LEXICON PHARMACEUTICALS, INC./DE
Form S-3
July 27, 2007

Table of Contents

AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON JULY 27, 2007
Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933
Lexicon Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**76-0474169**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

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

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

Copies to:

David P. Oelman	**Jeffrey L. Wade**
Vinson & Elkins L.L.P.	**Executive Vice President and General Counsel**
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(713) 758-3708	**(281) 863-3000**

Approximate date of commencement of proposed sale to the public:
From time to time after this registration statement becomes effective,
subject to market conditions and other factors.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, check the following box. o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. þ

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective

registration statement for the same offering. o

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Aggregate Offering Price Per Share (1)	Proposed Maximum Aggregate Offering Price (1)	Amount of Registration Fee
Common Stock, par value $0.001	7,650,622 shares	$3.335	$25,514,825	$784

(1) Estimated solely for the purpose of calculating the amount of the registration fee based on the high and low trading price for the common stock as reported on the Nasdaq Global Market on July 25, 2007, in accordance with Rule 457(c) under the Securities Act.

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

Table of Contents

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

SUBJECT TO COMPLETION, DATED JULY 27, 2007
7,650,622 Shares
Lexicon Pharmaceuticals, Inc.
Common Stock

This prospectus relates to the offer and sale of previously issued shares of our common stock by selling stockholders. The selling stockholders are offering up to 7,650,622 shares of our common stock. See Selling Stockholders beginning on page 14.

We will not receive any proceeds from the sale of the shares offered by the selling stockholders.

The selling stockholders may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices.

Our common stock is listed on The Nasdaq Global Market under the symbol LXRX . The last reported sale price on July 25, 2007 was $3.41 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page 4.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is July ___, 2007.

TABLE OF CONTENTS

	Page
Lexicon Pharmaceuticals, Inc.	3
Risk Factors	4
Special Note Regarding Forward-Looking Statements	14
Use of Proceeds	14
Selling Stockholders	14
Plan of Distribution	15
Legal Matters	17
Experts	17
Where You Can Find More Information	17
Documents Incorporated by Reference	18
Registration Rights Agreement	
Opinion of Vinson & Elkins L.L.P.	
Consent of Ernst & Young LLP	

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

In this prospectus, Lexicon, Lexicon Pharmaceuticals, we, us and our refer to Lexicon Pharmaceuticals, Inc. and its subsidiaries.

LexVision® and OmniBank® are registered trademarks and the Lexicon name and logo and Genome5000 are trademarks of Lexicon Pharmaceuticals, Inc.

Table of Contents

LEXICON PHARMACEUTICALS, INC.

Lexicon Pharmaceuticals is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We use our proprietary gene knockout technology to knock out, or disrupt, the function of genes in mice and then employ an integrated platform of advanced medical technologies to systematically discover the physiological and behavioral functions and pharmaceutical utility of the genes we have knocked out and the potential drug targets encoded by the corresponding human genes. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential small molecule, antibody and protein drugs. We have advanced drug candidates from two of these programs into human clinical trials, with drug candidates from two additional programs in preclinical development and a number of additional programs in various stages of preclinical research. We believe that our systematic, target biology-driven approach to drug discovery will enable us to substantially expand our clinical pipeline, and we have initiated our $10_{TO}10$ program with the goal of advancing ten drug candidates into human clinical trials by the end of 2010.

We have recently concluded a Phase 1b clinical trial of our most advanced drug candidate, LX6171, an orally-delivered small molecule compound that we are developing as a potential treatment for disorders characterized by cognitive impairment. We are conducting a Phase 1b clinical trial for another drug candidate, LX1031, an orally-delivered small molecule compound that we are developing as a potential treatment for irritable bowel syndrome. We have advanced drug candidates from two other drug discovery programs, LX2931, which we plan to develop as a potential treatment for rheumatoid arthritis and other autoimmune conditions, and LX1032, which we plan to develop as a potential treatment for conditions that may include gastrointestinal disorders and carcinoid syndrome, into preclinical development in preparation for regulatory filings for the commencement of clinical trials. We have compounds from a number of additional drug programs in various stages of preclinical research. Through the end of 2006, we had identified and validated in living mammals, or *in vivo,* more than 100 targets with promising profiles for drug discovery in the therapeutic areas of diabetes and obesity, cardiovascular disease, psychiatric and neurological disorders, cancer, immune system disorders and ophthalmic disease.

