LEXICON PHARMACEUTICALS, INC./DE
Form 424B5
October 17, 2012
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-171953

The information in this prospectus supplement is not complete and may be changed. The registration statement filed with the Securities and Exchange Commission relating to these securities has been declared effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 17, 2012

Preliminary prospectus supplement (To Prospectus dated November 7, 2011)

$

Common stock

We are offering $ of 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 October 16, 2012 was $2.55 per share.

	Per share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to $ of additional shares of our common stock at the public offering price less the underwriting discounts and commissions solely to cover over-allotments, if any.

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 October , 2012.

J.P. Morgan **Jefferies**

October , 2012

Table of Contents

Table of contents

Table of Contents

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, LexVision® and OmniBank® are registered trademarks and Genome5000 is a trademark of Lexicon Pharmaceuticals, Inc. All other trademarks or service marks appearing in this prospectus supplement are the property of their respective holders.

Table of Contents

Prospectus Supplement Summary

This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. In addition, please read the Risk Factors section of this prospectus supplement beginning on page S-7 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2011 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2012 and June 30, 2012.

Lexicon Pharmaceuticals, Inc.

Our business

Lexicon Pharmaceuticals is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We have 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 have identified and validated in living animals, or *in vivo*, more than 100 targets with promising profiles for drug discovery. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential new drugs.

We have multiple drug programs in various stages of clinical development:

We are developing LX4211, an orally-delivered small molecule compound, as a treatment for type 1 and type 2 diabetes. We have completed two Phase 2 clinical trials and are preparing for the initiation of pivotal Phase 3 clinical trials of LX4211 in type 2 diabetes patients and an initial Phase 2 clinical trial of LX4211 in type 1 diabetes patients. We are currently in discussions with both FDA and EMA regarding design of the Phase 3 program of LX4211 for type 2 diabetes. While we have not finalized the design of any Phase 3 trials, we presently expect the type 2 diabetes program to include six or more clinical studies which, in the aggregate, would enroll at least several thousand patients. We intend to seek a collaboration partner for Phase 3 development of LX4211 in type 2 diabetes;

We are developing LX1032, or telotristat etiprate, an orally-delivered small molecule compound, as a treatment for carcinoid syndrome and ulcerative colitis. We have completed two Phase 2 clinical trials and have initiated a pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients and are presently conducting an initial Phase 2 clinical trial of telotristat etiprate in ulcerative colitis patients. The Phase 3 clinical trial of telotristat etiprate is a 12-week, placebo-controlled study of approximately 105 patients with refractory carcinoid syndrome on background somatostatin analog therapy, followed by a 36-week, open-label extension where all patients will receive telotristat etiprate. Two dose levels of telotristat etiprate, 250mg and 500mg three times daily (TID), will be 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 stool form, a global assessment of symptoms associated with carcinoid syndrome and other factors. The Phase 3 program of telotristat etiprate is also expected

Table of Contents

to include an additional companion study for patients who do not meet the inclusion criteria for the pivotal Phase 3 clinical trial. The companion study will provide additional safety data for telotristat etiprate;

We are developing LX1033, an orally-delivered small molecule compound, as a treatment for irritable bowel syndrome and are presently conducting an initial Phase 2 clinical trial; and

We have completed a Phase 2a clinical trial and a subsequent dose-ranging study of LX2931, an orally-delivered small molecule compound that is in development as a treatment for rheumatoid arthritis, and a Phase 1 clinical trial of LX7101, a topically-delivered small molecule compound that is in development as a treatment for glaucoma. We are currently evaluating the results of these studies and intend to seek collaboration partners for their further development.

We have also advanced small molecule compounds from a number of additional drug discovery programs into various stages of preclinical development and research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline.

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

Recent developments

LX4211

We reported top-line data in June 2012 from a Phase 2b clinical trial evaluating the safety and tolerability of LX4211 and its effects on glycemic parameters associated with type 2 diabetes. The Phase 2b trial enrolled 299 patients with type 2 diabetes who were not adequately controlled on metformin monotherapy in a double-blind, randomized, placebo-controlled study of 75mg once daily, 200mg once daily, 200mg twice daily and 400mg once daily doses of LX4211, each administered in combination with standard metformin therapy over a 12-week treatment period. The primary efficacy endpoint under evaluation in the trial was the change in hemoglobin A1c, or HbA1c, from baseline to week 12. Secondary endpoints included a variety of other metabolic parameters.

Table of Contents

Top-line data from the study showed that treatment with LX4211 demonstrated statistically significant benefits in the primary and multiple secondary endpoints. Patients in each of the 75mg once daily, 200mg once daily, 200mg twice daily and 400mg once daily LX4211 treatment arms had mean HbA1C reductions from baseline of 0.43, 0.52, 0.79 and 0.95 percent, respectively ($p<0.001$ for all treatment arms), while in patients randomized to placebo, HbA1C decreased by 0.09 percent. We also observed that patients treated with LX4211 showed significant reductions in body weight and blood pressure. LX4211 was well tolerated and adverse events were generally mild to moderate, with the overall incidence of adverse events with LX4211 being similar to placebo.

