent notes offering and a concurrent private placement and cash on hand, for the clinical development of our drug candidates and our other nonclinical research and development efforts. We may also use a portion of the net proceeds to acquire or invest in complementary products and technologies or for general corporate purposes. We have no current plans or commitments as to any such acquisition or investment.

The amounts that we actually expend for research and development, acquisitions, investments or general corporate purposes 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 this offering and the net proceeds from the concurrent notes offering.

Pending such uses, we intend to invest the net proceeds from this offering, Artal s purchase of shares of our common stock in a concurrent private placement and the net proceeds from the concurrent notes offering in interest-bearing, investment-grade securities.

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Price range of common stock

Our common stock is quoted on The Nasdaq Global Select Market under the symbol LXRX. The following table sets forth, for the periods indicated, the range of the high and low sales prices per share of our common stock as reported on The Nasdaq Global Select Market, and previously on the Nasdaq Global Market.

	High	Low
Year ended December 31, 2012		
First Quarter	$ 2.01	$ 1.13
Second Quarter	2.36	1.45
Third Quarter	3.28	2.05
Fourth Quarter	2.75	1.55
Year ended December 31, 2013		
First Quarter	2.48	1.91
Second Quarter	2.41	1.84
Third Quarter	2.70	2.16
Fourth Quarter	3.18	1.70
Year ended December 31, 2014		
First Quarter	2.06	1.62
Second Quarter	1.86	1.25
Third Quarter	1.78	1.28
Fourth Quarter (through November 20, 2014)	1.51	0.96

As of November 18, 2014, there were approximately 310 holders of record of our common stock. On November 20, 2014, the reported last sale price of our common stock on The Nasdaq Global Select Market was $1.005 per share.

Dividend policy

We have never paid cash dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the expansion and operation of our business and do not anticipate paying cash dividends in the foreseeable future.

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Capitalization

The following table presents our unaudited capitalization and other data as of September 30, 2014:

- on an actual basis;
- as adjusted to give effect to the issuance and sale of (1) 49,751,244 shares of our common stock at the public offering price of $1.005 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and (2) 149,253,731 shares of our common stock to Artal in the concurrent private placement at $1.005 per share, the price per share to the public in this offering, after deducting estimated offering expenses payable by us; and
- as further adjusted to give effect to the issuance and sale of $80.0 million in aggregate principal amount of notes in the concurrent notes offering and our receipt of net proceeds therefrom, after deducting the initial purchasers discount and estimated offering expenses payable by us.

You should read the following table in conjunction with the consolidated financial statements and the related notes incorporated by reference into this prospectus supplement and the accompanying prospectus.

	As of September 30, 2014		
(in thousands, except share data)	**Actual**	**As Adjusted(1)**	**As Further Adjusted(1)**
Cash, cash equivalents, restricted cash and investments	$ 57,869	$ 254,569	$ 331,569
Long-term debt, net of current portion(2)			
5.25% Convertible Senior Notes due 2021(3)	$	$	$ 80,000
Stockholders equity:			
Preferred stock, $0.01 par value; 5,000,000 shares authorized, no shares issued and outstanding :			
Common stock, $0.001 par value; 900,000,000 shares authorized; 516,115,876 shares issued and 514,834,527 outstanding, actual; 715,120,851 shares issued and 713,839,502 outstanding, as adjusted and as further adjusted	516	715	715
Additional paid-in capital	1,181,015	1,377,516	1,377,516
Accumulated deficit	(1,101,319)	(1,101,319)	(1,101,319)
Accumulated other comprehensive gain	2	2	2
Treasury stock, at cost, 1,281,349 shares	(2,390)	(2,390)	(2,390)
Total Lexicon Pharmaceuticals, Inc. stockholders equity	77,824	274,524	274,524
Total capitalization	$ 77,824	$ 274,524	$ 354,524

(1) As adjusted, assumes successful completion of concurrent private placement and as further adjusted, assumes successful completion of the concurrent notes offering. We cannot assure you that the concurrent notes offering or the concurrent private placement will be completed.

(2)

Does not reflect the Company s mortgage on its facilities in The Woodlands, Texas, which is classified as a current maturity of long term debt. The mortgage had a principal balance of $20.6 million as of September 30, 2014. On November 14, 2014, the Company entered into an agreement to sell the facilities subject to the mortgage for a purchase price of $24.5 million, subject to customary closing conditions. The mortgage would be repaid with a portion of such proceeds.