LX6171, LX1031 and LX1032 are each subject to a clinical development financing arrangement under which we have licensed our intellectual property rights to those programs to Symphony Icon, Inc. and have received an exclusive option to purchase all of the equity of Symphony Icon, thereby allowing us to reacquire the programs.

We are working both independently and through strategic collaborations and alliances to capitalize on our technology and drug target discoveries and to develop and commercialize drug candidates emerging from our drug discovery and development programs. We are working with Bristol-Myers Squibb Company to discover and develop new small molecule drugs in the neuroscience field. We are working with Genentech, Inc. to discover the functions of secreted proteins and potential antibody targets identified through Genentech s internal drug discovery research, and to develop new biotherapeutic drugs based on certain targets selected from the alliance. We are working with N.V. Organon to discover, develop and commercialize new biotherapeutic drugs based on another group of secreted proteins and potential antibody targets. We are working with Takeda Pharmaceutical Company Limited for the discovery of new drugs for the treatment of high blood pressure. In addition, we have established collaborations and license agreements with other leading pharmaceutical and biotechnology companies, research institutes and academic institutions under which we receive 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 for use in the other organization s own drug discovery efforts.

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 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

RISK FACTORS

An investment in our common stock involves risks. You should carefully consider the following risk factors, together with all of the other information included in, or incorporated by reference into, this prospectus in evaluating an investment in our common stock. We believe that each of the following risk factors describe material risks to an investment in our common stock. If any of the following risks were to occur, our business, financial condition or results of operations would likely suffer, possibly materially. 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 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 March 31, 2007, we had cash, cash equivalents and short-term investments (net of restricted cash and investments) of $59.1 million. In June 2007, we entered into a series of agreements with Invus, L.P. under which, subject to the approval of our stockholders and customary closing conditions, Invus has agreed to purchase shares of our common stock for a total of approximately $205 million.

We anticipate that our existing capital resources, the cash we expect to receive from the investment in our common stock by Invus, and the cash and revenues we expect to derive from drug discovery and development alliances, collaborations for the discovery and, in some cases, analysis of the physiological effects of genes altered in knockout mice, government grants and contracts and technology licenses will enable us to fund our currently planned operations for at least the next twelve months. Our currently planned operations for that time period consist of the continuation of our efforts to discover the physiological functions of 5,000 human genes that we consider to be pharmaceutically important, the expansion of our medicinal chemistry, biotherapeutics and preclinical research operations and the initiation and conduct of additional clinical trials. However, we caution you that the investment in our common stock by Invus may not close as anticipated, whether as a result of the failure to obtain stockholder approval or otherwise, and we may otherwise 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 alliances, collaborations, government grants and contracts and technology licenses;
- the amount and timing of payments under such agreements;
- the level and timing of our research and development expenditures;
- future results from clinical trials that we initiate;
- the cost and timing of regulatory approvals of products that we successfully develop; and
- market acceptance of products that we successfully develop and commercially launch.

Our capital requirements will increase substantially to the extent we advance additional therapeutics into 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 the investment in our common stock by Invus does not close as anticipated, whether as a result of the failure to obtain stockholder approval or otherwise, or if our capital resources are otherwise insufficient to meet future capital requirements, we will have 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

Table of Contents

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; if so, we will be forced to significantly curtail or cease 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 $54.3 million for the year ended December 31, 2006, $36.3 million for the year ended December 31, 2005 and $47.2 million for the year ended December 31, 2004. We incurred net losses of $18.9 million for the quarter ended March 31, 2007. As of March 31, 2007, we had an accumulated deficit of $370.7 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 growth, if any, in our revenues and on the level of our expenses.