Telotristat etiprate (LX1032)

We reported top-line data in October 2012 from an open-label Phase 2 clinical trial evaluating the safety and tolerability of telotristat etiprate and its effects on symptoms associated with carcinoid syndrome. The Phase 2 trial enrolled 15 patients with metastatic carcinoid syndrome who were refractory to or could not tolerate somatostatin analog therapy in an open-label study of ascending doses of 150mg, 250mg, 350mg and 500mg of telotristat etiprate, administered three times daily, for 14 days on each dose until reaching the maximal dose, which was then continued until the completion of 12 weeks of therapy. The primary efficacy endpoint was the reduction of bowel movements from baseline to week 12. Secondary endpoints included relief of symptoms and reduction in serotonin synthesis.

Top-line data from the study showed that patients experienced a 46.4% median reduction from baseline at week 12, with the number of daily bowel movements steadily decreasing over time. All observed changes from baseline were statistically significant at $p<0.001$. This change corresponded with an increased proportion of patients reporting adequate relief of their carcinoid symptoms, a global assessment which also improved over time, with 75% of the patients with data at week 12 reporting improvement. Clinically relevant decreases from baseline were likewise seen for a number of key secondary endpoints, including statistically significant improvements in stool consistency ($p<0.001$) and trends of reductions in abdominal pain ($p=0.09$) and the number of cutaneous flushing episodes ($p=0.052$). The median percentage reductions from baseline of urinary 5-HIAA, a biomarker of serotonin synthesis, at weeks 8 and 12 were 68.3% ($p=0.019$) and 72.7% ($p=0.031$), respectively. Telotristat etiprate was well tolerated. There was no evidence of dose-limiting toxicity observed, and no patient discontinued from the study due to an adverse event. Only three patients reported a serious adverse event, none of which was related to telotristat etiprate.

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 our website should not be considered part of this prospectus.

Table of Contents

The offering

Common stock offered	shares
Common stock to be outstanding after this offering	shares
Use of proceeds	The net proceeds of this offering are estimated to be approximately $ million after deduction of underwriting discounts and commissions and estimated offering expenses. We currently intend to use the net proceeds for research and development, including the clinical development of our drug candidates and our other preclinical 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

Invus, L.P. and Invus C.V., which we collectively refer to as Invus, have the right, if they elect, to purchase from us at the price to the public in this offering, up to additional shares of our common stock, which is that number of shares that is sufficient to maintain their pro rata ownership of our common stock. This offering is not contingent on Invus election to exercise such rights, nor is this offering contingent upon Invus election not to exercise such rights. You should not elect to participate in this offering based on either Invus election to exercise or election not to exercise these rights. The election to exercise these rights is in Invus sole discretion and we can make no assurances as to whether this election will be exercised.

The number of shares of our common stock to be outstanding after this offering is based on 494,493,916 shares outstanding as of October 16, 2012, and excludes:

- 21,827,268 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price per share of $2.50;
- 4,053,775 shares of common stock issuable pursuant to outstanding restricted stock units; and
- 19,179,140 shares of common stock available for future grant or issuance under our equity incentive plans.

Unless we specifically state otherwise, all information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to additional shares of our common stock. To the extent that the underwriters exercise their over-allotment option and Invus exercises its preemptive rights with respect to this offering, Invus will have the right to purchase a number of additional shares of our common stock sufficient to permit Invus to maintain its percentage ownership of our outstanding common stock after giving effect to the underwriters exercise of their over-allotment option, which could be up to additional shares of our common stock if the underwriters exercise their over-allotment option in full.

Table of Contents

Summary financial data

The statement of operations data for each of the three years in the period ended December 31, 2011 has been derived from our financial statements that have been audited by Ernst & Young LLP, independent auditors. The statements of operations data for the six months ended June 30, 2012 and 2011, and the balance sheet data as of June 30, 2012, are unaudited, but include, in the opinion of management, all adjustments, consisting of only normal recurring adjustments, necessary for a fair presentation of such data. Our historical results for any prior or interim periods are not necessarily indicative of results to be expected for any future period.

The data presented below has been prepared in accordance with accounting principles generally accepted in the United States and should be read in conjunction with our financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

(in thousands, except per share data)	Year ended December 31, 2009	2010	2011	Six months ended June 30, 2011	2012
				(unaudited)	
Statements of Operations Data:					
Revenues	$ 10,700	$ 4,908	$ 1,849	$ 1,151	$ 499
Operating expenses:					
Research and development	81,238	78,520	91,828	44,066	42,392
Increase in fair value of Symphony Icon, Inc. purchase liability		2,710	6,766	2,862	4,243
General and administrative	19,418	19,396	17,350	9,285	8,727
Total operating expenses	100,656	100,626	115,944	56,213	55,362
Loss from operations	(89,956)	(95,718)	(114,095)	(55,062)	(54,863)
Interest and other income (expense), net	(3,463)	(6,083)	(2,120)	(1,205)	(936)
Consolidated net loss before taxes	(93,419)	(101,801)	(116,215)	(56,267)	(55,799)
Income tax benefit	102	26			
Consolidated net loss	(93,317)	(101,775)	(116,215)	(56,267)	(55,799)
Less: net loss attributable to noncontrolling interest in Symphony Icon, Inc.	10,537				
Net loss attributable to Lexicon Pharmaceuticals, Inc.	$ (82,780)	$ (101,775)	$ (116,215)	$ (56,267)	$ (55,799)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	$ (0.57)	$ (0.34)	$ (0.34)	$ (0.17)	$ (0.12)
Shares used in computing net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted share, basic and diluted	145,465	302,844	340,761	337,598	480,479

