

LEXICON PHARMACEUTICALS, INC./DE

Form 424B5

March 08, 2010

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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.

***PROSPECTUS SUPPLEMENT (Subject to Completion)***  
***(To Prospectus dated September 18, 2009)***

***Issued March 8, 2010***

**Filed Pursuant to Rule 424(b)(5)**  
**Registration No. 333-161696**

***\$95,000,000***

***Lexicon Pharmaceuticals, Inc.***

***COMMON STOCK***

***Lexicon is offering \$95,000,000 of shares of its common stock to the public.***

***Invus, L.P., Lexicon's largest stockholder, has the right, if it elects, to purchase from us at the price to the public in this offering up to approximately \$64,219,775 of additional shares of our common stock, which is that number of shares that is sufficient to maintain its pro rata ownership of our common stock. If Invus exercises such right, it will purchase such additional shares in a concurrent private placement.***

***Our common stock is listed on The Nasdaq Global Market under the symbol LXRX. On March 5, 2010, the reported last sale price of our common stock on The Nasdaq Global Market was \$1.78 per share.***

***Investing in our common stock involves risks. See Risk Factors beginning on page S-5 of this prospectus supplement.***

***PRICE \$ A SHARE***

	<i>Price to Public</i>	<i>Underwriting Discounts and Commissions</i>	<i>Proceeds to Lexicon Pharmaceuticals</i>
Per Share	\$	\$	\$
Total	\$	\$	\$

*The underwriters will not receive any compensation with respect to the shares being offered directly by Lexicon to Invus.*

*We have granted the underwriters the right to purchase up to an additional \$14,250,000 of shares to cover over-allotments.*

*The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.*

*The underwriters expect to deliver the shares to purchasers on \_\_\_\_\_, 2010.*

**MORGAN STANLEY**

**J.P.MORGAN**

**COWEN AND COMPANY**

**THOMAS WEISEL PARTNERS LLC**

*, 2010*

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You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. Neither we nor the underwriters have authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are offering to sell the shares of common stock, and are seeking offers to buy the shares of common stock, only in jurisdictions where offers and sales are permitted. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement, or the documents incorporated by reference, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sales of the shares of common stock.

In this prospectus supplement and the accompanying prospectus, unless otherwise indicated, 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. This prospectus supplement and the accompanying prospectus also include trademarks owned by other persons.

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**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 Risk Factors section of this prospectus supplement beginning on page S-5 and the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.*

**LEXICON PHARMACEUTICALS**

Lexicon Pharmaceuticals is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We have used our proprietary 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, focusing in the core therapeutic areas of immunology, metabolism, cardiology and ophthalmology.

We have announced positive results from Phase 2 clinical trials of each of our two most advanced drug candidates: LX1031, an orally-delivered small molecule compound that we are developing as a potential treatment for irritable bowel syndrome and other gastrointestinal disorders and LX4211, an orally-delivered small molecule compound that we are developing as a potential treatment for type 2 diabetes. We are presently conducting Phase 2 clinical trials of two other drug candidates: LX2931, an orally-delivered small molecule compound that we are developing as a potential treatment for rheumatoid arthritis and other autoimmune diseases and LX1032, an orally-delivered small molecule compound that we are developing as a potential treatment for the symptoms associated with carcinoid syndrome. We have advanced one other drug candidate into preclinical development: LX7101, a topically-delivered small molecule compound that we are developing as a potential treatment for glaucoma. We have small molecule compounds from a number of additional drug discovery programs in various stages of preclinical research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline.

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

**Recent Developments**

For the quarter ending March 31, 2010, we expect total operating expenses of between \$27.0 million and \$29.0 million (unaudited). As previously announced, we continue to expect total operating expenses for the 2010 fiscal year to be between \$100.0 and \$110.0 million. The primary factors that will affect the amount and timing of our 2010 operating expenses include the pace of enrollment of our ongoing and planned phase 2 clinical trials of LX1032 for carcinoid syndrome and LX2931 for rheumatoid arthritis and the design, timing of initiation and pace of enrollment of our other planned clinical trials, including our planned trials of LX1031 and LX4211. As a result of

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these factors and the other risk factors identified in this prospectus supplement, our operating expenses could be higher or lower than anticipated or vary significantly from quarter to quarter.