We derive substantially all of our revenues from drug discovery alliances, collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, government grants and contracts and technology licenses, and will continue to do so for the foreseeable future. Our future revenues from alliances, collaborations and government grants and contracts are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration. Our future revenues from technology licenses are uncertain because they depend, in part, on securing new agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators, granting agencies 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 early-stage nature 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, equipment and personnel. In addition, we expect to spend significant amounts to enhance our core technologies and fund our research and development activities, including the conduct of clinical trials and the advancement of additional potential therapeutics into clinical development. As a result, we expect that our operating expenses will continue to increase significantly as additional drug programs progress into human clinical trials and, consequently, we will need to generate significant 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 alliances, government grants and contracts, and technology licenses, and the timing of such arrangements;
- the expiration or other termination of collaborations and alliances, which may not be renewed or replaced;
- the success rate of our discovery efforts leading to opportunities for new collaborations, alliances 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

Table of Contents

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 Our Business

We are an early-stage company, and we may not successfully develop or commercialize any therapeutics that we have identified.

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

Biotechnology and pharmaceutical companies have successfully developed and commercialized only a limited number of genomics-derived pharmaceutical products to date. We have not proven our ability to develop or commercialize therapeutics or drug targets that we identify. We do not know that any pharmaceutical products based on our drug target discoveries can be successfully commercialized. In addition, we may experience unforeseen technical complications in the processes we use to discover and develop potential therapeutics. These complications could materially delay or limit the use of our resources, substantially increase the anticipated cost of generating them 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 United States Food and Drug Administration, or 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 dealing 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 test subjects. In addition, we must manufacture, or contract for the manufacture of, the product candidates that we use in our clinical trials under the FDA s current Good Manufacturing Practices.

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

Table of Contents

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.

We are dependent upon our collaborations with major pharmaceutical companies. If we are unable to achieve milestones under those collaborations or if our collaborators efforts fail to yield pharmaceutical products on a timely basis, our business will suffer.

We have derived a substantial majority of our revenues to date from collaborative drug discovery alliances with a limited number of major pharmaceutical companies. Revenues from our drug discovery alliances depend upon continuation of the collaborations, 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 we are unable to achieve milestones 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 alliances. In addition, some of our alliances are exclusive and preclude us from entering into additional collaborative arrangements with other parties in the field of exclusivity.

We have limited or no control over the resources that any collaborator may devote to the development and commercialization of products under our alliances. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us or otherwise fail to conduct product 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.

If we are unable to internally establish drug development and commercialization capabilities or arrange for the provision of such functions by third parties, our ability to develop and commercialize pharmaceutical products would be significantly impaired.

Our ability to develop and commercialize pharmaceutical products on our own will depend on our ability to internally develop preclinical, clinical, regulatory and sales and marketing capabilities, or enter into arrangements with third parties to provide these functions. It will be expensive and will require significant time for us to develop these capabilities internally. We may not be successful in developing these capabilities or entering into agreements with third parties on favorable terms, or at all. Further, our reliance upon third parties for these capabilities could reduce our control over such activities and could make us dependent upon these parties. 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, or our

Table of Contents

inability to develop or contract for these capabilities, would significantly impair our ability to develop and commercialize pharmaceutical products.

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

We face substantial competition in our drug discovery and product development efforts.

We face significant competition in our drug discovery and product development efforts from other biotechnology and pharmaceutical companies, as well as from universities and other not-for-profit institutions. In particular, certain competing companies such as Human Genome Sciences, Inc., Millennium Pharmaceuticals, Inc. and Exelixis, Inc. utilize a genetics-based approach to target discovery and validation that is similar to our own. Many of our competitors have substantially greater financial, scientific and human resources than we do. As a result, our competitors may succeed in developing products earlier than we do, obtaining regulatory approvals faster than we do and developing products that are more effective or safer than any that we may develop.

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

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

If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to successfully develop and commercialize our own products.

We are highly dependent on the principal members of our management and scientific staff. We do not carry key man insurance on any key personnel and the loss of any of these personnel could negatively impact our business, financial condition or results of operations and could inhibit our product development and commercialization efforts. Although we have entered into employment agreements with some of our key personnel, these employment agreements are all at will. In addition, not all key personnel have employment agreements.