Table of Contents

(in thousands)	As of June 30, 2012 Actual	As Adjusted(2)
		(unaudited)
Balance Sheet Data:		
Cash, cash equivalents, restricted cash and short-term investments(1)	$ 231,513	$
Working capital(1)	216,722	
Total assets	381,060	
Long-term debt, net of current portion	22,678	
Accumulated deficit	(845,420)	
Lexicon Pharmaceuticals, Inc. stockholders equity	244,896	

(1) Includes restricted cash and investments of $430 as of June 30, 2012.

(2) Reflects the net proceeds from the sale of an aggregate of shares of common stock in this offering after deducting estimated underwriting discounts and commissions and estimated offering expenses. For additional information with respect to additional net proceeds we may receive as a result of the exercise of the underwriters over-allotment option, see Use of Proceeds on page S-27.

Table of Contents

Risk factors

An investment in our common stock involves risks. You should carefully consider the following risk factors, as well as the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2011 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2012 and June 30, 2012, 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. 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 by entering into financing agreements on unattractive terms.

As of June 30, 2012, we had $231.5 million in cash, cash equivalents and investments. We anticipate that the net proceeds of this offering, our existing capital resources and the cash and revenues we expect to derive from collaborations, technology licenses and other sources will enable us to fund our currently planned operations for at least the next 12 months. Our currently planned operations for that time period consist of the completion of our ongoing clinical trials, the initiation and conduct of additional clinical trials and the continuation of our small molecule drug discovery and preclinical research efforts. However, we caution you that we may generate less cash and revenues or incur expenses more rapidly than we currently anticipate.

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

- our ability to obtain additional funds from collaborations, technology licenses and other sources;
- our ability to identify partners to help advance certain of our product candidates, including LX4211, LX2931 and LX7101 on terms acceptable to us;
- the amount and timing of payments under any such agreements identified in the bullets above;
- the level and timing of our research and development expenditures;
- the timing and progress of the clinical development of our drug candidates LX4211, LX1032, LX1033, LX2931 and LX7101, including the timing of any required regulatory actions and the outcome of our anticipated discussions with our regulators;
- future results from clinical trials of our drug candidates;
- the cost and timing of regulatory approvals of drug candidates that we successfully develop;
- market acceptance of products that we successfully develop and commercially launch;

Table of Contents

- 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.

Our capital requirements will 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 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 $116.2 million for the year ended December 31, 2011, $101.8 million for the year ended December 31, 2010 and $82.8 million for the year ended December 31, 2009. We incurred net losses of $55.8 million for the six months ended June 30, 2012. As of June 30, 2012, we had an accumulated deficit of $845.4 million. 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 have derived substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses, and will continue to do so for at least the next several years. Future revenues from our existing collaborations and technology licenses 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 and license agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine 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. 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 research and development activities, including the conduct of clinical trials, continued drug discovery efforts and the

Table of Contents

advancement of additional potential therapeutics into clinical development. To the extent that we elect to commercialize products on our own, we will be required to incur substantial expenditures in preparation for and to conduct commercialization activities. 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.

Risks related to discovery and development of our drug candidates

We have not proven our ability to successfully develop and commercialize drug candidates based on our drug target discoveries.

Our business strategy of using our discovery of the functions of genes using knockout mice to select promising drug targets and developing and commercializing drug candidates based on our target discoveries is unproven. Our success will depend upon our ability, on our own or through collaborations, to successfully generate, select and develop drug candidates for targets we consider to have pharmaceutical value and to select an appropriate commercialization strategy for each potential therapeutic we choose to pursue.

We have not proven our ability to develop or commercialize drug candidates based on our drug target discoveries. The generation and selection of potential drug candidates for a target is a difficult, expensive and time-consuming process that is subject to substantial technical and scientific challenges and uncertainties, without any assurance of ever identifying a drug candidate warranting clinical testing. The process involves the optimization of a wide variety of variables, including among many other things potency against the target, selectivity for the intended target relative to other proteins, absorption, metabolism, distribution and excretion characteristics, activity in animal models of disease and the results of other preclinical research, and feasibility and cost of manufacture, each of which may affect one or more of the others in ways that conflict with the desired profile.

Table of Contents

Furthermore, we do not know that any pharmaceutical products based on our drug target discoveries can be successfully developed or commercialized. Our strategy is 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, the drug candidates we develop 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.

