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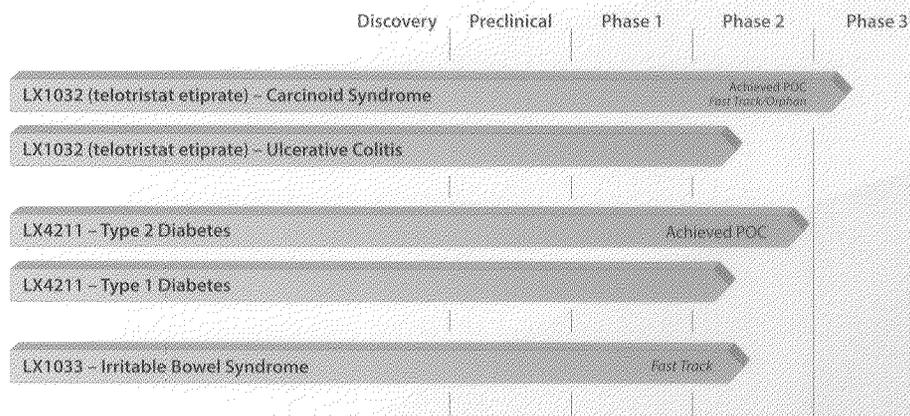
LEXICON PHARMACEUTICALS
2012 ANNUAL REPORT

To Our Shareholders,

The year 2012 witnessed an important transition to late stage development for the most advanced candidates in Lexicon's drug discovery and development pipeline. Telotristat etiprate (LX1032) became our first drug candidate to enter Phase 3 clinical development. The positive results from two Phase 2 studies in carcinoid syndrome encouraged us to pursue an international registrational trial of telotristat etiprate in this debilitating cancer syndrome with significant unmet medical need. Lexicon received Orphan Drug designation for telotristat etiprate from the U.S. Food and Drug Administration (FDA) for the treatment of carcinoid syndrome, having previously obtained Fast Track designation for the program in the U.S. and Orphan Drug status in Europe.

We obtained positive results from a Phase 2b study of LX4211, our dual SGLT1 and SGLT2 inhibitor, in patients with type 2 diabetes. In the study, LX4211 demonstrated a favorable safety profile with significantly positive effects on multiple parameters of glycemic control and cardiovascular health. In addition, we are carrying out clinical studies in type 2 diabetes patients with renal impairment and in type 1 diabetes patients and making preparations for the Phase 3 program of LX4211 for type 2 diabetes.

Pipeline of Advanced Drug Candidates with Breakthrough Potential



We made significant progress in our Phase 2 trial of LX1033 in patients with diarrhea-predominant irritable bowel syndrome (IBS). We expect results from this study in the second half of 2013 and anticipate making preparations for the Phase 3 program of LX1033 based on a positive outcome. We received Fast Track designation from the FDA for the development of LX1033 in this disease.

Our research team achieved meaningful progress in multiple, early-stage programs, all based on our use of genetics to guide drug discovery and development.

In 2013, we look forward to furthering our transition to late-stage development and to preparing for commercialization as we remain focused on our mission to discover breakthrough treatments for human disease.

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

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

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FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT
For the Fiscal Year Ended December 31, 2012

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE
For the Transition Period from _____ to _____

Commission File Number: 000-30111

Lexicon Pharmaceuticals, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware

(State or Other Jurisdiction of Incorporation or Organization)

76-0474169

(I.R.S. Employer Identification Number)

8800 Technology Forest Place
The Woodlands, Texas 77381

(Address of Principal Executive Offices and Zip Code)

(281) 863-3000

(Registrant's Telephone Number,
Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class

Name of Each Exchange on which Registered

Common Stock, par value \$0.001 per share

Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act of 1933. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Securities Exchange Act of 1934. (check one): Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes No

The aggregate market value of voting stock held by non-affiliates of the registrant as of the last day of the registrant's most recently completed second quarter was approximately \$446.3 million, based on the closing price of the common stock on the Nasdaq Global Select Market on June 29, 2012 of \$2.25 per share. For purposes of the preceding sentence only, our directors, executive officers and controlling stockholders are assumed to be affiliates. As of March 8, 2013, 513,002,541 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2013 annual meeting of stockholders, which proxy statement will be filed under the Securities Exchange Act of 1934 within 120 days of the end of the registrant's fiscal year ended December 31, 2012, are incorporated by reference into Part III of this annual report on Form 10-K.

Lexicon Pharmaceuticals, Inc.

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The Lexicon name and logo, OmniBank[®] and LexVision[®] are registered trademarks and Genome5000[™] is a trademark of Lexicon Pharmaceuticals, Inc.

In this annual report on Form 10-K, “Lexicon Pharmaceuticals,” “Lexicon,” “we,” “us” and “our” refer to Lexicon Pharmaceuticals, Inc. and its subsidiaries.

This annual report on Form 10-K contains forward-looking statements. These statements relate to future events or our future financial performance. We have attempted to identify forward-looking statements by terminology including “anticipate,” “believe,” “can,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “should” or “will” or the negative of these terms or other comparable terminology. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under “Item 1A. Risk Factors,” that may cause our or our industry’s actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. We are not under any duty to update any of the forward-looking statements after the date of this annual report on Form 10-K to conform these statements to actual results, unless required by law.

PART I

Item 1. *Business*

Overview

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

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

- We are developing LX4211, an orally-delivered small molecule compound, as a treatment for type 1 and type 2 diabetes. We have completed two Phase 2 clinical trials and are preparing for the initiation of pivotal Phase 3 clinical trials of LX4211 in type 2 diabetes patients. We have also initiated a clinical trial of LX4211 in type 2 diabetes patients with renal impairment and an initial Phase 2 clinical trial of LX4211 in type 1 diabetes patients;
- We are developing LX1032, or telotristat etiprate, an orally-delivered small molecule compound, as a treatment for carcinoid syndrome and ulcerative colitis. We have completed two Phase 2 clinical trials and have initiated a pivotal Phase 3 clinical trial of telotristat etiprate in carcinoid syndrome patients and are presently conducting an initial Phase 2 clinical trial of telotristat etiprate in ulcerative colitis patients;
- We are developing LX1033, an orally-delivered small molecule compound, as a treatment for irritable bowel syndrome and are presently conducting an initial Phase 2 clinical trial; and
- We have completed a Phase 2 clinical trial and a subsequent dose-ranging study of LX2931, an orally-delivered small molecule compound that is in development as a treatment for rheumatoid arthritis, and a Phase 1 clinical trial of LX7101, a topically-delivered small molecule compound that is in development as a treatment for glaucoma.

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

We are working both independently and through strategic collaborations and alliances to capitalize on our technology, drug target discoveries and drug discovery and development programs. Consistent with this approach, we seek to retain exclusive rights to the benefits of certain 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 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 leading pharmaceutical and biotechnology companies which generated near-term cash while offering us the potential to retain economic participation in products developed from the collaborations. In addition, we have established collaborations and license agreements with other leading pharmaceutical and biotechnology companies, research institutes and academic institutions under which we received fees and, in some cases, are eligible to receive milestone and royalty payments, in return for granting access to some of our technologies and discoveries.

Lexicon Pharmaceuticals 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 annual report on Form 10-K.

control, demonstrated statistically significant benefits in the primary and multiple secondary efficacy endpoints and demonstrated a favorable safety profile. In the Phase 1 clinical trial, LX4211 was well tolerated at all dose levels and produced a dose-dependent increase in urinary glucose excretion.

LX4211 was internally generated by our medicinal chemists and inhibits both sodium-glucose cotransporter type 2, or SGLT2, a transporter responsible for most of the glucose reabsorption performed by the kidney, and sodium-glucose cotransporter type 1, or SGLT1, a transporter responsible for glucose and galactose absorption in the gastrointestinal tract, and to a lesser extent than SGLT2, glucose reabsorption in the kidney. Our scientists identified mice lacking either SGLT1 or SGLT2 as having potent anti-diabetic phenotypes across multiple measures of glucose control and metabolism. In preclinical studies, animals treated with LX4211 demonstrated improvements in multiple measures of glycemic control and increased urinary glucose excretion, with urinary glucose excretion returning to baseline after treatment was discontinued.

LX1032 (Telotristat etiprate)

LX1032, or telotristat etiprate, is an orally-delivered small molecule compound that we are developing for the treatment of carcinoid syndrome and ulcerative colitis. We initiated a single, pivotal Phase 3 clinical trial of telotristat etiprate in October 2012 evaluating the safety and tolerability of telotristat etiprate and its effect on symptoms associated with carcinoid syndrome. The trial is expected to enroll approximately 105 patients with refractory carcinoid syndrome on background somatostatin analog therapy in a randomized, double-blind, placebo-controlled study of 250mg three times daily and 500mg three time daily doses of telotristat etiprate over a 12-week treatment period, followed by a 36-week, open-label extension where all patients will receive 500mg three times daily doses of telotristat etiprate. The primary efficacy endpoint under evaluation in the trial is the number of daily bowel movements, with secondary efficacy endpoints including stool form, a global assessment of symptoms associated with carcinoid syndrome and other factors. The Phase 3 program of telotristat etiprate is also expected to include an additional companion study for patients who do not meet the inclusion criteria for the pivotal Phase 3 clinical trial.