Table of Contents

Recruiting and retaining qualified scientific personnel to perform future research and development work will be critical to our success. Competition for experienced scientists is intense. Failure to recruit and retain scientific personnel on acceptable terms could prevent us from achieving our business objectives.

Any contamination among our knockout mouse population could negatively affect the reliability of our scientific research or cause us to incur significant remedial costs.

Our generation and analysis of knockout mice are conducted in a specific pathogen-free environment. Any contamination of our knockout mouse population could distort or compromise the quality of our research and negatively impact the reliability of our scientific discoveries. Although we have expended substantial resources in order to secure our facilities from such risk, in the event such a contamination were to occur, our drug discovery efforts could be significantly harmed or delayed and our reputation within the scientific community could be eroded. In addition, we may incur significant remedial costs relating to the elimination of any pathogens present in our facilities.

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

Our OmniBank mouse clone library and its backup are stored in liquid nitrogen freezers located at our facility in The Woodlands, Texas, and our knockout mouse research operations are carried out entirely at the same facility. While we have developed redundant and emergency backup systems to protect these 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 these resources are maintained, our business could be disrupted until we could regenerate the affected resources and, as a result, our stock price could decline. Our business interruption insurance may not be sufficient to compensate us in the event of a major interruption due to such a disaster.

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

Our research and development processes involve the use of hazardous materials, including chemicals and radioactive and biological materials. Our operations also produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge or any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages in the event of an improper or unauthorized release of, or exposure of individuals to, these hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development or production efforts. We do not currently maintain insurance coverage that would cover these types of environmental liabilities.

Risks Related to Our Industry

Our ability to patent our inventions is uncertain because patent laws and their interpretation are highly uncertain and subject to change.

The patent positions of pharmaceutical and biotechnology companies generally are highly uncertain and involve complex legal and factual questions that will determine who has the right to develop or use a particular technology or product. No clear policy has emerged regarding the scope of protection provided in gene, drug target and biopharmaceutical patents. In addition, certain uses of technologies and products covered by some of these patents may be subject to statutory exemptions from infringement under applicable law. The biopharmaceutical patent situation outside the United States is similarly uncertain. Changes in, or different interpretations of, patent laws in the United States or other countries might allow others to use our inventions or to develop and commercialize any technologies or products that we may develop without any compensation to us. We anticipate that these uncertainties will continue for a significant period of time.

Table of Contents

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could negatively impact 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 technologies and future products. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets.

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. 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. Others may be able to design around these patents or develop unique products providing effects similar to any products that we may develop. Other companies or institutions may challenge our or our collaborators patents or independently develop similar products that could result in an interference proceeding in the United States Patent and Trademark Office or a legal action.

Patent applications can take many years to issue and there may be currently pending patent applications of our competitors that later result in issued patents covering our discoveries. 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 therapeutic 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 therapeutic product, the holder of a patent covering the use of that technology or therapeutic product could exclude us from selling a product that is based on the same use of that product.

Additionally, significant aspects of our intellectual property are not protected by patents. As a result, we seek to protect the proprietary nature of this intellectual property as trade secrets through proprietary information agreements and other measures. While we have entered into proprietary information agreements with all of our employees, consultants, advisers and collaborators, we may not be able to prevent the disclosure of our trade secrets. In addition, other companies or institutions may independently develop substantially equivalent information and techniques.

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. This risk will increase as the biotechnology industry expands and as other companies and institutions obtain more patents covering the sequences, functions and uses of genes and the drug targets they encode. We are aware that other companies and institutions have conducted research on many of the same targets that we have identified and have filed patent applications potentially covering many of the genes and encoded drug targets that are the focus of our drug discovery programs. 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. 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 any resulting therapeutic products. 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 resulting therapeutic products or may force us to terminate such activities or manufacturing and marketing efforts.