In addition, we may experience unforeseen technical complications in the processes we use to identify potential drug targets or discover and develop potential drug candidates. These complications could materially delay or limit the use of our resources, substantially increase the anticipated cost of conducting our drug target or drug candidate discovery efforts or prevent us from implementing our processes at appropriate quality and throughput levels.

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.

Clinical trials are inherently risky and the results from preclinical 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. Negative or inconclusive results from a preclinical study or a clinical trial could cause us, one of our collaborators or the FDA to terminate a preclinical study or clinical trial or require that we repeat it. 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 preclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. 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

Table of Contents

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.

Our drug candidates, 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 trial of telotristat etiprate and our interactions with 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 provide compelling evidence of clinically meaningful benefit in order to warrant consideration for marketing approval. If the FDA determines that our Phase 3 results do not have a clinically meaningful benefit, or if the FDA requires us to conduct additional Phase 3 clinical trials of telotristat etiprate prior to seeking approval, we will incur significant additional development costs and commercialization of telotristat etiprate may be prevented or delayed. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. For example, we will need to complete carcinogenicity studies on a pre-approval basis in connection with our diabetes program and on a post-approval basis with respect to our carcinoid syndrome program. 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

Table of Contents

development or approval periods of our drug candidates may cause delays in the approval or rejection of an application. 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 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.

Table of Contents

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 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 the price we might establish for products that we may develop, which would result in lower product revenues to us.

Table of Contents

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.

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,

Table of Contents

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 LX4211, which are in more advanced stages of development than LX4211. 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 preclinical 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. 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. In addition, we currently intend to seek a collaboration partner for Phase 3 development of LX4211 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

Table of Contents

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 preclinical 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.

We lack the capability to manufacture materials for preclinical 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 preclinical 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,

Table of Contents

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 practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative 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 technologies, 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. Moreover, we may be blocked from using or developing some of our existing or proposed technologies and products, or may be required to obtain a license that may not be available on reasonable terms, if at all. Further, others may discover uses for our technologies or products 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

Table of Contents

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 discovery and development and planned commercialization activities. We may not prevail in any such litigation or other dispute or be able to obtain required licenses.

Our discovery and 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 are the focus of our drug discovery programs 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 discovery or 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

Table of Contents

intellectual property indemnification undertakings that 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 use intellectual property that we license from third parties. If we do not comply with these licenses, we could lose our rights under them.

We rely, in part, on licenses to use certain technologies that are important to our business, and we do not own the patents that underlie these licenses. Most of these licenses, however, have terms that extend for the life of the licensed patents. Our rights to use these technologies and practice the inventions claimed in the licensed patents are subject to our abiding by the terms of those licenses and the licensors not terminating them. We believe we are currently in material compliance with all requirements of these licenses. In many cases, we do not control the filing, prosecution or maintenance of the patent rights to which we hold licenses and rely upon our licensors to prosecute infringement of those rights. The scope of our rights under our licenses may be subject to dispute by our licensors or third parties.

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.

Table of Contents

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 and the continuation of existing collaborations. Recruiting and retaining qualified clinical and scientific personnel will be critical to support activities related to advancing our clinical and preclinical development programs, and supporting our collaborative arrangements and our internal proprietary research and development efforts. Competition is intense for experienced clinical personnel, in particular, and we may be unable to retain or recruit 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 research and 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 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 maybe 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.

Because most of our operations are located at a single facility, the occurrence of a disaster could significantly disrupt our business.

Most of our operations are conducted at our facility in The Woodlands, Texas. While we have developed redundant and emergency backup systems to protect our resources and the facilities in which they are stored, they may be insufficient in the event of a severe fire, flood, hurricane, tornado, mechanical failure or similar disaster. If such a disaster significantly damages or destroys the facility in which our resources are maintained, our business could be disrupted until we could regenerate the affected resources. Our business interruption insurance may not be sufficient to compensate us in the event of a major interruption due to such a disaster.

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 involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations produce 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

Table of Contents

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.

Risks related to our common stock

Invus, L.P., Invus C.V. and their affiliates own a controlling interest in our outstanding common stock and may have interests which conflict with those of our other stockholders.

Invus, L.P. and Invus C.V., which we collectively refer to as Invus, and their affiliates currently own approximately 56.7% of the outstanding shares of our 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.

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 actions in accordance with our obligations under the stockholders agreement to (1) increase the number of directors to the number specified by

Table of Contents

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 four members of the compensation committee and one of the three members of 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.

Invus has preemptive rights under the stockholders agreement to participate in future equity issuances by us (including this offering), subject to certain exceptions, so as to maintain its then-current percentage ownership of our capital stock. Subject to certain limitations, Invus will be required to exercise its preemptive rights in advance with respect to certain marketed offerings, in which case it will be obligated to buy its pro rata share of the number of shares being offered in such marketed offering, including any 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%.

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.

Table of Contents

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;
- 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.

Table of Contents

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.

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 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. 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.

Table of Contents

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.