The quarter ended March 31, 2010 is not yet complete, and the total operating expenses for the quarter and the 2010 fiscal year set forth above are preliminary, based on information available to us as of the date of this prospectus supplement. Our independent public accountants have not audited, reviewed or performed any procedures with respect to such anticipated total operating expenses and accordingly do not express an opinion or any other form of assurance with respect thereto.

Lexicon 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 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](http://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 supplement or the accompanying prospectus and should not be considered part of this document.



**Table of Contents****THE OFFERING**

*The following summary contains basic information about this offering. The summary is not intended to be complete. You should read the full text and more specific details contained elsewhere in this document. For a more detailed description of our common stock, see the description of common stock contained in the accompanying prospectus.*

Issuer	Lexicon Pharmaceuticals, Inc.
Common stock offered to public	shares
Common stock to be outstanding after this offering	265,083,300 shares <sup>(1) (2)</sup>
Use of proceeds	The net proceeds of this offering are estimated to be approximately \$89.4 million after deduction of underwriting discounts and commissions and estimated offering expenses based on an assumed public offering price of \$1.78 per share, which is the reported last sales price of our common stock on March 5, 2010. We currently intend to use the net proceeds for research and development. 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.
Nasdaq Global Market symbol	LXRX
Risk Factors	See Risk Factors beginning on page S-5 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.

Invus, L.P., or Invus, has the right, if it elects, 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 its pro rata ownership of our common stock. If Invus exercises such right, it will purchase such additional shares in a concurrent private placement.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters over-allotment option in this offering. To the extent that the underwriters exercise their over-allotment option, 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.

- (1) Assumes the issuance of 53,370,787 shares in this offering and 36,078,525 additional shares offered directly by us to Invus in a concurrent private placement pursuant to Invus' right to purchase up to the number of shares that is sufficient to maintain its pro rata ownership of our common stock, in each case based on an assumed public offering price of \$1.78 per share, which is the reported last sale price of our common stock on March 5, 2010. While Invus has indicated interest in purchasing such shares, an indication of interest is not a binding commitment or agreement to purchase shares and, as a result, Invus may purchase fewer or no shares.

- (2) Based on 175,633,988 shares of our common stock outstanding as of February 28, 2010 and excludes:  
20,297,813 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price per share of \$3.79;  
387,100 shares of common stock issuable pursuant to outstanding restricted stock units (phantom stock); and  
10,659,425 shares of common stock available for future grant or issuance under our stock incentive plans.

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The statement of operations data for each of the three years in the period ended December 31, 2009 has been derived from our financial statements that have been audited by Ernst & Young LLP, independent auditors. 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.

	<b>Year Ended December 31,</b>		
	<b>2007</b>	<b>2008</b>	<b>2009</b>
	<b>(in thousands, except per share data)</b>		
<b>Statements of Operations Data:</b>			
Revenues	\$ 50,118	\$ 32,321	\$ 10,700
Operating expenses:			
Research and development	103,237	107,232	81,238
General and administrative	21,835	21,624	19,418
Total operating expenses	125,072	128,856	100,656
Loss from operations	(74,954)	(96,535)	(89,956)
Interest and other income (expense), net	3,721	(349)	(3,463)
Consolidated net loss before taxes	(71,233)	(96,884)	(93,419)
Income tax benefit			102
Consolidated net loss	(71,233)	(96,884)	(93,317)
Less: net loss attributable to noncontrolling interest in Symphony Icon, Inc.	12,439	20,024	10,537
Net loss attributable to Lexicon Pharmaceuticals, Inc.	\$ (58,794)	\$ (76,860)	\$ (82,780)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	\$ (0.59)	\$ (0.56)	\$ (0.57)
Shares used in computing net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	99,798	136,797	145,465

**As of December 31, 2009**  
**Actual**      **As Adjusted<sup>(2)</sup>**  
**(unaudited)**  
**(in thousands)**

**Balance Sheet Data:**

Cash, cash equivalents, restricted cash and short-term investments <sup>(1)</sup>	\$ 157,096	\$ 310,691
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Short-term investments held by Symphony Icon, Inc.	5,417	5,417
Working capital <sup>(1)</sup>	118,730	272,325
Total assets	257,761	411,356
Long-term debt, net of current portion	28,482	28,482
Accumulated deficit	(570,175)	(570,175)
Lexicon Pharmaceuticals, Inc. stockholders' equity	163,787	317,382

(1) Includes restricted cash and investments of \$430 as of December 31, 2009.