(3) The Company is currently evaluating the conversion features of the notes offered hereby to determine the proper accounting treatment for such features. The table above shows the aggregate principal amount of the notes without regard to any separate accounting for the conversion features. Determination of the final accounting treatment may result in a different presentation than what is provided in the table above.

The table above excludes:

24,313,195 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price per share of $2.16;

3,162,232 shares of common stock issuable pursuant to outstanding restricted stock units;

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13,843,239 shares of common stock available for future grant or issuance under our equity incentive plans; and

the shares of our common stock to be reserved for issuance upon conversion of the notes being offered by us in connection with the concurrent notes offering.

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Dilution

As of September 30, 2014, our net tangible book value was approximately $(20.3) million, or approximately $(0.04) per share. Net tangible book value per share represents the amount of our total tangible assets, excluding goodwill and other intangible assets, less total liabilities divided by the 514,834,527 shares of our common stock outstanding as of September 30, 2014. After giving effect to our sale of the shares of common stock in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses, and the sale of additional shares of our common stock in a concurrent private placement, the net tangible book value as of September 30, 2014 would have been approximately $176.4 million, or approximately $0.247 per share. This represents an immediate increase in net tangible book value of $0.286 per share to existing stockholders and an immediate dilution in net tangible book value of $0.758 per share to new investors purchasing shares of common stock at the public offering price.

The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 1.005
Net tangible book value per share as of September 30, 2014	$ (0.039)	
Increase in net tangible book value per share attributable to new investors	0.286	
Net tangible book value per share as of September 30, 2014 after giving effect to this offering	0.247	
Dilution in net tangible book value per share to new investors		$ 0.758

As of September 30, 2014, there were 24,313,195 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $2.16 per share and 3,162,232 shares of common stock issuable pursuant to outstanding restricted stock units. To the extent that any of these shares are issued upon exercise of stock options or vesting of restricted stock units, there may be further dilution to new public investors. In addition, the foregoing discussion and table do not take into account further dilution to new investors that could occur upon the issuance of notes in the concurrent notes offering.

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Concurrent convertible notes offering

Concurrently with this offering of common stock, we are offering $80.0 million aggregate principal amount of our 5.25% Convertible Senior Notes due 2021 (or a total of $95.0 million aggregate principal amount of the notes if the initial purchasers in that offering exercise their over-allotment option in full) in an offering exempt from registration under the Securities Act. Invus has waived their right to purchase from us any notes. Through this offering, the concurrent notes offering and the concurrent private placement, we intend to raise gross proceeds of approximately $280.0 million (up to $302.5 million if the underwriters in this offering exercise in full their option to purchase additional shares and the initial purchasers in the concurrent notes offering exercise in full their over-allotment option). This offering is not contingent upon the completion of the concurrent notes offering, and the concurrent notes offering is not contingent upon the completion of this offering. We cannot assure you that any of these offerings will be completed.

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Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Goldman, Sachs & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities LLC	24,626,866
Goldman, Sachs & Co.	20,149,254
Needham & Company, LLC	2,487,562
Stifel, Nicolaus & Company, Incorporated	2,487,562
Total	49,751,244

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.03618 per share. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters.

The underwriters have an option to buy up to 7,462,687 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $0.0603 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	No exercise	Full exercise
Per Share	$ 0.0603	$ 0.0603
Total	$ 3,000,000	$ 3,450,000

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $200,000.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage

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account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock, (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock (regardless of whether any of the transactions described in clauses (i) or (ii) above are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), or (iii) file any registration statement with the SEC relating to the offering of any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock, in each case without the prior written consent of each of J.P. Morgan Securities LLC and Goldman, Sachs & Co. for a period of 90 days after the later of the date of the final offering memorandum relating to the concurrent sale of our convertible notes or the date of this prospectus supplement. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

The restrictions described in the immediately preceding paragraph do not apply, subject to certain conditions, to the following:

- the sale of shares of common stock in this offering, the sale of the notes in the concurrent notes offering, or the sale of shares of common stock in the concurrent private placement;

- the issuance by us of any shares of common stock upon the exercise of an option or warrant, the conversion of a security outstanding on the date of this prospectus supplement or the conversion of the notes;