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

Upon completion of this offering, we will have outstanding an aggregate of 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. Sales of a substantial number of shares of our common stock in the public markets following this 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 Jefferies & Company, Inc. See Underwriters.

Table of Contents

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 and anticipated trends in our business. Discussions containing forward-looking statements may be found, among other places, in 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.

Table of Contents

Use of proceeds

We estimate that the net proceeds from the sale of shares of common stock that we are offering will be approximately $ million after deducting estimated underwriting discounts and commissions and estimated offering expenses. If the underwriters exercise their option to purchase additional shares in this offering, we estimate the aggregate net proceeds to us will be approximately $ million.

We currently intend to use the net proceeds from this offering for research and development, including the clinical development of our drug candidates and our other preclinical 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.

Pending such uses, we intend to invest the net proceeds from this offering in interest-bearing, investment-grade securities.

Table of Contents

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, 2010		
First Quarter	$ 2.87	$ 1.20
Second Quarter	1.69	1.19
Third Quarter	1.63	1.17
Fourth Quarter	1.91	1.22
Year ended December 31, 2011		
First Quarter	2.30	1.44
Second Quarter	1.87	1.33
Third Quarter	1.85	0.92
Fourth Quarter	1.31	0.81
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 (through October 16, 2012)	2.75	2.32

As of October 16, 2012, there were approximately 388 holders of record of our common stock. On October 16, 2012, the reported last sale price of our common stock on The Nasdaq Global Select Market was $2.55 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.

Table of Contents

Capitalization

The following table presents our unaudited capitalization and other data as of June 30, 2012 on an actual basis and as adjusted to give effect to the sale by us of shares of common stock to the public in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses. To the extent the underwriters exercise their over-allotment option, our net proceeds will be adjusted in proportion to such changes. See Use of Proceeds on page S-27. 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.

(in thousands, except share data)	As of June 30, 2012 Actual	As Adjusted
Cash, cash equivalents, restricted cash and investments	$ 231,513	$
Long-term debt, net of current portion	$ 22,678	$
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; 481,167,650 shares issued, actual; shares issued, as adjusted	481	
Additional paid-in capital	1,090,485	
Accumulated deficit	(845,420)	
Accumulated other comprehensive loss	(20)	
Treasury stock, at cost, 380,443 shares	(630)	
Total Lexicon Pharmaceuticals, Inc. stockholders equity	244,896	
Total capitalization	$ 267,574	$

The table above excludes 22,463,983 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $2.52 per share, 4,097,000 shares of common stock issuable pursuant to outstanding restricted stock units and 18,968,390 shares of common stock available for future grant or issuance under our stock incentive plans, in each case as of June 30, 2012.

The table above also does not reflect the issuance of 13,237,519 shares of our common stock on July 30, 2012 to certain designees of Symphony Icon Holdings LLC.

Table of Contents

Dilution

As of June 30, 2012, our net tangible book value was approximately $146.8 million, or approximately $0.31 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 480,787,207 shares of our common stock outstanding as of June 30, 2012. 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, the net tangible book value as of June 30, 2012 would have been approximately $ million, or approximately $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ 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:

Assumed public offering price per share		$
Net tangible book value per share as of June 30, 2012	$ 0.31	
Increase in net tangible book value per share attributable to new investors		
Net tangible book value per share as of June 30, 2012 after giving effect to this offering		
Dilution in net tangible book value per share to new investors		$

As of June 30, 2012, there were 22,463,983 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $2.52 per share and 4,097,000 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.

The table above also does not reflect the issuance of 13,237,519 shares of our common stock on July 30, 2012 to certain designees of Symphony Icon Holdings LLC.

Table of Contents

Underwriting

We are offering the shares of common stock described in this prospectus supplement through J.P. Morgan Securities LLC and Jefferies & Company, Inc., who are acting as joint bookrunners of the offering. 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 the underwriters have severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to their respective names in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Jefferies & Company, Inc.	
Total	

The underwriters are committed to purchase all the shares of common stock 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 shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $ per share. After the 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 an additional shares of our 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 supplement to exercise this over-allotment option. If any shares are purchased with this over-allotment option, 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 $ 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.

	Without over-allotment exercise	With full over-allotment exercise
Per Share	$	$
Total	$	$

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

Table of Contents

A prospectus supplement in electronic format may be made available on the website maintained by the underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters to 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 Jefferies & Company, Inc. for a period of 90 days after 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 pursuant to the underwriting agreement;
- the issuance by us of any shares of common stock upon the exercise of an option or warrant, vesting of a restricted stock unit (phantom stock) or the conversion of a security outstanding on the date of this prospectus supplement;
- the grant of options to purchase our common stock or restricted stock units (phantom stock) pursuant to which shares of our common stock are issuance, in each case under our equity incentive plans; 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 us or on our behalf.