(2) Reflects the net proceeds from the sale of an assumed aggregate of 53,370,787 shares of common stock in this offering, based on an assumed public offering price of \$1.78 per share, which is the reported last sale price of our common stock on March 5, 2010, after deducting estimated underwriting discounts and commissions and estimated offering expenses, and an assumed 36,078,525 shares of common stock to Invus in a concurrent private placement, based on the assumed public offering price. For additional information with respect to our net proceeds from this offering without giving effect to Invus' participation, as well as the 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-24.

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**RISK FACTORS**

*An investment in our common stock involves risks. You should carefully consider the following risk factors, together with all of the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus in evaluating an investment in our common stock. 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 December 31, 2009, we had \$157.1 million in cash, cash equivalents and investments, including \$56.0 million of auction rate securities and related rights, and \$5.4 million in investments held by Symphony Icon, Inc. 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;
- the amount and timing of payments under such agreements;
- the level and timing of our research and development expenditures;
- the timing and progress of the clinical development of our drug candidates LX1031, LX4211, LX2931 and LX1032;
- our election whether to exercise our exclusive option to acquire all of the equity of Symphony Icon, thereby allowing us to reacquire LX1031 and LX1032;
- 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;
- 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 we advance our drug candidates 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

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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.

***Invus, L.P., our largest stockholder, may decline to grant its consent which is required for us to conduct additional equity offerings at prices less than \$4.50 per share. In addition, we can provide no assurance that Invus will exercise its rights to require us to initiate up to two pro rata rights offerings in which it would be obligated to purchase its pro rata portion of the offering.***

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus made an initial investment of \$205.4 million to purchase 50,824,986 shares of our common stock in August 2007 and has the right to require us to initiate up to two pro rata rights offerings to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount of up to \$344.5 million, less the proceeds of any qualified offerings that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share. We have not completed any such qualified offering. Invus may exercise its right to require us to conduct the first rights offering by giving us notice within a period of one year beginning on November 28, 2009 (which we refer to as the first rights offering trigger date). Invus may exercise its right to require us to conduct a second rights offering by giving us notice within a period of one year beginning on the date that is 90 days after Invus exercise of its right to require us to conduct the first rights offering or, if Invus does not exercise its right to require us to conduct the first rights offering, within a period of one year beginning on the first anniversary of the first rights offering trigger date. If Invus elects to exercise its right to require us to initiate a rights offering, Invus would be required to purchase its pro rata portion of the offering.

Under the securities purchase agreement, until the later of the completion of the second rights offering or the expiration of the period following the second rights offering trigger date during which Invus may require us to initiate the second 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 initiate a rights offering, Invus will have a period of 10 business days in which to exercise its right to require us to conduct a rights offering, in which case we would be required to forego the proposed public offering and proceed with the rights offering. Although Invus may consent to this offering, if we are not able to issue common stock at prices equal to or greater than \$4.50 per share in the future, due to market conditions or otherwise, this obligation will limit our ability to raise capital by issuing additional equity securities without the consent of Invus. In the event Invus declines to grant such consent and, in addition, elects not to exercise its right to require us to initiate the first rights offering, or elects to limit the size of the first rights offering, our ability during this period to satisfy our future capital requirements by issuing equity securities will be limited if we are unable to do so by issuing common stock at prices equal to or greater than \$4.50 per share.

***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 \$82.8 million for the year ended December 31, 2009, \$76.9 million for the year ended December 31, 2008 and \$58.8 million for the year ended December 31, 2007. As of December 31, 2009, we had an accumulated deficit of \$570.2 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 derive substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses, and will continue to do so for the foreseeable future. Our future revenues from collaborations and technology licenses are uncertain because our existing agreements have fixed terms or relate to specific projects of limited duration and future revenues from such agreements, if any, depend 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

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future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine, as we have to date with respect to our four clinical drug candidates, 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 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 our drug programs progress into and through 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.

***We have licensed the intellectual property, including commercialization rights, to our drug candidates LX1031 and LX1032 to Symphony Icon and will not receive any future royalties or revenues with respect to these drug candidates unless we exercise our option to purchase Symphony Icon.***

Our option to purchase all of the equity of Symphony Icon, thereby allowing us to reacquire these drug candidates, is exercisable by us at any time, in our sole discretion, until June 15, 2011 at an exercise price of (a) \$81 million, if the purchase option is exercised before June 15, 2010 and (b) \$90 million, if the purchase option is exercised on or after June 15, 2010 and before June 15, 2011. The purchase option exercise price may be paid in cash or a combination of cash and common stock, at our sole discretion, provided that the common stock portion may not exceed 40% of the purchase option exercise price. Any such issuance of common stock may also be subject to Invus providing its consent to such issuance as required by our securities purchase agreement with Invus.