We reported top-line data in October 2012 from an open-label Phase 2 clinical trial evaluating the safety and tolerability of telotristat etiprate and its effects on symptoms associated with carcinoid syndrome. The Phase 2 trial enrolled 15 patients with metastatic carcinoid syndrome who were refractory to or could not tolerate somatostatin analog therapy in an open-label study of ascending doses of 150mg, 250mg, 350mg and 500mg of telotristat etiprate, administered three times daily, for 14 days on each dose until reaching the maximal dose, which was then continued until the completion of 12 weeks of therapy. The primary efficacy endpoint under evaluation in the trial was the reduction of bowel movements from baseline to week 12, with secondary endpoints including relief of symptoms and reduction in serotonin synthesis. Top-line data from the study showed that patients experienced a 46.4% median reduction from baseline at week 12, with the number of daily bowel movements steadily decreasing over time. All observed changes from baseline were statistically significant at $p < 0.001$. This change corresponded with an increased proportion of patients reporting adequate relief of their carcinoid symptoms, a global assessment which also improved over time, with 75% of the patients with data at week 12 reporting improvement. Clinically relevant decreases from baseline were likewise seen for a number of key secondary endpoints, including statistically significant improvements in stool consistency ($p < 0.001$) and trends of reductions which did not achieve statistical significance in abdominal pain and the number of cutaneous flushing episodes. The median percentage reductions from baseline of urinary 5-HIAA, a biomarker of serotonin synthesis, at weeks 8 and 12 were 68.3% and 72.7%, respectively (each, $p < 0.05$). Telotristat etiprate was well tolerated in the study, with no dose-limiting toxicity observed. Three patients reported serious adverse events, none of which were related to telotristat etiprate, and no patient discontinued from the study due to an adverse event.

We reported top-line data in August 2011 from a Phase 2 clinical trial evaluating the safety and tolerability of telotristat etiprate and its effects on symptoms associated with carcinoid syndrome. The Phase 2 trial enrolled 23 patients with symptomatic carcinoid syndrome who were refractory to octreotide therapy in a double-blind, randomized, placebo-controlled study of 150mg, 250mg, 350mg and 500mg doses of telotristat etiprate, each administered three times daily over a 28-day treatment period in combination with octreotide therapy. The efficacy endpoints under evaluation in the trial included the number of daily bowel movements, stool form, urgency, a global assessment of symptoms associated with carcinoid syndrome, flushing episodes and an assessment of pain and discomfort. Top-line data from the trial showed evidence of efficacy across multiple endpoints, including improvements in bowel movement frequency, decreased levels of urinary 5-HIAA, the primary metabolite of serotonin and a biomarker for serotonin production, and improvements in the assessment of pain and discomfort. Telotristat etiprate demonstrated a favorable safety profile in the trial, with no dose-limiting toxicities observed. Adverse events were generally mild to moderate and similarly distributed across all groups, including the placebo group.

We initiated a Phase 2 clinical trial in February 2012 to evaluate the safety and tolerability of telotristat etiprate and its effect on symptoms associated with ulcerative colitis. The trial is expected to enroll approximately 60 patients with mild to moderate ulcerative colitis who are also taking mesalamine, a standard therapy, in a randomized, double-blind, placebo-

controlled study of 500mg once daily and 500mg three times daily doses of telotristat etiprate over an eight-week treatment period. The primary efficacy endpoint under evaluation in the trial is the safety and tolerability of telotristat etiprate in patients with mild to moderate ulcerative colitis, with secondary endpoints including the change from baseline in patients' modified MAYO scores and other efficacy measures.

We previously completed a Phase 1a single ascending-dose study and a Phase 1b multiple ascending-dose study of telotristat etiprate. In Phase 1 clinical trials, telotristat etiprate was generally well tolerated at all dose levels, and results demonstrated a potent dose-dependent reduction in both blood serotonin levels and urinary 5-HIAA which was consistent with the reductions observed in preclinical animal models.

Telotristat etiprate was internally generated by our medicinal chemists and inhibits tryptophan hydroxylase, or TPH, the rate-limiting enzyme for serotonin production found primarily in enterochromaffin, or EC, cells of the gastrointestinal tract. Our scientists found that mice lacking the non-neuronal form of this enzyme, TPH1, have virtually no serotonin in the gastrointestinal tract, but maintain normal levels of serotonin in the brain. Telotristat etiprate was specifically designed to achieve enhanced systemic exposure to address disorders such as carcinoid syndrome that require regulation of serotonin levels beyond the enterochromaffin cells in the gastrointestinal tract without impacting brain serotonin production. In preclinical studies, telotristat etiprate was able to reduce peripheral serotonin levels in several different species without affecting serotonin levels in the brain. Telotristat etiprate has received Fast Track status and Orphan Drug designation from the United States Food and Drug Administration, or FDA, for the treatment of gastrointestinal symptoms associated with carcinoid syndrome in patients who no longer respond to standard care. Telotristat etiprate has also received Orphan Drug designation from the Committee for Orphan Medical Products of the European Medicines Agency for the treatment of carcinoid tumors in certain patients.

LX1033

LX1033 is an orally-delivered small molecule compound that we are developing for the treatment of irritable bowel syndrome. We initiated a Phase 2 clinical trial in February 2012 to evaluate the safety and tolerability of LX1033 and symptoms associated with irritable bowel syndrome. The trial is expected to enroll up to 360 patients suffering from diarrhea-predominant irritable bowel syndrome in a randomized, double-blind, placebo-controlled study of 500mg twice daily, 500mg three times daily and 1,000mg twice daily doses of LX1033 over a four-week treatment period. The primary efficacy endpoint under evaluation in the trial is stool consistency, with secondary efficacy endpoints including a global assessment of adequate relief and symptom severity evaluation (bloating, urgency and pain).

We previously completed a Phase 1 multiple ascending-dose study exploring safety and tolerability and the pharmacokinetics of LX1033. In the Phase 1 study, all dose levels were well tolerated, no dose-limiting toxicities were observed and LX1033 produced reductions in both plasma and urinary 5-HIAA comparable to those observed with our first-generation serotonin synthesis inhibitor, LX1031, but with a substantially lower and less frequent dosing regimen. Data from a previous Phase 2 clinical trial of LX1031 in 155 patients with either diarrhea-predominant or mixed irritable bowel syndrome showed that treatment with 1,000mg of LX1031 four times daily produced a statistically significant improvement in the global assessment of relief of irritable bowel syndrome pain and discomfort over the four-week treatment period compared to placebo.

LX1033 was internally generated by our medicinal chemists as an inhibitor of TPH, the same target as telotristat etiprate, but LX1033 is chemically distinct and was designed to reduce production of serotonin in the gastrointestinal tract and therefore reduce the serotonin available for receptor activation without affecting serotonin levels in the brain. In preclinical studies, LX1033 demonstrated dose-dependent reductions of serotonin levels in the gastrointestinal tract of multiple species without affecting brain serotonin levels.

LX2931

LX2931 is an orally-delivered small molecule compound that is in development for the treatment of autoimmune diseases such as rheumatoid arthritis. We reported top-line data in December 2010 from a Phase 2 clinical trial evaluating the safety and tolerability of LX2931 and its effects on symptoms and signs associated with rheumatoid arthritis. The Phase 2 trial enrolled 208 patients with rheumatoid arthritis who were also taking methotrexate, a standard therapy, in a double-blind, randomized, placebo-controlled study of 70mg, 110mg and 150mg doses of LX2931, each administered once daily over a 12-week treatment period. The primary efficacy endpoint under evaluation in the trial was ACR20 at 12 weeks, with secondary endpoints including ACR20/50/70 and DAS28 at four, eight and 12 weeks. Top-line data from the study suggested that patients treated with 150mg of LX2931 once daily showed an improvement in ACR20 at 12 weeks (60% versus 49% for placebo), which did not achieve statistical significance. Patients treated with 70mg and 110mg of LX2931 once daily did not indicate improvement relative to placebo. The greatest improvements in ACR20 were observed in patients with the highest serum drug

levels of LX2931, suggesting higher dose levels may be required to achieve appropriate clinical benefit. LX2931 was well tolerated, with no notable differences in adverse events observed between placebo and any of the treatment groups.

We reported top-line data in August 2012 from a Phase 1 dose-ranging study exploring higher doses of LX2931 in patients with rheumatoid arthritis. The dose-ranging study enrolled 10 patients with rheumatoid arthritis in a double-blind, randomized, placebo-controlled study of ascending doses of LX2931 beginning at 50mg once daily and escalating to 500mg once daily over a 12-week treatment period. The primary efficacy endpoint under evaluation in the study was an evaluation of the safety and tolerability of escalating doses of LX2931, with secondary endpoints including a variety of pharmacokinetic and disease activity measures. LX2931 was well tolerated at all dose levels, with no serious adverse events and no withdrawals due to adverse events.