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 date of this prospectus supplement, may not, without the prior written consent of each of J.P. Morgan Securities LLC and Jefferies & Company, Inc., (1) 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 beneficially owned, or any other securities so owned convertible into or

Table of Contents

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 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 or restricted stock units (phantom stock) pursuant to which shares of common stock are issuable) 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 restricted stock units (phantom 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, provided that in the case of any transfer or distribution pursuant to clause (2) (4), (i) each transferee agrees in writing to be bound by the restrictions set forth above and pursuant to clause (1) (4), (ii) 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, except to reflect the surrender of shares of Common Stock to us pursuant to clause (1) above to cover withholding tax obligations upon the vesting of, in the aggregate, approximately 200,000 restricted stock units issued to certain of our executive officers; 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.

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

Table of Contents

the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing 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 over-allotment option 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 over-allotment option, 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 over-allotment option. 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, 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 representative of the underwriters purchases common stock in the open market in stabilizing transactions or to cover short sales, the representative 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 supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement 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

Table of Contents

jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

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 supplement 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 it may, with effect from and including the Relevant Implementation Date, make an offer of shares 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 supplement 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 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, 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.

Table of Contents

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, 2011, 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. 333-171953) 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, 2011;

Our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2012 and June 30, 2012;

Table of Contents

Our Current Reports on Form 8-K filed on February 24, 2012, April 27, 2012, and July 30, 2012; and

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, 2012 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

Table of Contents

$200,000,000

Lexicon Pharmaceuticals, Inc.

Common Stock

Preferred Stock

Debt Securities

Warrants

Rights

Units

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

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

Our common stock is listed on The Nasdaq Global Select Market under the symbol LXRX . The prospectus supplement will contain information, where applicable, regarding any other listing on The Nasdaq Global Select Market or any securities exchange of the securities covered by the prospectus supplement. The last reported sale price of our common stock on November 2, 2011 was $1.09 per share.

Investing in our securities involves risks. See Risk Factors on page 4.

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

The date of this prospectus is November 7, 2011.

Table of Contents

TABLE OF CONTENTS

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

Table of Contents

LEXICON PHARMACEUTICALS, INC.

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

We have four drug programs for which we have completed Phase 2 clinical trials:

- We have completed a Phase 2a clinical trial and are presently conducting a Phase 2b clinical trial of LX4211, an orally-delivered small molecule compound that we are developing as a treatment for type 2 diabetes;

- We have completed a Phase 2a clinical trial of LX1031, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome and other gastrointestinal disorders, and Phase 1 clinical trials of LX1033, a more potent back-up molecule that we plan to advance into Phase 2 clinical trials;

- We have completed a Phase 2a clinical trial and are presently conducting an additional Phase 2 clinical trial of LX1032, an orally-delivered small molecule compound that we are developing as a treatment for the symptoms associated with carcinoid syndrome; and

- We have completed a Phase 2a clinical trial and have initiated a dose-ranging study to explore higher doses of LX2931, an orally-delivered small molecule compound that we are developing as a treatment for rheumatoid arthritis and other autoimmune diseases.

We have also advanced small molecule compounds from a number of additional drug programs into various stages of preclinical development and research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline.

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

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

Our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, or Exchange Act, are made available free of charge on our corporate website located at www.lexpharma.com as soon as reasonably practicable after the filing of those reports with the Securities and Exchange Commission, or SEC. Information found on our website is not incorporated by reference into this prospectus and should not be considered part of this document.

Table of Contents

RISK FACTORS

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

For a discussion of these risks, please see:

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

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

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 900 million shares of common stock, $0.001 par value, and five million shares of preferred stock, $0.01 par value. As of September 30, 2011, there were 337,895,522 shares of our common stock issued and outstanding, 217,658 shares of our common stock issued and held in treasury and no shares of preferred stock outstanding.

The following summary description of our capital stock is based on the provisions of our restated certificate of incorporation, as amended, restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our restated certificate of incorporation, as amended, restated bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our restated certificate of incorporation, as amended, and restated bylaws, see Where You Can Find More Information on page 24 of this prospectus.

Common Stock

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

Preferred Stock

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

Table of Contents

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

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

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

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

The Delaware General Corporation Law provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

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

Table of Contents

Arrangements with Invus, L.P. and Its Affiliates

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment of approximately $205.5 million to purchase 50,824,986 shares of our common stock in August 2007. Under the securities purchase agreement, as amended and supplemented (the securities purchase agreement), and after accounting for the $181.5 million in net proceeds from our public offering and concurrent private placement of common stock in March 2010, Invus, L.P. and its affiliate Invus C.V., which we collectively refer to as Invus, have the right to require us to initiate a pro rata rights offering to our stockholders providing all stockholders with non-transferable rights to acquire shares of our common stock in an aggregate amount of up to approximately $163.0 million. Invus may exercise its right to require us to conduct such a rights offering by giving us notice within a period of one year beginning on February 28, 2011, which will be extended by the number of days during such period that Invus is not permitted under the securities purchase agreement to initiate the rights offering as a result of any blackout period in connection with certain public offerings of our common stock. If Invus elects to exercise its right to require us to initiate a rights offering, Invus would be required to purchase its pro rata portion of the offering, subject to certain customary closing conditions, including (1) the expiration or termination of any applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, (2) the accuracy (subject to materiality and material adverse effect qualifications) of our representations and warranties and our compliance in all material respects with the covenants to be performed by us in the securities purchase agreement and related ancillary agreements as of the closing of the rights offering and (3) the delivery of an officer s certificate certifying as to the satisfaction of the closing conditions set forth in clause (2) above, an opinion of counsel reasonably satisfactory to Invus (as specified in the securities purchase agreement) and certain certificates of good standing.