If we elect to exercise the purchase option, we will be required to make a substantial cash payment or to make a lesser but still substantial cash payment and issue a substantial number of shares of our common stock, which may in turn require us to enter into a financing arrangement or license arrangement with one or more third parties. The amount of any such cash payment would reduce our capital resources. Payment in shares of our common stock could result in dilution to our stockholders at that time. Other financing or licensing alternatives may be expensive or impossible to obtain. If we do not exercise the purchase option prior to its expiration, our rights to purchase all of the equity in Symphony Icon and to reacquire LX1031 and LX1032 will terminate. We may not have the financial resources to exercise the option, which may result in our loss of these rights. Additionally, we may not receive clinical data from future clinical trials of LX1031 before the expiration of our option on June 15, 2011 or the clinical data available to us may otherwise be insufficient for us to make a determination of whether we should exercise the option prior to June 15, 2010 or June 15, 2011.

***At December 31, 2009, we held \$56.2 million (par value), with an estimated fair value of \$46.3 million, of auction rate securities for which auctions have failed and, as a result, we may not be able to access at least a portion of these funds without a loss of principal.***

At December 31, 2009, we held \$56.2 million (par value), with an estimated fair value of \$46.3 million, of investments with an auction interest rate reset feature, known as auction rate securities. Until February 2008, the market for our auction rate securities was highly liquid. However, starting in February 2008, a substantial number of auctions failed, meaning that there was not enough demand to sell all of the securities that holders desired to sell at auction.

In November 2008, we accepted an offer from UBS AG, the investment bank that sold us our auction rate securities, providing us with certain rights related to our auction rate securities. The rights permit us to require UBS to purchase our auction rate securities from us at par value during the period from June 30, 2010 through July 2, 2012.

Conversely, UBS has the right, in its discretion, to purchase or sell the securities at any time by paying us the par value of the securities. In connection with our acceptance of UBS's offer, in January 2009, we entered into a credit line agreement with UBS Bank USA that provides, as of December 31, 2009, up to an aggregate amount of \$37.5 million in the form of an uncommitted, demand, revolving line of credit. The credit line is secured only by the

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auction rate securities and advances under the credit line will be made on a no net cost basis, meaning that the interest paid by us on advances will not exceed the interest or dividends paid to us by the issuer of the auction rate securities. As of December 31, 2009, we had \$37.4 million outstanding under this credit line.

Although we have accessed substantially the maximum amount permitted under the credit line and expect to exercise the rights and sell our auction rate securities to UBS on June 30, 2010, the earliest date allowable under the rights, we will have no means to access approximately \$18.7 million (par value), as of December 31, 2009, invested in auction rate securities before such date without a loss of principal. Further, UBS and its affiliates may not be able to maintain the financial resources necessary to perform its obligations under the rights or credit line. UBS and the Swiss government are currently engaged in discussions with the United States government regarding the disclosure, pursuant to an August 2009 settlement between UBS and the United States government, of the identities of certain UBS customers subject to an ongoing investigation of tax fraud, the outcome of which could also impact UBS' ability to perform its obligations under the rights or credit line. As a result, we cannot provide any assurance that we will be able to access the funds invested in auction rate securities without a loss of principal, unless a future auction on these investments is successful or the issuer redeems the securities.

***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 expiration or other termination of collaborations and technology licenses, which may not be renewed or replaced;

the pace of enrollment of our ongoing and planned Phase 2 clinical trials of LX1032 for carcinoid syndrome and LX2931 for rheumatoid arthritis and the design, timing of initiation and pace of enrollment of our other planned clinical trials, including our planned trials of LX1031 and LX4211;

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 are an early-stage company, and 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, in significant part through collaborations, is unproven. Our success will depend upon our ability to successfully generate, select and develop drug candidates for 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.

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-

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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.

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. For example, we are presently seeking to develop an improved formulation of LX1031 in preparation for use in future clinical trials and cannot provide assurance that we will be able to develop a commercially viable formulation.

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 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.

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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. 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. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our drug candidates may cause delays in the approval or rejection of an application. 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

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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;

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