We previously completed two Phase 1a single ascending-dose studies and a Phase 1b multiple ascending-dose study of LX2931 in healthy subjects. In these Phase 1 studies, LX2931 demonstrated a dose-dependent reduction in circulating lymphocytes. An episode of acute abdominal pain resolving within 24 hours was observed in two out of 24 subjects in the single ascending-dose trials, with other mild to moderate adverse events equally distributed across all groups, including the placebo group.

LX2931 was internally generated by our medicinal chemists to target sphingosine-1-phosphate lyase, or S1P lyase, an enzyme in the sphingosine-1 phosphate (S1P) pathway associated with the activity of lymphocytes. Lymphocytes are a cellular component and key driver of the immune system, and are involved in a number of autoimmune and inflammatory disorders. Our scientists discovered that mice lacking this enzyme have increased retention of immune cells in the thymus and spleen with a corresponding reduction in the deployment of T-cells and B-cells into the circulating blood. In preclinical studies, LX2931 produced a consistent reduction in circulating lymphocyte counts in multiple species, and reduced joint inflammation and prevented arthritic destruction of joints in mouse and rat models of arthritis.

LX7101

LX7101 is a topically-delivered small molecule compound that is in development for the treatment of glaucoma. We reported top-line data in August 2012 from an initial Phase 1 clinical trial evaluating the safety, tolerability and pharmacokinetics of LX7101 in glaucoma patients. The Phase 1 trial enrolled 63 patients with glaucoma in a double-blind, randomized, placebo-controlled study of 0.125% solution and 0.25% solution doses of LX7101, each given as an eye drop, over a two-week treatment period. Patients in the trial received a single daily dose of LX7101 or placebo during the first week of the study and two daily doses during the second week. The primary endpoint under evaluation in the trial was the safety and tolerability of LX7101 compared with vehicle, with secondary endpoints including measures of intraocular pressure, taken at multiple time points on day -1, day 1, day 7 and day 14. LX7101 was well tolerated at all dose levels, with no serious adverse events and no withdrawals due to adverse events. Mean intraocular pressure changes from baseline at day 14 for each LX7101 dose level compared to vehicle at eight hours post-dose were 3.18 mmHg for 0.125% and 2.32 mmHg for 0.25%, compared to 0.40 mmHg for vehicle ($p < 0.01$ for 0.125% and $p < 0.05$ for 0.25%). Reductions from baseline at day 14 in the diurnal mean intraocular pressure, representing mean changes across all daily time points, were also statistically significant at 3.37mmHg for 0.125% and 3.52 mmHg for 0.25%, compared to 2.17 mmHg for vehicle.

LX7101 was internally generated by our medicinal chemists to target LIMK2, a kinase associated with the regulation of intraocular pressure, and is designed to lower intraocular pressure by enhancing the fluid outflow facility of the eye. Our scientists discovered that mice lacking LIMK2 exhibited lower intraocular pressure compared to normal mice. In preclinical studies, LX7101 significantly reduced intraocular pressure in animal models of ocular hypertension.

Preclinical Development and Discovery Programs

We have advanced small molecule compounds from a number of additional drug programs into various stages of preclinical development and research and have identified and validated, *in vivo*, more than 100 targets with promising profiles for drug discovery.

Our Drug Discovery and Development Process

Our drug discovery and development process began with our Genome5000 program, in which we used our gene knockout and medical evaluative technologies to discover the putative physiological and behavioral functions of almost 5,000 human genes through analysis of the corresponding mouse knockout models. In our Genome5000 program, we used gene knockout technologies to generate knockout mice – mice whose DNA has been modified to disrupt, or knock out, the function

of the altered gene – by altering the DNA of genes in a special variety of mouse cells, called embryonic stem cells, which were then cloned and used to generate mice with the altered gene. We then studied the physiology and behavior of the knockout mice using a comprehensive battery of advanced medical technologies, each of which was adapted specifically for the analysis of mouse physiology. This systematic use of these evaluative technologies allowed us to discover, *in vivo*, the physiological and behavioral functions of the genes we knocked out and assess the prospective pharmaceutical utility of the potential drug targets encoded by the corresponding human genes. The study of the effects of knocking out genes in mice has historically proven to be a powerful tool for understanding human genes because of the close similarity of gene function and physiology between mice and humans, with approximately 99% of all human genes having a counterpart in the mouse genome.

We engage in programs for the discovery of potential small molecule drugs for those *in vivo*-validated drug targets that we consider to have high pharmaceutical value. We have established extensive internal small molecule drug discovery capabilities, in which we use our own sophisticated libraries of drug-like chemical compounds in high-throughput screening assays to identify “hits,” or chemical compounds demonstrating activity, against these targets. We then employ medicinal chemistry efforts to optimize the potency and selectivity of these hits and to identify lead compounds for potential development. We have established extensive internal capabilities to characterize the absorption, distribution, metabolism and excretion of our potential drug candidates and otherwise evaluate their safety in mammalian models in preparation for preclinical and clinical development. In all of our drug discovery programs, we use a parallel physiological analysis technology platform that we used in the discovery of gene function to analyze the *in vivo* activity and safety profiles of drug candidates in mice as part of our preclinical research efforts.

Once we identify a potential drug candidate, we initiate formal preclinical development studies in preparation for regulatory filings for the commencement of human clinical trials. We have established internal expertise in each of the critical areas of preclinical and clinical development, including clinical trial design, study implementation and oversight, and regulatory affairs.

We believe that our systematic, biology-driven approach provides us with substantial advantages over alternative approaches to drug target discovery. In particular, we believe that the comprehensive nature of our approach has allowed us to identify potential drug targets within the context of mammalian physiology that might have been missed by more narrowly focused efforts. We also believe our approach is more likely to reveal those side effects that may be a direct result of inhibiting or otherwise modulating the drug target and may limit the utility of potential therapeutics directed at the drug target. We believe these advantages have contributed to better target selection and, therefore, to a greater likelihood of success for our drug discovery and development efforts.

Our Commercialization Strategy

We are working both independently and through strategic collaborations and alliances with leading pharmaceutical and biotechnology companies, research institutes and academic institutions 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 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 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.

Drug Discovery and Development Collaborations

Bristol-Myers Squibb. We established a drug discovery alliance with Bristol-Myers Squibb Company in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. Bristol-Myers Squibb extended the target discovery term of the alliance in May 2006. We initiated the alliance with a number of neuroscience drug discovery programs at various stages of development and used our gene knockout technologies to identify additional drug targets with promise in the neuroscience field. For those targets that were selected for the alliance, we and Bristol-Myers Squibb are working together, on an exclusive basis, to identify, characterize and carry out the preclinical development of small molecule drugs, and share equally both in the costs and in the work attributable to those efforts. As drugs resulting from the alliance enter clinical trials, Bristol-Myers Squibb will have the first option to assume full responsibility for clinical development and commercialization.

We received \$86 million in upfront payments and research funding under the agreement during the target discovery portion of the alliance, which expired in October 2009. In addition, we are entitled to receive clinical and regulatory milestone payments ranging, depending on the timing and extent of our efforts in the alliance, up to \$76 million for each drug developed

by Bristol-Myers Squibb under the alliance. We will also earn royalties on sales of drugs commercialized by Bristol-Myers Squibb under the alliance.

Genentech. We established a drug discovery alliance with Genentech, Inc. in December 2002 to discover novel therapeutic proteins and antibody targets. We and Genentech expanded the alliance in November 2005 for the advanced research, development and commercialization of new biotherapeutic drugs. Under the original alliance agreement, we used our target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. In the expanded alliance, we conducted additional, advanced research on a broad subset of those proteins and targets. We have exclusive rights to develop and commercialize biotherapeutic drugs for two of these targets, while Genentech has exclusive rights to develop and commercialize biotherapeutic drugs for the other targets. We retain certain other rights to discoveries made in the alliance, including non-exclusive rights, along with Genentech, for the development and commercialization of small molecule drugs addressing the targets included in the alliance.

We received \$58 million in upfront payments, research funding and research milestone payments under the agreement during the research collaboration term, which expired in November 2008. In addition, we are entitled to receive clinical and regulatory milestone payments ranging, depending on the extent of our efforts in the alliance, up to \$25 million for each drug target for which Genentech develops a biotherapeutic drug under the alliance. We will also earn royalties on sales of biotherapeutic drugs commercialized by Genentech under the alliance. Genentech is entitled to receive milestone payments and royalties on sales of biotherapeutic drugs which we develop or commercialize under the alliance.