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

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

In the event that the number of shares of our common stock owned by Invus and its affiliates ever exceeds 50% of the total number of shares of our common stock then outstanding (not counting for such purpose any shares acquired by Invus from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders agreement), from and after that time, Invus will have the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, rounded up to the nearest whole number of directors. The directors appointed by Invus have proportionate representation on the compensation committee and corporate governance committee of our board of directors.

Table of Contents

Invus rights with respect to the designation of members of our board of directors and its compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus will also have the right to terminate these provisions at any time following the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders agreement).

Preemptive Rights. Invus has preemptive rights under the stockholders agreement to participate in future equity issuances by us (including any qualified offering), subject to certain exceptions, so as to maintain its then-current percentage ownership of our capital stock. Subject to certain limitations, Invus will be required to exercise its preemptive rights in advance with respect to certain marketed offerings, in which case it will be obligated to buy its pro rata share of the number of shares being offered in such marketed offering, including any 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%.

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

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

solicit proxies to vote any of our voting securities or any voting securities of our subsidiaries;

submit to our board of directors a written proposal for any merger, recapitalization, reorganization, business combination or other extraordinary transaction involving an acquisition of us or any of our subsidiaries or any of our or our subsidiaries securities or assets by Invus and its affiliates;

enter into discussions, negotiations, arrangements or understandings with any third party with respect to any of the foregoing; or

request us or any of our representatives, directly or indirectly, to amend or waive any of these standstill provisions.

The standstill provisions of the stockholders agreement will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all of the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders agreement), (d) the date on which any third party makes a public proposal to acquire (by

Table of Contents

purchase, exchange, merger or otherwise) assets or business constituting 50% or more of our revenues, net income or assets or 50% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction or (e) the date on which any third party acquires beneficial ownership (by purchase, exchange, merger or otherwise) of assets or business constituting 20% or more of our revenues, net income or assets or 20% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction.

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

The provisions of the stockholders agreement relating to sales to third parties will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, and (c) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders agreement).

Voting of Shares. In any election of persons to serve on our board of directors, Invus will be obligated to vote all of the shares of common stock held by it and its affiliates in favor of the directors nominated by our board of directors, as long as we have complied with our obligation with respect to the designation of members of our board of directors described above and the individuals designated by Invus for election to our board of directors have been nominated, and, if applicable, are serving on our board of directors. With respect to all other matters submitted to a vote of the holders of our common stock, Invus will be obligated to vote any shares that it acquired from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders agreement, in the same proportion as all the votes cast by other holders of our common stock, unless Invus and we (acting with the approval of the unaffiliated board) agree otherwise. Invus may vote all other shares of our common stock held by it in its sole discretion.

The provisions of the stockholders agreement relating to voting will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock held by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties after June 17, 2007 in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the provisions of the stockholders agreement), and (d) the termination of the standstill provisions in accordance with the stockholders agreement.

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

Table of Contents

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

Registration Rights. Concurrently with the execution of the securities purchase agreement, we entered into a registration rights agreement with Invus, L.P., pursuant to which Invus, L.P. and its affiliates have certain demand and piggyback registration rights with respect to shares of our common stock held by them. Invus, L.P. and its affiliates which hold our common stock have waived these registration rights with respect to any offerings of our securities pursuant to this prospectus.

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

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

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

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

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

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

Transfer Agent and Registrar

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

Table of Contents

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus and the related indenture. While the terms summarized below will apply generally to any debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any debt securities offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

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

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

General

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

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

- the title of the debt securities;
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which we will pay the principal on the debt securities;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and premium and interest on, the debt securities will be payable;
- the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities;

Table of Contents

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities;

the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;

if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, or premium or interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any conversion provisions, including the conversion price, the conversion period, provisions as to whether conversion will be mandatory, at the option of the holder or at our option, the events requiring an adjustment of the conversion price and provisions affecting conversion if such series of debt securities are redeemed;

whether the debt securities will be senior debt securities or subordinated debt securities and, if applicable, a description of the subordination terms thereof;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities; and

any other terms of the debt securities, which may modify, delete, supplement or add to any provision of the indenture as it applies to that series.