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

10

Table of Contents

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, such as certain gene targeting technology licensed from GenPharm International, Inc. and conditional knockout technology licensed from DuPont Pharmaceuticals Company, now a subsidiary of Bristol-Myers Squibb Company. We do not own the patents that underlie these licenses. Most of these licenses, however, including those licensed from GenPharm and DuPont, 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 are currently in 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. In addition, most of our gene trapping patents and our licensed gene targeting patents cover only the United States and do not apply to discovery activities conducted outside of the United States or, in some circumstances, to importing into the United States products developed using this technology.

Our industry is subject to extensive and uncertain government regulatory requirements, which could significantly hinder our ability, or the ability of our collaborators, to obtain, in a timely manner or at all, regulatory approval of potential therapeutic products, or to commercialize such products.

Our drug candidates, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA or other equivalent foreign regulatory agencies. Our failure to obtain regulatory approval for a drug candidate would prevent us from commercializing that drug candidate. The regulatory approval process is expensive, time-consuming and can vary substantially depending on the modality, complexity and novelty of the drug candidate. The regulatory process includes extensive preclinical studies and human clinical trials, which can take many years and may require substantial expenditures. Such preclinical studies or clinical trials may fail to produce results satisfactory to the FDA or other equivalent foreign regulatory agencies. Even if we obtain regulatory approval, the FDA or other equivalent foreign regulatory agency may impose restrictions as to the approved use and labeling of our product or the types of patients to which we can market and sell our product. We have limited internal resources with respect to the regulatory process and have only limited experience in the preparation and filing of the applications necessary to obtain regulatory 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

Table of Contents

domestic and foreign government regulation of, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of our products and product 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.

Moreover, several of our product development areas involve relatively new technology and have not been the subject of extensive product testing in humans. The regulatory requirements governing these products and related clinical procedures remain uncertain and the products themselves may be subject to substantial review by foreign governmental regulatory authorities that could prevent or delay approval in those countries. Regulatory requirements ultimately imposed on any products that we may develop could limit our ability to test, manufacture and, ultimately, commercialize such products.

The uncertainty of pharmaceutical pricing and reimbursement may decrease the commercial potential of any products that we or our collaborators may develop and affect our ability to raise capital.

Our ability and the ability of our collaborators to successfully commercialize pharmaceutical products will depend, in part, on the extent to which reimbursement for the cost of such products and related treatment will be available from government health administration authorities, private health coverage insurers and other organizations. The pricing, availability of distribution channels and reimbursement status of newly approved pharmaceutical products is highly uncertain. As a result, adequate third-party coverage may not be available for us to maintain price levels sufficient for realization of an appropriate return on our investment in product discovery and development.

In certain foreign markets, pricing or profitability of healthcare products is subject to government control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental control. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on pharmaceutical pricing. While we cannot predict the adoption of any such legislative or regulatory proposals or the effect such proposals or managed care efforts may have on our business, the announcement of such proposals or efforts could harm our ability to raise capital, and the adoption of such proposals or efforts could harm our results of operations. Further, to the extent that such proposals or efforts harm other pharmaceutical companies that are our prospective collaborators, our ability to establish corporate collaborations would be impaired. In addition, third-party payers are increasingly challenging the prices charged for medical products and services. We do not know whether consumers, third-party payers and others will consider any products that we or our collaborators develop to be cost-effective or that reimbursement to the consumer will be available or will be sufficient to allow us or our collaborators to sell such products on a profitable basis.

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.

Public perception of ethical and social issues may limit or discourage the use of our technologies, which could reduce our revenues.

Our success will depend, in part, upon our ability to develop products discovered through our knockout mouse technologies. Governmental authorities could, for ethical, social or other purposes, limit the use of genetic processes or prohibit the practice of our knockout mouse technologies. Claims that genetically engineered products are unsafe for consumption or pose a danger to the environment may influence public perceptions. The subject of

Table of Contents

genetically modified organisms, like knockout mice, has received negative publicity and aroused public debate in some countries. Ethical and other concerns about our technologies, particularly the use of genes from nature for commercial purposes and the products resulting from this use, could reduce the likelihood of maintaining market acceptance of our technologies.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this prospectus contain certain information regarding our financial projections, plans and strategies that are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and 21E of the Securities Exchange Act of 1934. We have attempted to identify forward-looking statements by terminology including anticipate, believe, can, continue, could, estimat expect, intend, may, plan, potential, predict, should or will or the negative of these terms or other comp terminology. These statements, which are only predictions and involve known and unknown risks, uncertainties and other important factors may include, among other things, statements which address our strategy and operating performance, events or developments that we expect or anticipate will occur in the future, such as projections of our future results of operations or of our financial condition, the status of any collaborative agreements, 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 other sections of the documents incorporated by reference into this prospectus. 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.