Schering-Plough/Organon. We established a drug discovery alliance with N.V. Organon in May 2005 to discover, develop and commercialize novel biotherapeutic drugs. In the collaboration, we created and analyzed knockout mice for 300 genes selected by the parties that encode secreted proteins or potential antibody targets, including two of our preexisting drug discovery programs. We and Organon agreed to equally share costs of and responsibility for research, preclinical and clinical activities, jointly determine the manner in which collaboration products would be commercialized, and equally benefit from product revenue. Organon, formerly a subsidiary of Akzo Nobel N.V., was acquired by Schering-Plough Corporation in November 2007, which subsequently merged with Merck & Co., Inc. in November 2009. In February 2010, we entered into a revised collaboration and license agreement with Organon and Schering Corporation, acting through its Schering-Plough Research Institute division, amending the terms of the alliance to provide that Schering-Plough would assume the full cost of research activities conducted by either party in the alliance, and would assume the full cost of and responsibility for preclinical, clinical and commercialization activities with respect to biotherapeutic drugs resulting from the alliance. In accordance with the terms of the revised agreement, certain targets were released from the alliance, with both parties having rights to pursue such targets independent of the other party, and the remaining targets were subsequently released or exclusive rights granted to us.

We received \$52.5 million in upfront payments and research funding under the agreement during the target discovery portion of the alliance, which expired in December 2009.

Takeda. We established a drug discovery alliance with Takeda Pharmaceutical Company Limited in July 2004 to discover new drugs for the treatment of high blood pressure. In the collaboration, we used our gene knockout technologies to identify drug targets that control blood pressure. Takeda is responsible for the screening, medicinal chemistry, preclinical and clinical development and commercialization of drugs directed against targets selected for the alliance, and bears all related costs.

We received \$18.5 million in upfront payments and research milestone payments under the agreement during the target discovery portion of the alliance, which expired in July 2007. In addition, we are entitled to receive clinical development and product launch milestone payments of up to \$29 million for each drug developed by Takeda under the alliance. We will also earn royalties on sales of drugs commercialized by Takeda under the alliance.

Other Collaborations and Licenses

Taconic Farms. We established a collaboration with Taconic Farms, Inc. in November 2005 for the marketing, distribution and licensing of certain lines of our knockout mice. Taconic is an industry leader in the breeding, housing, quality control and global marketing and distribution of rodent models for medical research and drug discovery. Under the terms of the collaboration, we are presently making available through Taconic more than 3,600 distinct lines of knockout mice, and in some cases, phenotypic data relating to such lines of knockout mice, for use by pharmaceutical and biotechnology companies, academic and non-profit institutions and other researchers. We receive license fees and royalties from payments received by Taconic from customers obtaining access to knockout mice and any related phenotypic data.

Research Collaborations. We have established research collaborations with a number of leading pharmaceutical and biotechnology companies, research institutes and academic institutions under which we received fees in exchange for generating knockout mice for genes requested by the collaborator, providing phenotypic data with respect to such knockout mice or otherwise granting access to some of our technologies and discoveries. In some cases, we are also eligible to receive milestone and royalty payments on products that our collaborators discover or develop using our technology.

Our Executive Officers

Our executive officers and their ages and positions are listed below.

| <u>Name</u> | <u>Age</u> | <u>Position with the Company</u> |
|------------------------------|------------|---|
| Arthur T. Sands, M.D., Ph.D. | 51 | President and Chief Executive Officer and Director |
| Pablo Lapuerta, M.D. | 49 | Executive Vice President, Clinical Development and Chief Medical Officer |
| Alan J. Main, Ph.D. | 59 | Executive Vice President of Pharmaceutical Research |
| Jeffrey L. Wade, J.D. | 48 | Executive Vice President, Corporate Development and Chief Financial Officer |
| Brian P. Zambrowicz, Ph.D. | 50 | Executive Vice President and Chief Scientific Officer |
| James F. Tessmer | 53 | Vice President, Finance and Accounting |

Arthur T. Sands, M.D., Ph.D. co-founded our company and has been our president and chief executive officer and a director since September 1995. At Lexicon, Dr. Sands pioneered the development of large-scale gene knockout technology for use in drug discovery. Before founding our company, Dr. Sands served as an American Cancer Society postdoctoral fellow in the Department of Human and Molecular Genetics at Baylor College of Medicine. Dr. Sands received his B.A. in economics and political science from Yale University and his M.D. and Ph.D. from Baylor College of Medicine.

Pablo Lapuerta, M.D. has been our executive vice president, clinical development and chief medical officer since February 2013 and previously served as our senior vice president, clinical development and chief medical officer from March 2011 until February 2013. From 2009 through 2010, Dr. Lapuerta served as vice president at Bristol-Myers Squibb Company with responsibility for global development of an Alzheimer's disease drug candidate. From 2007 through 2009, Dr. Lapuerta was senior vice president, clinical strategy and chief medical officer of Cogentus Pharmaceuticals, Inc. and prior to that served in a variety of clinical development leadership roles at Bristol-Myers Squibb, where he worked for 11 years before joining Cogentus. He holds a B.A. in biology from Harvard College and an M.D. from Harvard Medical School.

Alan J. Main, Ph.D. has been our executive vice president of pharmaceutical research since February 2007 and served as our senior vice president, Lexicon Pharmaceuticals from July 2001 until February 2007. Dr. Main was president and chief executive officer of Coelacanth Corporation, a leader in using proprietary chemistry technologies to rapidly discover new chemical entities for drug development, from January 2000 until our acquisition of Coelacanth in July 2001. Dr. Main was formerly senior vice president, U.S. Research at Novartis Pharmaceuticals Corporation, where he worked for 20 years before joining Coelacanth. Dr. Main holds a B.S. from the University of Aberdeen, Scotland and a Ph.D. in organic chemistry from the University of Liverpool, England and completed postdoctoral studies at the Woodward Research Institute.

Jeffrey L. Wade, J.D. has been our executive vice president, corporate development and chief financial officer since May 2010. Mr. Wade served as our executive vice president and general counsel from February 2000 until May 2010 and was our senior vice president and chief financial officer from January 1999 to February 2000. From 1988 through December 1998, Mr. Wade was a corporate securities and finance attorney with the law firm of Andrews & Kurth L.L.P., for the last two years as a partner, where he represented companies in the biotechnology, information technology and energy industries. Mr. Wade is a member of the board of directors of the Texas Healthcare and Bioscience Institute. He received his B.A. and J.D. from the University of Texas.

Brian P. Zambrowicz, Ph.D. co-founded our company and has been our executive vice president and chief scientific officer since February 2007. Dr. Zambrowicz served as our executive vice president of research from August 2002 until February 2007, senior vice president of genomics from February 2000 to August 2002, vice president of research from January 1998 to February 2000 and senior scientist from April 1996 to January 1998. From 1993 to April 1996, Dr. Zambrowicz served as a National Institutes of Health postdoctoral fellow at the Fred Hutchinson Cancer Center in Seattle, Washington, where he studied gene trapping and gene targeting technology. Dr. Zambrowicz received his B.S. in biochemistry from the University of Wisconsin. He received his Ph.D. from the University of Washington, where he studied tissue-specific gene regulation using transgenic mice.

James F. Tessmer has been our vice president, finance and accounting since November 2007 and previously served as our senior director of finance from February 2004 to November 2007 and director of finance from April 2001 to February

2004. From January 1997 to April 2001, Mr. Tessmer was assistant controller for Mariner Health Network, Inc. and prior to that served in a variety of financial and accounting management positions for HWC Distribution Corp. and American General Corporation. Mr. Tessmer is a certified public accountant and received his B.B.A. from the University of Wisconsin – Milwaukee and his M.B.A. from the University of Houston.

Patents and Proprietary Rights

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that those rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. Accordingly, patents and other proprietary rights are an essential element of our business. We own patent applications, and in some cases issued patents, covering each of our drug candidates in clinical and preclinical development, including:

- worldwide patent applications that claim LX4211 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including four in the United States;
- worldwide patent applications that claim LX1032, or telotristat etiprate, and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including ten in the United States;
- worldwide patent applications that claim LX1033 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including ten in the United States;
- worldwide patent applications that claim LX2931 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including five in the United States; and
- worldwide patent applications that claim LX7101 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including two in the United States.

Additionally, we hold rights to a number of patents and patent applications under license agreements with third parties. Many of these licenses are nonexclusive, although some are exclusive in specified fields. Most of the licenses have terms that extend for the life of the licensed patents.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. We have filed patent applications and hold issued patents covering each of our drug candidates in clinical development. No United States patent that has issued or may issue based on a patent application we have filed relating to one of our drug candidates in clinical development has a normal expiration date earlier than 2026.

All of our employees, consultants and advisors are required to execute a proprietary information agreement upon the commencement of employment or consultation. In general, the agreement provides that all inventions conceived by the employee or consultant, and all confidential information developed or made known to the individual during the term of the agreement, shall be our exclusive property and shall be kept confidential, with disclosure to third parties allowed only in specified circumstances. We cannot assure you, however, that these agreements will provide useful protection of our proprietary information in the event of unauthorized use or disclosure of such information.

Our patent and intellectual property rights are subject to certain rights and uncertainties. See “Risks Related to Our Intellectual Property” under “Item 1A. Risk Factors.”