- the grant of options to purchase our common stock under our equity incentive plans;

- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that the plan does not provide for the transfer of common stock during the restricted period except as otherwise permitted, and no public announcement or filing under the Exchange Act regarding the establishment of such plan shall be required of or voluntarily made by us or on our behalf; and

- the issuance by us of shares of common stock to Holdings or its designee or designees in partial satisfaction of our contingent payment obligations under the Amended and Restated Purchase Option Agreement, dated July 30, 2010, between us, Holdings and Symphony Icon, Inc. triggered by our receipt of an upfront payment of $23 million under the License and Collaboration Agreement, dated October 21, 2014, between us and Ipsen, and the filing of a registration statement (or amendment thereto) with the Commission relating to the resale of such shares of common stock.

Our directors, executive officers and Invus have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions described below, for a period of 90 days after the later of the date of the final offering memorandum relating to the concurrent sale of our convertible notes or the date of this prospectus supplement, may not, without the prior written consent of each of J.P. Morgan Securities LLC and Goldman, Sachs & Co., (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any

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option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned (in accordance with the rules and regulations of the SEC), or any other securities so owned convertible into or exercisable or exchangeable for common stock or (2) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise. Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90- day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

The restrictions described in the immediately preceding paragraph do not apply, subject to certain conditions, to, among other things, the following:

transactions relating to shares of common stock or other securities acquired in open market transactions after the completion of this offering, provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of such shares of common stock or other securities;

(1) any surrender of shares of common stock (or options to purchase shares of common stock) to us in satisfaction of (i) any federal, state or local taxes required by law to be withheld with respect to the vesting of shares of common stock or the exercise of stock options to purchase common stock and/or (ii) the exercise price payable to us with respect to the exercise of stock options to purchase common stock; (2) transfers of shares of common stock or any security convertible into common stock as a bona fide gift; (3) distributions of shares of common stock or any security convertible into common stock to limited partners or stockholders of the transferor; (4) transfers to immediate family members of the transferor, to a trust established for the benefit of the transferor or an immediate family member, or to a corporation, partnership, limited partnership or limited liability company wholly owned by the transferor and members of his or her immediate family, in each case for estate planning purposes, purposes; provided that (i) in the case of any transfer or distribution pursuant to clause (2)-(4) each transferee agrees in writing to be bound by the restrictions set forth above and (ii) in the case of any surrender, transfer or distribution pursuant to clause (1)-(4), no filing under Section 16(a) of the Exchange Act, reporting a reduction in beneficial ownership of shares of common stock, is required or voluntarily made during the restricted period, subject to certain exceptions; and

the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that the plan does not provide for the transfer of common stock during the restricted period except as otherwise permitted, and no public announcement or filing under the Exchange Act regarding the establishment of such plan shall be required of or voluntarily made by or on behalf of the director, executive officer, Invus or us.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our common stock is listed on The Nasdaq Global Select Market under the symbol LXRX.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing

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transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering the underwriters may engage in passive market making transactions in our common stock on The Nasdaq Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

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This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling with Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). The securities are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), from and including the date on which the European Union Prospectus Directive (the EU Prospectus Directive) was implemented in that Relevant Member State (the Relevant Implementation Date) an offer of securities described in this prospectus may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus may be made to the public in that Relevant Member State at any time:

- to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or
- in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an offer of securities to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the EU Prospectus Directive in that Member State. The expression EU Prospectus Directive means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future. Certain of the underwriters, including the representatives, are acting as initial purchasers in our concurrent convertible notes offering for which they will receive customary discounts.

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Legal matters

Vinson & Elkins L.L.P., Houston, Texas, will pass upon the validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus for us. Ropes & Gray LLP has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2013, as set forth in their report, which is incorporated by reference in this prospectus supplement. 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 annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information that we file with the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information 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 corporate 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 supplement or the accompanying prospectus and does not constitute a part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement and the accompanying prospectus relate to our effective registration statement on Form S-3 (Registration No. 333-198493) we filed with the SEC. As permitted by SEC rules, this prospectus supplement and the accompanying prospectus do 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 should 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 or through its website.