USE OF PROCEEDS

All of the shares offered by this prospectus are being offered and sold by the selling stockholders. We will not receive any proceeds from the sale of the shares of common stock offered by the selling stockholders.

We will pay all expenses for the registration of the selling stockholders offer and sale of the shares of common stock covered by this prospectus, including registration fees, the costs and expenses of our counsel and independent public accountants and the reasonable fees of one counsel for the selling stockholders. The selling stockholders will pay any underwriting discounts and commissions which they incur in selling shares of our common stock.

SELLING STOCKHOLDERS

We issued the shares of common stock covered by this prospectus to Symphony Icon Holdings LLC, or Holdings, in connection with our entry into a series of related agreements in June 2007 providing for the financing of the clinical development of LX6171, LX1031, LX1032 and other pharmaceutical compositions modulating the same targets as those drug candidates. Holdings subsequently transferred the shares to the selling stockholders in transactions exempt from the registration requirements of the Securities Act of 1933.

In connection with these clinical development financing transactions, we entered into a registration rights agreement pursuant to which we agreed to register the resale of the shares of common stock issued to Holdings and to keep the registration statement effective until the earlier of (a) the date on which the selling stockholders may sell all of the common stock covered by the registration statement without restriction under Rule 144(k) under the Securities Act of 1933 or (b) the date on which the selling stockholders have sold all of the common stock covered by the registration statement. All of the shares to be offered by the selling stockholders using this prospectus were originally issued by us in transactions exempt from the registration requirements of the Securities Act of 1933.

The selling stockholders, or their donees of 500 or fewer shares, may offer the shares of common stock covered by this prospectus from time to time. Our registration of the selling stockholders offer and sale of such shares does not necessarily mean that the selling stockholders will sell any or all of their shares. We do not know when or in what amounts the selling stockholders may offer shares for sale. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholders after completion of the offering.

Table of Contents

If a selling stockholder transfers more than 500 shares of common stock by gift, pledge or other non-sale transfer after the effective date of the registration statement of which this prospectus is a part, the donee, pledgee or transferee may make no offer or sale under this prospectus unless and until a supplement to this prospectus has been filed or an amendment to the related registration statement has become effective.

The table below sets forth the beneficial ownership of all common stock held by each selling stockholder as of July 25, 2007 and the number of such shares of common stock offered by this prospectus. Percentage of ownership is based on 85,965,249 shares of common stock outstanding on July 25, 2007.

We prepared this table based on information supplied to us by each selling stockholder named in the table, and we have not sought to independently verify such information.

	Beneficial Ownership Prior to Offering		
Name of Selling Stockholder	Number of Shares Beneficially Owned	Percentage ownership	Shares Offered Hereby
Symphony Capital Partners, L.P.	4,954,745	5.8%	4,954,745
Symphony Strategic Partners, LLC	374,869	*	374,869
RRD International, LLC	86,070	*	86,070
Howard Hughes Medical Institute	703,997	*	620,816
Stormlaunch & Co. for the benefit of Morgan Stanley Private Markets Fund III LP	496,653	*	496,653
Sailorshell & Co. for the benefit of Morgan Stanley AIP Global Diversified Fund LP	248,327	*	248,327
Mellon Bank, N.A. as Trustee for the Weyerhaeuser Company Master Retirement Trust	248,327	*	248,327
Sailorpier & Co. for the benefit of Aurora Cayman Limited	74,498	*	74,498
Nuclear Electric Insurance Ltd.	49,665	*	49,665
Factory Mutual Insurance Company	49,665	*	49,665
Stormbay & Co. for the benefit of Vijverpoort Huizen C.V.	49,665	*	49,665
Stormstar & Co. for the benefit of Morgan Stanley Private Markets Fund Employee Investors III LP	24,833	*	24,833
WHI Morula Fund, LLC	124,163	*	124,163
UBS O Connor LLC for the benefit of O Connor Global Convertible Arbitrage Master Limited	124,163	*	124,163
UBS O Connor LLC for the benefit of O Connor PIPEs Corporate Strategies Master Ltd.	124,163	*	124,163