Competition

The biotechnology and pharmaceutical industries are highly competitive and characterized by rapid technological change. We face significant competition in each of the aspects of our business from other pharmaceutical and biotechnology companies. In addition, a large number of universities and other not-for-profit institutions, many of which are funded by the U.S. and foreign governments, are also conducting research to discover genes and their functions and to identify potential therapeutic products. Many of our competitors have substantially greater research and product development capabilities and

financial, scientific, marketing and human resources than we do. As a result, our competitors may succeed in developing products earlier than we do, obtaining approvals from the FDA or other regulatory agencies for those products more rapidly than we do, or developing products that are more effective than those we propose to develop. Similarly, our collaborators face similar competition from other competitors who may succeed in developing products more quickly, or developing products that are more effective, than those developed by our collaborators. Any products that we may develop or discover are likely to be in highly competitive markets.

The competition for our drug candidates includes both marketed products and drug candidates that are being developed by others, including drug candidates that are currently in a more advanced stage of clinical development than are our own drug candidates. These competitive marketed products and drug candidates include compounds that employ different mechanisms of action in addressing diseases and conditions for which we are developing our own drug candidates and, in some cases such as LX4211, that employ the same or similar mechanisms of action.

We believe that our ability to successfully compete with these potentially competitive drug candidates and other competitive products currently on the market will depend on, among other things:

- the efficacy, safety and reliability of our drug candidates;
- our ability, and the ability of our collaborators, to complete preclinical testing and clinical development and obtain regulatory approvals for our drug candidates;
- the timing and scope of regulatory approvals for our drug candidates;
- our ability, and the ability of our collaborators, to obtain product acceptance by physicians and other health care providers and reimbursement for product use in approved indications;
- our ability, and the ability of our collaborators, to manufacture and sell commercial quantities of our products;
- the skills of our employees and our ability to recruit and retain skilled employees;
- protection of our intellectual property; and
- the availability of substantial capital resources to fund development and commercialization activities.

Government Regulation

Regulation of Pharmaceutical Products

The development, manufacture and sale of any drug or biologic products developed by us or our collaborators will be subject to extensive regulation by United States and foreign governmental authorities, including federal, state and local authorities. In the United States, new drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act and the regulations promulgated thereunder, or the FDC Act, and biologic products are subject to regulation both under certain provisions of the FDC Act and under the Public Health Services Act and the regulations promulgated thereunder, or the PHS Act. The FDA regulates, among other things, the development, preclinical and clinical testing, manufacture, safety, efficacy, record keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution and export of small molecule and biotherapeutic drugs.

The standard process required by the FDA before a drug candidate may be marketed in the United States includes:

- preclinical laboratory and animal tests performed under the FDA's current Good Laboratory Practices regulations;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for its intended use;

- for drug candidates regulated as small molecule drugs, submission of a New Drug Application, or NDA, and, for drug candidates regulated as biotherapeutic drugs, submission of a Biologic License Application, or BLA, with the FDA; and
- FDA approval of the NDA or BLA prior to any commercial sale or shipment of the product.

This process for the testing and approval of drug candidates requires substantial time, effort and financial resources. Preclinical development of a drug candidate can take from one to several years to complete, with no guarantee that an IND based on those studies will become effective to even permit clinical testing to begin. Before commencing the first clinical trial of a drug candidate in the United States, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial. In such a case, we and the FDA must resolve any outstanding concerns before the clinical trial may begin. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, and the FDA must grant permission for each clinical trial to start and continue. Further, an independent institutional review board for each medical center proposing to participate in the clinical trial must review and approve the plan for any clinical trial before it commences at that center. Regulatory authorities or an institutional review board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

For purposes of NDA or BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1 clinical trials are conducted in a limited number of healthy human volunteers or, in some cases, patients, to evaluate the safety, dosage tolerance, absorption, metabolism, distribution and excretion of the drug candidate;
- Phase 2 clinical trials are conducted in groups of patients afflicted with a specified disease or condition to obtain preliminary data regarding efficacy as well as to further evaluate safety and optimize dosing of the drug candidate; and
- Phase 3 clinical trials are conducted in larger patient populations at multiple clinical trial sites to obtain statistically significant evidence of the efficacy of the drug candidate for its intended use and to further test for safety in an expanded patient population.

In addition, the FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after a drug receives approval.

Completion of the clinical trials necessary for an NDA or BLA submission typically takes many years, with the actual time required varying substantially based on, among other things, the nature and complexity of the drug candidate and of the disease or condition. Success in earlier-stage clinical trials does not ensure success in later-stage clinical trials. Furthermore, data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent proceeding with further clinical trials, filing or acceptance of an NDA or BLA, or obtaining marketing approval.

After completion of clinical trials, FDA approval of an NDA or BLA must be obtained before a new drug may be marketed in the United States. An NDA or BLA, depending on the submission, must contain, among other things, information on chemistry, manufacturing controls and potency and purity, non-clinical pharmacology and toxicology, human pharmacokinetics and bioavailability and clinical data. There can be no assurance that the FDA will accept an NDA or BLA for filing and, even if filed, that approval will be granted. Among other things, the FDA reviews an NDA to determine whether a product is safe and effective for its intended use and a BLA to determine whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may deny approval of an NDA or BLA if the applicable regulatory criteria are not satisfied, or it may require additional clinical data or an additional pivotal Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval. Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Limited indications for use or other conditions could also be placed on any approvals that could restrict the commercial applications of a product or impose costly procedures in connection with the commercialization or use of the product.

In addition to obtaining FDA approval for each product, each drug manufacturing establishment must be inspected and approved by the FDA. All manufacturing establishments are subject to inspections by the FDA and by other federal, state and local agencies and must comply with current Good Manufacturing Practices requirements. Non-compliance with these requirements can result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing and withdrawal, suspension or revocation of marketing approvals.

Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information. Product changes as well as certain changes in a manufacturing process or facility would necessitate additional FDA review and approval. Other post-approval changes may also necessitate further FDA review and approval. Additionally, a manufacturer must meet other requirements including those related to adverse event reporting and record keeping.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Violations of the FDC Act, the PHS Act or regulatory requirements may result in agency enforcement action, including voluntary or mandatory recall, license suspension or revocation, product seizure, fines, injunctions and civil or criminal penalties.

In addition to regulatory approvals that must be obtained in the United States, drugs are also subject to regulatory approval in other countries in which they are marketed. The conduct of clinical trials of drugs in countries other than the United States is likewise subject to regulatory oversight in such countries. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary widely from country to country. No action can be taken to market any drug in a country until the regulatory authorities in that country have approved an appropriate application. FDA approval does not assure approval by other regulatory authorities. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In some countries, the sale price of a drug or biologic product must also be approved. The pricing review period often begins after marketing approval is granted. Even if a foreign regulatory authority approves a drug, it may not approve satisfactory prices for the product.

Other Regulations

In addition to the foregoing, our business is and will be subject to regulation under various state and federal environmental laws, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act and the Toxic Substances Control Act. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in and wastes generated by our operations. We believe that we are in material compliance with applicable environmental laws and that our continued compliance with these laws will not have a material adverse effect on our business. We cannot predict, however, whether new regulatory restrictions will be imposed by state or federal regulators and agencies or whether existing laws and regulations will adversely affect us in the future.

Research and Development Expenses

In 2012, 2011 and 2010, respectively, we incurred expenses of \$82.6 million, \$91.8 million and \$78.5 million in company-sponsored as well as collaborative research and development activities, including \$3.7 million, \$3.2 million and \$3.2 million of stock-based compensation expense in 2012, 2011 and 2010, respectively.

Employees and Consultants

We believe that our success will be based on, among other things, achieving and retaining scientific and technological superiority and identifying and retaining capable management. We have assembled a highly qualified team of scientists as well as executives with extensive experience in the biotechnology industry.

As of February 28, 2013, we employed 230 persons, of whom 61 hold M.D., Ph.D. or D.V.M. degrees and another 38 hold other advanced degrees. We believe that our relationship with our employees is good.

Item 1A. Risk Factors

The following risks and uncertainties are important factors that could cause actual results or events to differ materially from those indicated by forward-looking statements. The factors described below are not the only ones we face and additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

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, 2012, we had \$223.2 million in cash, cash equivalents and investments. We anticipate that our existing capital resources and the cash and revenues we expect to derive from collaborations, technology licenses and other sources will enable us to fund our currently planned operations for at least the next 12 months. Our currently planned operations for that time period consist of the completion of our ongoing clinical trials, the initiation and conduct of additional clinical trials and the continuation of our small molecule drug discovery and preclinical research efforts. However, we caution you that we may generate less cash and revenues or incur expenses more rapidly than we currently anticipate.