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

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

Table of Contents

Transfer and Exchange

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

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

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

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Covenants

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

Consolidation, Merger and Sale of Assets

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

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

Events of Default

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

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of that default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

Table of Contents

default in the payment of principal of or premium on any debt security of that series when due and payable;

default in the deposit of any sinking fund payment, when and as due in respect of any debt security of that series;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 90 days after we receive written notice from the trustee or we and the trustee receive written notice from the holders of not less than a majority in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain events of bankruptcy, insolvency or reorganization of our company; and

any other event of default provided with respect to debt securities of that series that is described in the applicable prospectus supplement accompanying this prospectus.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under our bank credit agreements in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of, and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an event of default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

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

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

that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and

Table of Contents

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

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

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

Modification and Waiver

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

reduce the amount of debt securities whose holders must consent to an amendment or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of, or premium or interest on, any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security.

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

14

Table of Contents

security of the series affected; *provided, however*, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

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

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

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

- we may omit to comply with the covenant described under the heading Consolidation, Merger and Sale of Assets and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

- any omission to comply with those covenants will not constitute a default or an event of default with respect to the debt securities of that series, or covenant defeasance.

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, foreign government obligations, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

Table of Contents

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

Foreign Government Obligations means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars:

direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged which are not callable or redeemable at the option of the issuer thereof; or

obligations of a person controlled or supervised by or acting as an agency or instrumentality of that government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government which are not callable or redeemable at the option of the issuer thereof.

Governing Law

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

DESCRIPTION OF WARRANTS

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

General

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

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

Table of Contents

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any; or

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

Exercise of Warrants

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

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

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

as all or part of the exercise price for warrants.

Governing Law

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

Table of Contents

Enforceability of Rights by Holders of Warrants

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

DESCRIPTION OF RIGHTS

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

General

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

Each series of rights will be issued under a separate rights agreement or other arrangements that 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 any rights agreement and the rights certificates relating to each series of rights with the SEC, and incorporate them by reference as an exhibit to the registration statement of which this prospectus is a part on or before the time we issue a series of rights.

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

- the date of determining the stockholders entitled to the rights distribution;
- the number of rights issued or to be issued to each stockholder;
- the exercise price payable for each share of common stock, preferred stock, debt securities or other securities upon the exercise of the rights;
- the number and terms of the shares of common stock, preferred stock, debt securities or other securities which may be purchased per each right;

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

Special Considerations for Indirect Holders

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

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

Global Securities

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

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under Special Situations When a Global Security Will Be Terminated. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

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

Special Considerations for Global Securities

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

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

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

An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

Table of Contents

An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

The depositary s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor s interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary s actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way;

The depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

Financial institutions that participate in the depositary s book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

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

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

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this prospectus contain certain information regarding our financial projections, plans and strategies that are forward-looking statements within the meaning of Section 27A of the Securities Act and 21E of the Exchange Act. We have attempted to identify forward-looking statements by terminology including anticipate, believe, can, continue, could, estimate, intend, may, plan, potential, predict, should or will or the negative of these terms or other comparable terminology. These statements, only predictions and involve known and unknown risks, uncertainties and other important factors may include, among other things, statements which

23

Table of Contents

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, 2010 and in the nine-month period ended September 30, 2011. 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:

		Fiscal years ended December 31,				
	Nine months ended September 30, 2011	2010	2009	2008	2007	2006
Ratio of earnings to fixed charges (1)						

(1) For the nine months ended September 30, 2011, and the fiscal years ended December 31, 2010, 2009, 2008, 2007 and 2006, our earnings were insufficient to cover fixed charges by $82.4 million, $101.8 million, $82.9 million, $76.9 million, $58.8 million and $54.4 million, respectively.

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

USE OF PROCEEDS

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

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

Table of Contents

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.

Table of Contents

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

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

We may offer securities through agents in connection with a distribution to our stockholders of rights to purchase such securities (including, without limitation, rights offered in a rights offering conducted pursuant to Invus right to require us to initiate a rights offering). The terms of any such sales will be described in the prospectus supplement relating thereto. Pursuant to any standby underwriting agreement entered into in connection with a rights offering to our stockholders, persons acting as standby underwriters may receive a commitment fee for all securities underlying the rights that the underwriter commits to purchase on a standby basis. Additionally, prior to the expiration date with respect to any rights, any standby underwriters in a rights offering to our stockholders may offer such securities on a when-issued basis, including securities to be acquired through the purchase and exercise of rights, at prices set from time to time by the standby underwriters. After the expiration date with respect to such rights, the underwriters may offer securities of the type underlying the rights, whether acquired pursuant to a standby underwriting agreement, the exercise of the rights or the purchase of such securities in the market, to the public at a price or prices to be determined by the underwriters. The standby underwriters may thus realize profits or losses independent of the underwriting discounts or commissions paid by us. If we do not enter into a standby underwriting agreement in connection with a rights offering to our stockholders, we may elect to retain a dealer-manager to manage such a rights offering for us. We also may enter into a standby arrangement with other purchasers pursuant to which such purchasers may be required to purchase any securities remaining unsubscribed for after such offering. Any such dealer-manager may offer securities of the type underlying the rights acquired or to be acquired pursuant to the purchase and exercise of rights and may thus realize profits or losses independent of any dealer-manager fee paid by us.

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

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

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

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

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

Table of Contents

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 included in our Annual Report on Form 10-K for the year ended December 31, 2010, 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.