* Represents beneficial ownership of less than 1 percent.

PLAN OF DISTRIBUTION

The shares covered by this prospectus may be offered and sold from time to time by any selling stockholder. The term selling stockholders includes donees selling 500 or fewer shares received from a selling stockholder as a gift after the effective date of the registration statement of which this prospectus is a part. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges or in the over-the-counter market or otherwise, at prices and under terms

15

Table of Contents

then prevailing or at prices related to the then current market price or in negotiated transactions. The selling stockholders have advised us that they may offer and sell the shares of common stock offered by this prospectus in one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of the Nasdaq Global Market;
- through the Nasdaq Global Market or any other securities exchange or association that quotes the common stock;
- in privately negotiated transactions; and
- in options transactions.

In addition, the selling stockholders have advised us that they may sell shares of common stock in compliance with Rule 144, if available, or pursuant to other available exemptions from the registration requirements under the Securities Act of 1933, rather than pursuant to this prospectus.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with distributions of the shares or otherwise, the selling stockholders have advised us that they may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with the selling stockholders. The selling stockholders have advised us that they may also sell the common stock short and redeliver the shares to close out such short positions. The selling stockholders have advised us that they may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling stockholders have advised us that they may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution may effect sales of the pledged shares pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by a selling stockholder may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholders in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus, the selling stockholders and any broker-dealers who execute sales for any such selling stockholder may be deemed to be underwriters within the meaning of the Securities Act of 1933 in connection with such sales. Any profits realized by a selling stockholder and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

In order to comply with the securities laws of certain states, if applicable, the shares must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

The selling stockholders have advised us that they may sell their shares at market prices prevailing at the time of sale, at prices related to such prevailing market prices, at negotiated prices or at fixed prices and that the transactions listed above may include cross or block transactions.

16

Table of Contents

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934 may apply to their sales of common stock and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act of 1933. The selling stockholders have advised us that they may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act of 1933.

At the time a particular offer of shares is made, if required, a prospectus supplement will be distributed that will set forth the number of shares being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

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

All shares offered by this prospectus by the selling stockholders will be sold subject to the terms and conditions of the registration rights agreement described in the section entitled Selling Stockholders.

LEGAL MATTERS

The validity of the issuance of the common stock 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, 2006, and management s assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management s assessment are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission, or SEC, a registration statement on Form S-3 under the Securities Act of 1933 regarding the offer and sale of shares of common stock under this prospectus by the selling stockholders. This prospectus, which constitutes a part of the registration statement, does not contain all of the information contained in the registration statement or the exhibits to the registration statement, as permitted by the rules and regulations of the SEC. For further information about us and our common stock, please review the registration statement and the exhibits filed as a part of it. Statements made in this prospectus that describe documents may not necessarily be complete. We recommend that you review the documents that we have filed with the registration statement to obtain a more complete understanding of these documents. A copy of the registration statement, including the exhibits filed as a part of it, may be inspected without charge at the SEC s Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from the SEC upon the payment of fees prescribed by it. You may obtain information on the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding companies that file electronically with it.

We are subject to the information and reporting requirements of the Securities Exchange Act of 1934 and will file periodic reports, proxy statements and other information with the SEC. You may inspect any of these documents as described in the preceding paragraph.