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

- our ability to obtain additional funds from collaborations, technology licenses and other sources;
- our ability to identify partners to help advance certain of our product candidates, including LX4211, LX2931 and LX7101, on terms acceptable to us;
- the amount and timing of payments under such agreements;
- the level and timing of our research and development expenditures;
- the timing and progress of the clinical development of our drug candidates LX4211, LX1032, LX1033, LX2931 and LX7101, including the timing of any required regulatory actions and the outcome of our anticipated discussions with regulators;
- future results from clinical trials of our drug candidates;
- the cost and timing of regulatory approvals of drug candidates that we successfully develop;
- market acceptance of products that we successfully develop and commercially launch;
- the effect of competing programs and products, and of technological and market developments;
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and
- the cost and timing of establishing or contracting for sales, marketing and distribution capabilities.

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

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

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

We have incurred net losses since our inception, including net losses of \$110.2 million for the year ended December 31, 2012, \$116.2 million for the year ended December 31, 2011 and \$101.8 million for the year ended December 31, 2010. As of December 31, 2012, we had an accumulated deficit of \$899.8 million. We are unsure when we will become profitable, if ever. The size of our net losses will depend, in part, on the rate of decline or growth in our revenues and on the level of our expenses.

We have derived substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses, and will continue to do so for at least the next several years. Future revenues from our existing collaborations and technology licenses are uncertain because they depend, to a large degree, on the achievement of milestones and payment of royalties we earn from any future products developed under the collaborations. As a result, we depend, in part, on securing new collaboration and license agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine, as we have with certain of our 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 current stage of our operations, we do not currently derive any revenues from sales of pharmaceutical products.

A large portion of our expenses is fixed, including expenses related to facilities and equipment. In addition, we expect to spend significant amounts to fund our research and development activities, including the conduct of clinical trials, continued drug discovery efforts and the advancement of additional potential therapeutics into clinical development. To the extent that we elect to commercialize products on our own, we will be required to incur substantial expenditures in preparation for and to conduct commercialization activities. As a result, we will need to generate substantial additional revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

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

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

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

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

Risks Related to Discovery and Development of Our Drug Candidates

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

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

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

Furthermore, we do not know that any pharmaceutical products based on our drug target discoveries can be successfully developed or commercialized. Our strategy is focused principally on the discovery and development of drug candidates for targets that have not been clinically validated in humans by drugs or drug candidates generated by others. As a result, the drug candidates we develop are subject to uncertainties as to the effects of modulating the human drug target as well as to those relating to the characteristics and activity of the particular compound.

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

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

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

Clinical trials are inherently risky and the results from preclinical testing of a drug candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger-scale, advanced stage clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving positive results in earlier trials. Negative or inconclusive results from a preclinical study or a clinical trial could cause us, one of our collaborators or the FDA to terminate a preclinical study or clinical trial or require that we repeat it. Furthermore, we, one of our collaborators or a regulatory agency with jurisdiction over the trials may suspend clinical trials at any time if the subjects or patients participating in such trials are being exposed to unacceptable health risks or for other reasons.

Any preclinical or clinical test may fail to produce results satisfactory to the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. The FDA or institutional review boards at the medical institutions and healthcare facilities where we sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. Clinical trials must be conducted in accordance with the FDA's current Good Clinical Practices. The FDA and these institutional review boards have authority to oversee our clinical trials, and the FDA may require large numbers of subjects or patients. In addition, we must manufacture, or contract for the manufacture of, the drug candidates that we use in our clinical trials under the FDA's current Good Manufacturing Practices.

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

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

Risks Related to Regulatory Approval of Our Drug Candidates

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

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

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

If we or our collaborators obtain initial regulatory approvals from the FDA or foreign regulatory authorities for any products that we may develop, we or our collaborators will be subject to extensive and rigorous ongoing domestic and foreign government regulation of, among other things, the research, development, testing, manufacture, labeling, promotion, advertising, distribution and marketing of our products and drug candidates. The failure to comply with these requirements or the identification of safety problems during commercial marketing could lead to the need for product marketing restrictions, product withdrawal or recall or other voluntary or regulatory action, which could delay further marketing until the product is brought into compliance. The failure to comply with these requirements may also subject us or our collaborators to stringent penalties.

Risks Related to Commercialization of Products

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

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

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

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

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

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

Our ability to commercialize any products that we may develop will be highly dependent on the extent to which coverage and reimbursement for our products will be available from third-party payors, including governmental payors, such as Medicare and Medicaid, and private health insurers, including managed care organizations and group purchasing organizations. Many patients will not be capable of paying themselves for some or all of the products that we may develop and will rely on third-party payors to pay for, or subsidize, their medical needs. If third-party payors do not provide coverage or reimbursement for any products that we may develop, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for our products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

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

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

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

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

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

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

Our competitors may develop products that make our products obsolete.

The biotechnology industry is highly fragmented and is characterized by rapid technological change. We face, and will continue to face, intense competition from biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research and development activities similar to ours. In addition, significant delays in the development of our drug candidates could allow our competitors to bring products to market before us, which would impair our ability to commercialize our drug candidates. Any products that we develop will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop products that would render our products, and those of our collaborators, obsolete and noncompetitive. For example, drug candidates are currently being developed by other pharmaceutical companies for the treatment of type 2 diabetes that act through SGLT2, one of the targets of LX4211, which are in more advanced stages of development than LX4211. In addition, there may be drug candidates of which we are not aware at an earlier stage of development that may compete with our drug candidates.

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

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

Risks Related to Our Relationships with Third Parties

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

We have derived a substantial majority of our revenues to date from collaborative drug discovery and development alliances with a limited number of major pharmaceutical companies. In addition, we currently intend to seek a collaboration partner for Phase 3 development of LX4211 in type 2 diabetes and we cannot be certain that we will be successful in establishing such a collaborative alliance on terms acceptable to us, if at all.

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

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

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

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

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

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

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

We currently do not have the manufacturing capabilities or experience necessary to produce materials for preclinical studies, clinical trials or commercial sales and intend in the future to continue to rely on collaborators and third-party contractors to produce such materials. We will rely on selected manufacturers to deliver materials on a timely basis and to comply with applicable regulatory requirements, including the current Good Manufacturing Practices of the FDA, which relate

to manufacturing and quality control activities. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. In addition, there are a limited number of manufacturers that operate under the FDA's current Good Manufacturing Practices and that are capable of producing such materials, and we may experience difficulty finding manufacturers with adequate capacity for our needs. If we are unable to contract for the production of sufficient quantity and quality of materials on acceptable terms, our product development and commercialization efforts may be delayed. Moreover, noncompliance with the FDA's current Good Manufacturing Practices can result in, among other things, fines, injunctions, civil and criminal penalties, product recalls or seizures, suspension of production, failure to obtain marketing approval and withdrawal, suspension or revocation of marketing approvals.

Risks Related to Our Intellectual Property

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

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

Because patent applications can take many years to issue, there may be currently pending applications which may later result in issued patents that cover the production, manufacture, commercialization or use of our technologies, drug targets or drug candidates. If any such patents are issued to other entities, we will be unable to obtain patent protection for the same or similar discoveries that we make. Moreover, we may be blocked from using or developing some of our existing or proposed technologies and products, or may be required to obtain a license that may not be available on reasonable terms, if at all. Further, others may discover uses for our technologies or products other than those covered in our issued or pending patents, and these other uses may be separately patentable. Even if we have a patent claim on a particular technology or product, the holder of a patent covering the use of that technology or product could exclude us from selling a product that is based on the same use of that product.

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

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

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

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

We may need to pursue litigation against others to enforce our patents and intellectual property rights and may be the subject of litigation brought by third parties to enforce their patent and intellectual property rights. In addition, we may become involved in litigation based on intellectual property indemnification undertakings that we have given to certain of our collaborators. Patent litigation is expensive and requires substantial amounts of management attention. The eventual outcome of any such litigation is uncertain and involves substantial risks.

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

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

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

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

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

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

Many of our employees and independent contractors were previously employed at universities, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and divert management's attention. If we fail in

defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain drug candidates, which could severely harm our business.

Risks Related to Employees, Advisors and Facilities Operations

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

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

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

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their availability to us. Although these advisors and collaborators generally agree not to perform competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In such a circumstance, our development efforts with respect to the matters on which they were working maybe significantly delayed or otherwise adversely affected. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

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

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

Risks Related to Environmental and Product Liability

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

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

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

We may be sued for product liability.

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

Risks Related to Our Common Stock

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

Invus, L.P. and Invus C.V., which we collectively refer to as Invus, and their affiliates currently own approximately 55.2% of the outstanding shares of our common stock and are thereby able to control the election and removal of our directors and determine our corporate and management policies, including potential mergers or acquisitions, asset sales, the amendment of our articles of incorporation or bylaws and other significant corporate transactions. This concentration of ownership may delay or deter possible changes in control of our company, which may reduce the value of an investment in our common stock. The interests of Invus and its affiliates may not coincide with the interests of other holders of our common stock.

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

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

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

The provisions of the stockholders' agreement relating to Invus' rights to designate members of our board of directors and its audit, compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus also has the right to terminate these provisions at any time in its discretion.