The SEC allows us to incorporate by reference the information we have filed with it, which means that we can disclose important information by referring you to those documents. The information we incorporate by reference is an important part of this prospectus supplement and the accompanying 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:

- Our Annual Report on Form 10-K for the year ended December 31, 2013;
- Our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2014, June 30, 2014 and September 30, 2014;
- Our Current Reports on Form 8-K filed on January 13, 2014, April 24, 2014, July 8, 2014, October 24, 2014, November 14, 2014 and November 20, 2014; and

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The description of our common units contained in our Registration Statement on Form 8-A (File No. 000-30111) filed with the SEC on March 27, 2000 and any subsequent amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus supplement and the accompanying prospectus 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 supplement and prior to the termination of the offering. You may obtain any of the documents incorporated by reference in this prospectus supplement from the SEC through the SEC s website at the address provided above. We will provide you a copy of any or all of the information that has been incorporated by reference in this prospectus supplement (including exhibits to those documents specifically incorporated by reference in this document), at no cost, upon your written or oral request to us at the following address or telephone number:

Lexicon Pharmaceuticals, Inc.

Investor Relations

8800 Technology Forest Place

The Woodlands, Texas 77381

(281) 863-3000

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$150,000,000

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. 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 August 28, 2014 was $1.50 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 September 12, 2014.

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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 are 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 these securities.

In this prospectus, Lexicon, Lexicon Pharmaceuticals, we, us and our refer to Lexicon Pharmaceuticals, Inc. and 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 are registered trademarks of Lexicon Pharmaceuticals, Inc.

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LEXICON PHARMACEUTICALS, INC.

Lexicon Pharmaceuticals, Inc. is a biopharmaceutical company focused on the development of breakthrough treatments for human disease. We have advanced multiple drug candidates into clinical development. We are presently devoting most of our resources to the development of our two most advanced drug candidates:

- We are developing LX4211, an orally-delivered small molecule drug candidate, as a treatment for type 1 and type 2 diabetes. We have completed two Phase 2 clinical trials of LX4211 in type 2 diabetes patients and an additional clinical trial of LX4211 in type 2 diabetes patients with renal impairment. We have also completed a Phase 2 clinical trial of LX4211 in type 1 diabetes patients. We are presently preparing for the initiation of pivotal Phase 3 clinical trials of LX4211 in both type 1 and type 2 diabetes patients; and

- We are developing telotristat etiprate, or LX1032, an orally-delivered small molecule drug candidate, as a treatment for carcinoid syndrome. We have completed two Phase 2 clinical trials and are presently conducting a pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients.

Our most advanced drug candidates, as well as compounds from a number of additional drug discovery and development programs that we have advanced into various stages of clinical and preclinical development, originated from our own internal drug discovery efforts. These efforts were driven by a systematic, target biology-driven approach in which we used gene knockout technologies 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 identified and validated in living animals, or *in vivo*, more than 100 targets with promising profiles for drug discovery.

We are working both independently and through strategic collaborations and alliances with third parties to capitalize on our drug target discoveries, and we intend to pursue the same strategy for our drug candidates in clinical development. Consistent with this approach, we seek to retain exclusive rights to the benefits of certain drug discovery and development programs by developing and commercializing drug candidates from those programs internally and to collaborate with other pharmaceutical and biotechnology companies with respect to the development and commercialization of drug candidates from other programs, particularly when the collaboration may provide us with access to expertise and resources that we do not possess internally or are complementary to our own. We also seek to collaborate with other pharmaceutical and biotechnology companies, research institutes and academic institutions to capitalize on our drug target 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, as amended, or the 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. Information found on our website is not incorporated by reference into this prospectus and should not be considered part of this document.

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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 Securities and Exchange Commission, or SEC, that are incorporated by reference into this prospectus.

For more information about our SEC filings, please see Where You Can Find More Information and Documents Incorporated By Reference on page 26 of this prospectus. See also Special Note Regarding Forward-Looking Statements on page 22 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 June 30, 2014, there were 514,665,316 shares of our common stock issued and outstanding, 1,281,349 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 amended and restated certificate of incorporation, second amended and 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 amended and restated certificate of incorporation, second amended and restated bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our amended and restated certificate of incorporation and second amended and restated bylaws, see Where You Can Find More Information on page 25 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 amended and 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

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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.

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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

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. purchased 50,824,986 shares of our common stock in August 2007. Invus, L.P. and its affiliates have subsequently purchased additional shares of our common stock and currently own approximately 55.0% of our outstanding common stock.