Table of Contents

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus, except for information superseded by information in this prospectus. We incorporate by reference the documents listed below that we have previously filed with the SEC and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, prior to the termination of the offering of the securities covered by this prospectus:

- our annual report on Form 10-K for the year ended December 31, 2006;
- our quarterly report on Form 10-Q for the quarterly period ended March 31, 2007;
- our current reports on Form 8-K dated December 31, 2006 and February 13, February 26, June 15 and June 17, 2007; and
- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on March 27, 2000 pursuant to Section 12 of the Securities Exchange Act of 1934, including any amendments and reports filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as so modified or superseded. You may rely on any statement contained in this prospectus or in documents incorporated or deemed to be incorporated in this prospectus, unless that statement has been subsequently modified or superseded as described above prior to the time you make your investment decision.

Upon your written or oral request, we will provide you at no cost a copy of any or all of the documents incorporated by reference in this prospectus, other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into this prospectus. You may request a copy of these documents by contacting:

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

Table of Contents

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

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

SEC Registration Fee	$ 784
Printing Expenses	5,000
Accounting Fees and Expenses	10,000
Legal Fees and Expenses	10,000
Transfer Agent and Registrar Fees	
Miscellaneous Expenses	1,216
Total	$ 27,000

The reasonable fees of one counsel for the selling stockholders is included under Legal Fees and Expenses in the foregoing table. The selling stockholders will pay any underwriting discounts and commissions, which discounts and commissions are not included in the foregoing table.

Item 15. Indemnification of Directors and Officers.

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

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

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

Table of Contents

services as a director, officer, employee, agent or fiduciary to Lexicon, any subsidiary of Lexicon or to any other company or enterprise for which the person provides services at Lexicon s request.

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

Item 16. Exhibits.

Exhibit No.	Description
3.1	Restated Certificate of Incorporation, as amended (filed as Exhibit 3.1 to the Company s Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated by reference herein).
3.2	Restated Bylaws (filed as Exhibit 3.2 to the Company s Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
*4.1	Registration Rights Agreement, dated June 15, 2007, with Symphony Icon Holdings LLC
*5.1	Opinion of Vinson & Elkins L.L.P.
*23.1	Consent of Ernst & Young LLP
*23.2	Consent of Vinson & Elkins L.L.P. (contained in Exhibit 5.1)
*24.1	Power of Attorney (contained in signature page)

* Filed herewith.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

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

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

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

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

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

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

Table of Contents

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

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

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions described in Item 15, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

Table of Contents

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of The Woodlands, in the State of Texas, on July 27, 2007.

Lexicon Pharmaceuticals, Inc.

By: /s/ Arthur T. Sands

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ Arthur T. Sands Arthur T. Sands, M.D., Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	July 27, 2007
/s/ Julia P. Gregory Julia P. Gregory	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	July 27, 2007
/s/ Samuel L. Barker Samuel L. Barker, Ph.D.	Chairman of the Board of Directors	July 27, 2007
/s/ Robert J. Lefkowitz Robert J. Lefkowitz, M.D.	Director	July 27, 2007
/s/ Barry Mills Barry Mills, J.D., Ph.D.	Director	July 27, 2007

/s/ Alan S. Nies	Director	July 27, 2007
Alan S. Nies, M.D.		
/s/ Frank P. Palantoni	Director	July 27, 2007
Frank P. Palantoni		
/s/ Clayton S. Rose	Director	July 27, 2007
Clayton S. Rose, Ph.D.		
/s/ Kathleen M. Wiltsey	Director	July 27, 2007
Kathleen M. Wiltsey		

Table of Contents

EXHIBIT INDEX

Exhibit No.	Description
3.1	Restated Certificate of Incorporation, as amended (filed as Exhibit 3.1 to the Company s Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated by reference herein).
3.2	Restated Bylaws (filed as Exhibit 3.2 to the Company s Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
*4.1	Registration Rights Agreement, dated June 15, 2007, with Symphony Icon Holdings LLC
*5.1	Opinion of Vinson & Elkins L.L.P.
*23.1	Consent of Ernst & Young LLP
*23.2	Consent of Vinson & Elkins L.L.P. (contained in Exhibit 5.1)
*24.1	Power of Attorney (contained in signature page)

* Filed herewith.