Invus has preemptive rights under the stockholders' agreement to participate in future equity issuances by us, subject to certain exceptions, so as to maintain its then-current percentage ownership of our capital stock. Subject to certain limitations, Invus will be required to exercise its preemptive rights in advance with respect to certain marketed offerings, in which case it will be obligated to buy its pro rata share of the number of shares being offered in such marketed offering, including any over-allotment (or such lesser amount specified in its exercise of such rights), so long as the sale of the shares were priced within a range within 10% above or below the market price on the date we notified Invus of the offering and we met certain other conditions.

The provisions of the stockholders' agreement relating to preemptive rights will terminate on the earlier to occur of August 28, 2017 and the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%.

Invus is entitled to certain consent rights under the stockholders' agreement, including with respect to (a) the creation or issuance of any new class or series of shares of our capital stock (or securities convertible into or exercisable for shares of

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

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

Our stock price may be extremely volatile.

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

- adverse results or delays in clinical trials;
- announcement of FDA approval or non-approval, or delays in the FDA review process, of our or our collaborators' product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators' or our competitors' clinical trials;
- the announcement of new products by us or our competitors;
- quarterly variations in our or our competitors' results of operations;
- conflicts or litigation with our collaborators;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- failure to achieve operating results projected by securities analysts;
- changes in earnings estimates or recommendations by securities analysts;
- financing transactions;
- developments in the biotechnology or pharmaceutical industry;
- sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;
- departures of key personnel or board members;
- developments concerning current or future collaborations;
- FDA or international regulatory actions;
- third-party reimbursement policies;
- acquisitions of other companies or technologies;
- disposition of any of our subsidiaries, drug programs or other technologies; and
- other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

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

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

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

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

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

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

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

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently own approximately 260,000 square feet of space for our corporate offices and laboratories in buildings located in The Woodlands, Texas, a suburb of Houston, Texas, and lease approximately 42,000 square feet of space for offices and laboratories near Princeton, New Jersey.

In April 2004, we purchased our facilities in The Woodlands, Texas from the lessor under our previous synthetic lease agreement. In connection with such purchase, we obtained a \$34.0 million mortgage which has a ten-year term with a 20-year amortization and bears interest at a fixed rate of 8.23%. The mortgage had a principal balance outstanding of \$23.5 million as of December 31, 2012.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a lease for our facility in Hopewell, New Jersey. Effective December 31, 2012, this lease was amended and now extends until June 2018. The amended lease provides for escalating yearly base rent payments starting at \$836,000 and increasing to \$941,000 in the final year of the lease. We are the guarantor of the obligations of our subsidiary under the lease.

We believe that our facilities are well-maintained, in good operating condition and acceptable for our current operations.

Item 3. *Legal Proceedings*

We are from time to time party to claims and legal proceedings that arise in the normal course of our business and that we believe will not have, individually or in the aggregate, a material adverse effect on our results of operations, financial condition or liquidity.

Item 4. *[Reserved]*

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

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

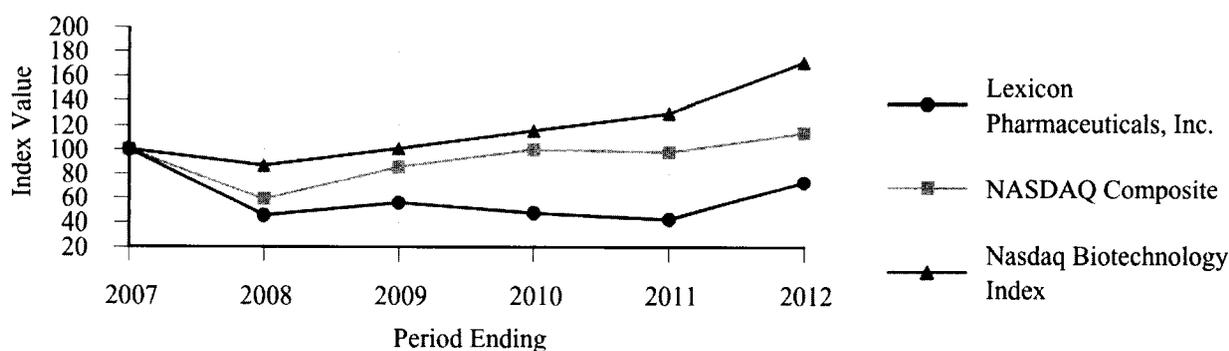
| | High | Low |
|----------------|---------|---------|
| 2011 | | |
| First Quarter | \$ 2.30 | \$ 1.44 |
| Second Quarter | \$ 1.87 | \$ 1.33 |
| Third Quarter | \$ 1.85 | \$ 0.92 |
| Fourth Quarter | \$ 1.31 | \$ 0.81 |
| 2012 | | |
| First Quarter | \$ 2.01 | \$ 1.13 |
| Second Quarter | \$ 2.36 | \$ 1.45 |
| Third Quarter | \$ 3.28 | \$ 2.05 |
| Fourth Quarter | \$ 2.75 | \$ 1.55 |

As of February 28, 2013, there were approximately 374 holders of record of our common stock.

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

Performance Graph

The following performance graph compares the performance of our common stock to the Nasdaq Composite Index and the Nasdaq Biotechnology Index for the period beginning December 31, 2007 and ending December 31, 2012. The graph assumes that the value of the investment in our common stock and each index was \$100 at December 31, 2007, and that all dividends were reinvested.



| | December 31, | | | | | |
|-------------------------------|---------------------|-------------|-------------|-------------|-------------|-------------|
| | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
| Lexicon Pharmaceuticals, Inc. | 100 | 46 | 56 | 48 | 43 | 73 |
| Nasdaq Composite Index | 100 | 59 | 86 | 100 | 98 | 114 |
| Nasdaq Biotechnology Index | 100 | 87 | 101 | 116 | 130 | 171 |

The foregoing stock price performance comparisons shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference by any general statement incorporating by reference this annual report on Form 10-K into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate such comparisons by reference.

Item 6. Selected Financial Data

The statements of comprehensive loss data for the years ended December 31, 2012, 2011 and 2010 and the balance sheet data as of December 31, 2012 and 2011 have been derived from our audited financial statements included elsewhere in this annual report on Form 10-K. The statements of comprehensive loss data for the years ended December 31, 2009 and 2008, and the balance sheet data as of December 31, 2010, 2009 and 2008 have been derived from our audited financial statements not included in this annual report on Form 10-K. Our historical results are not necessarily indicative of results to be expected for any future period. The data presented below has been derived from financial statements that have been prepared in accordance with accounting principles generally accepted in the United States and should be read with our financial statements, including the notes, and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this annual report on Form 10-K.

| | Year Ended December 31, | | | | |
|--|---------------------------------------|---------------------|---------------------|--------------------|--------------------|
| | 2012 | 2011 | 2010 | 2009 | 2008 |
| Statements of Comprehensive Loss Data: | (in thousands, except per share data) | | | | |
| Revenues | \$ 1,089 | \$ 1,849 | \$ 4,908 | \$ 10,700 | \$ 32,321 |
| Operating expenses: | | | | | |
| Research and development, including stock-based compensation of \$3,673 in 2012, \$3,249 in 2011, \$3,170 in 2010, \$3,022 in 2009 and \$3,941 in 2008 | 82,574 | 91,828 | 78,520 | 81,238 | 107,232 |
| Increase in fair value of Symphony Icon, Inc. purchase liability | 9,887 | 6,766 | 2,710 | — | — |
| General and administrative, including stock-based compensation of \$2,822 in 2012, \$2,458 in 2011, \$2,308 in 2010, \$2,252 in 2009 and \$2,559 in 2008 | 17,043 | 17,350 | 19,396 | 19,418 | 21,624 |
| Total operating expenses | 109,504 | 115,944 | 100,626 | 100,656 | 128,856 |
| Loss from operations | (108,415) | (114,095) | (95,718) | (89,956) | (96,535) |
| Interest and other income (expense), net | (1,796) | (2,120) | (6,083) | (3,463) | (349) |
| Consolidated net loss before taxes | (110,211) | (116,215) | (101,801) | (93,419) | (96,884) |
| Income tax benefit | — | — | 26 | 102 | — |
| Consolidated net loss | (110,211) | (116,215) | (101,775) | (93,317) | (96,884) |
| Less: net loss attributable to noncontrolling interest in Symphony Icon, Inc. | — | — | — | 10,537 | 20,024 |
| Net loss attributable to Lexicon Pharmaceuticals, Inc. | <u>\$ (110,211)</u> | <u>\$ (116,215)</u> | <u>\$ (101,775)</u> | <u>\$ (82,780)</u> | <u>\$ (76,860)</u> |
| Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted | <u>\$ (0.23)</u> | <u>\$ (0.34)</u> | <u>\$ (0.34)</u> | <u>\$ (0.57)</u> | <u>\$ (0.56)</u> |
| Shares used in computing net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted | 489,707 | 340,761 | 302,844 | 145,465 | 136,797 |
| | As of December 31, | | | | |
| | 2012 | 2011 | 2010 | 2009 | 2008 |
| Balance Sheet Data: | (in thousands) | | | | |
| Cash, cash equivalents and short-term investments, including restricted cash and investments of \$430 | \$ 223,208 | \$ 281,692 | \$ 211,111 | \$ 157,096 | \$ 86,502 |
| Short-term investments held by Symphony Icon, Inc. | — | — | — | 5,417 | 16,610 |
| Long-term investments | — | — | — | — | 55,686 |
| Working capital | 212,650 | 264,400 | 203,963 | 118,730 | 87,991 |
| Total assets | 371,778 | 430,512 | 366,884 | 257,761 | 261,508 |
| Long-term debt, net of current portion | 21,877 | 23,451 | 27,345 | 28,482 | 29,529 |
| Accumulated deficit | (899,832) | (789,621) | (673,406) | (570,175) | (487,395) |
| Lexicon Pharmaceuticals, Inc. stockholders' equity | 266,678 | 297,568 | 247,024 | 163,787 | 185,580 |