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, L.P. and Invus C.V., which we collectively refer to as Invus, 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. Invus has designated three of the nine current members of our board of directors. While Invus has not presently exercised its director designation rights in full, it may exercise them at any time in the future in its sole discretion. To facilitate the exercise of such rights, we have agreed, upon written request from Invus, to take all necessary actions in accordance with our obligations under the stockholders agreement to (a) increase the number of directors to the number specified by Invus (which number shall be no greater than reasonably necessary for the exercise of Invus director designation rights under the stockholders agreement) and (b) cause the appointment to the newly created directorships of directors so designated by Invus pursuant to its rights under the stockholders agreement.

Invus also has the right to require proportionate representation of Invus-appointed directors on the audit, compensation and corporate governance committees of our board of directors, subject to certain restrictions. Invus-designated directors currently serve as one of the three members of each of the compensation committee and the corporate governance committee of our board of directors.

The provisions of the stockholders agreement relating to Invus rights to designate members of our board of directors and its audit, 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 also has the right to terminate these provisions at any time in its discretion.

Preemptive Rights. Invus has preemptive rights under the stockholders agreement to participate in future equity issuances by us, 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 overallotment (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%.

Consent Rights. Invus is entitled to certain consent rights under the stockholders agreement, including with respect to (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

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amendment to the certificate of incorporation or bylaws of any of our subsidiaries, in a manner adversely affecting Invus rights under the securities purchase agreement and the related agreements, (c) the repurchase, retirement, redemption or other acquisition of our or our subsidiaries capital stock (or securities convertible into or exercisable for shares of our or our subsidiaries capital stock), (d) any increase in the size of our board of directors to more than 12 members and (e) the adoption or proposed adoption of any stockholders rights plan, poison pill or other similar plan or agreement, unless Invus is exempt from the provisions of such plan or agreement.

The provisions of the stockholders agreement relating to consent rights 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 also entered into a registration rights agreement with Invus, L.P., pursuant to which Invus 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 amended and restated certificate of incorporation 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 amended and restated certificate of incorporation:

- 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 second amended and 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 amended and restated certificate of incorporation. 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 second amended and restated bylaws also limit who may call a special meeting of stockholders.

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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 Computershare Inc. 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 so 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;

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the place or places where principal of, and interest, if any, 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.

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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.

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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

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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.

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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

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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;

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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.

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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. 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;

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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.

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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.

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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 depositary on behalf of other financial institutions that participate in the depositary 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 depositary or its nominee. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary 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 depositary 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 depositary 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.

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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;

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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.

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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 of 1933, as amended, or the Securities Act, and 21E of the Exchange Act. We have attempted to identify forward-looking statements by terminology including anticipate, believe, can, continue, coul estimate, expect, intend, may, plan, potential, predict, should or will or the negative of these terms o 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, 2013 and in the six-month period ended June 30, 2014. 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:

	Six months ended June 30, 2014	Fiscal years ended December 31, 2013	2012	2011	2010	2009
Ratio of earnings to fixed charges (1)						

(1) For the six months ended June 30, 2014, and the fiscal years ended December 31, 2013, 2012, 2011, 2010 and 2009, our earnings were insufficient to cover fixed charges by $56.9 million, $104.1 million, $110.2 million, $116.2 million, $101.8 million and $82.9 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.

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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 reallowed 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 reallowed 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. 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-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.

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

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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, 2013, 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 annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information that we file with the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information 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 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 should 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 or through its website.

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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, 2013;
- our quarterly reports on Form 10-Q for the quarterly periods ended March 31 and June 30, 2014;
- our current reports on Form 8-K dated January 8, April 24 and July 7, 2014; 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 Exchange Act, 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

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49,751,244 Shares

Common Stock

Prospectus Supplement

J.P. Morgan

Goldman, Sachs & Co.

Needham & Company

Stifel

November 20, 2014

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement and accompanying prospectus or any free writing prospectus that we or the underwriters provide you in connection with the offering. We take no responsibility for, and cannot provide any assurance as to the reliability of, any other information that others may give you. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in or incorporated by reference in this prospectus supplement and accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement.

No action is being taken in any jurisdiction outside the United States to permit a public offering of shares of our common stock or possession or distribution of this prospectus supplement in that jurisdiction. Persons who come into possession of this prospectus supplement in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement applicable to that jurisdiction.