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis should be read with "Selected Financial Data" and our financial statements and notes included elsewhere in this annual report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We have used gene knockout technologies and an integrated platform of advanced medical technologies to identify and validate, *in vivo*, more than 100 targets with promising profiles for drug discovery. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential new drugs. We have multiple drug programs in various stages of clinical development and have advanced small molecule compounds from a number of additional drug programs into various stages of preclinical development and research.

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 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 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 leading pharmaceutical and biotechnology companies which generated near-term cash while offering us the potential to retain economic participation in products developed from the collaborations. 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.

We have derived substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses, and will continue to do so for the foreseeable future. To date, we have generated a substantial portion of our revenues from a limited number of sources.

Our operating results and, in particular, our ability to generate additional revenues are dependent on many factors, including our success in establishing new collaborations and licenses, the success rate of our discovery and development efforts leading to opportunities for new collaborations and licenses, the timing and willingness of collaborators to commercialize products that would result in milestone payments and royalties and their success in such efforts, and general and industry-specific economic conditions which may affect research and development expenditures. Future revenues from our existing collaborations and licenses are uncertain because they depend, to a large degree, on the achievement of milestones and payment of royalties we earn from any future products developed under the collaboration. As a result, we depend, in part, on securing new collaborations and license agreements. Our ability to secure future revenue-generating agreements will depend upon our ability to address the needs of our potential future collaborators and licensees, and to negotiate agreements that we believe are in our long-term best interests. We may determine, as we have with certain of our 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. Because of these and other factors, our operating results have fluctuated in the past and are likely to do so in the future, and we do not believe that period-to-period comparisons of our operating results are a good indication of our future performance.

Since our inception, we have incurred significant losses and, as of December 31, 2012, we had an accumulated deficit of \$899.8 million. Our losses have resulted principally from costs incurred in research and development, general and administrative costs associated with our operations, and non-cash stock-based compensation expenses associated with stock options and restricted stock granted to employees and consultants. Research and development expenses consist primarily of salaries and related personnel costs, external research costs related to our preclinical and clinical efforts, material costs, facility costs, depreciation on property and equipment, and other expenses related to our drug discovery and development programs. General and administrative expenses consist primarily of salaries and related expenses for executive and administrative personnel, professional fees and other corporate expenses, including information technology, facilities costs and general legal activities. We expect to continue to incur significant research and development costs in connection with our drug discovery and development programs. As a result, we will need to generate significantly higher revenues to achieve profitability.

Critical Accounting Policies

Revenue Recognition

We recognize revenues when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable, and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned.

Upfront fees under our drug discovery and development alliances are recognized as revenue on a straight-line basis over the estimated period of service, generally the contractual research term, as this period is our best estimate of the period over which the services will be rendered, to the extent they are non-refundable. We have determined that the level of effort we perform to meet our obligations is fairly constant throughout the estimated periods of service. As a result, we have determined that it is appropriate to recognize revenue from such agreements on a straight-line basis, as we believe this reflects how the research is provided during the initial period of the agreement. When it becomes probable that a collaborator will extend the research period, we adjust the revenue recognition method as necessary based on the level of effort required under the agreement for the extension period.

Research funding under these alliances is recognized as services are performed to the extent they are non-refundable, either on a straight-line basis over the estimated service period, generally the contractual research term; or as contract research costs are incurred. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Payments received under target validation collaborations and government grants and contracts are recognized as revenue as we perform our obligations related to such research to the extent such fees are non-refundable. Non-refundable technology license fees are recognized as revenue upon the grant of the license, when performance is complete and there is no continuing involvement.

Revenues recognized from multiple element contracts are allocated to each element of the arrangement based on the relative fair value of the elements. An element of a contract can be accounted for separately if the delivered elements have standalone value to the collaborator and the fair value of any undelivered elements is determinable through objective and reliable evidence. If an element is considered to have standalone value but the fair value of any of the undelivered items cannot be determined, all elements of the arrangement are recognized as revenue over the period of performance for such undelivered items or services.

A change in our revenue recognition policy or changes in the terms of contracts under which we recognize revenues could have an impact on the amount and timing of our recognition of revenues.

Research and Development Expenses

Research and development expenses consist of costs incurred for research and development activities solely sponsored by us as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred.

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

- LX4211, an orally-delivered small molecule compound that we are developing as a treatment for type 1 and type 2 diabetes;
- LX1032, or telotristat etiprate, an orally-delivered small molecule compound that we are developing as a treatment for carcinoid syndrome and ulcerative colitis;
- LX1033, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome;
- LX2931, an orally-delivered small molecule compound that is in development as a treatment for rheumatoid arthritis and other autoimmune diseases; and
- LX7101, a topically-delivered small molecule compound that is in development as a treatment for glaucoma.

We have also advanced small molecule compounds from a number of additional drug programs into various stages of preclinical development and research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline. The drug development process takes many years to complete. The cost and length of time varies due to many factors including the type, complexity and intended use of the drug candidate. We estimate that drug development activities are typically completed over the following periods:

| <u>Phase</u> | <u>Estimated Completion Period</u> |
|-------------------------|------------------------------------|
| Preclinical development | 1-2 years |
| Phase 1 clinical trials | 1-2 years |
| Phase 2 clinical trials | 1-2 years |
| Phase 3 clinical trials | 2-4 years |

We expect research and development costs to increase in the future as our existing clinical drug programs advance to later stage clinical trials and new drug programs enter preclinical and clinical development. Due to the variability in the length of time necessary for drug development, the uncertainties related to the cost of these activities and ultimate ability to obtain governmental approval for commercialization, accurate and meaningful estimates of the ultimate costs to bring our potential drug candidates to market are not available.

We record significant accrued liabilities related to unbilled expenses for products or services that we have received from service providers, specifically related to ongoing preclinical studies and clinical trials. These costs primarily relate to clinical study management, monitoring, laboratory and analysis costs, drug supplies, toxicology studies and investigator grants. We have multiple drugs in concurrent preclinical studies and clinical trials at clinical sites throughout the world. In order to ensure that we have adequately provided for ongoing preclinical and clinical development costs during the period in which we incur such costs, we maintain accruals to cover these expenses. Substantial portions of our preclinical studies and clinical trials are performed by third-party laboratories, medical centers, contract research organizations and other vendors. For preclinical studies, we accrue expenses based upon estimated percentage of work completed and the contract milestones remaining. For clinical studies, expenses are accrued based upon the number of patients enrolled and the duration of the study. We monitor patient enrollment, the progress of clinical studies and related activities to the extent possible through internal reviews of data reported to us by the vendors and clinical site visits. Our estimates depend on the timeliness and accuracy of the data provided by our vendors regarding the status of each program and total program spending. We periodically evaluate the estimates to determine if adjustments are necessary or appropriate based on information we receive. Although we use consistent milestones or subject or patient enrollment to drive expense recognition, the assessment of these costs is a subjective process that requires judgment. Upon settlement, these costs may differ materially from the amounts accrued in our consolidated financial statements.

We record our research and development costs by type or category, rather than by project. Significant categories of costs include personnel, facilities and equipment costs, laboratory supplies and third-party and other services. In addition, a significant portion of our research and development expenses is not tracked by project as it benefits multiple projects. Consequently, fully-loaded research and development cost summaries by project are not available.

Stock-based Compensation Expense

We recognize compensation expense in our statements of comprehensive loss for share-based payments, including stock options issued to employees, based on their fair values on the date of the grant, with the compensation expense recognized over the period in which an employee is required to provide service in exchange for the stock award. Stock-based compensation expense for awards without performance conditions is recognized on a straight-line basis. Stock-based compensation expense for awards with performance conditions is recognized over the period from the date the performance condition is determined to be probable of occurring through the time the applicable condition is met. We had stock-based compensation expense of \$6.5 million for the year ended December 31, 2012, or \$0.01 per share. As of December 31, 2012, stock-based compensation cost for all outstanding unvested options was \$10.2 million, which is expected to be recognized over a weighted-average vesting period of 1.3 years.

The fair value of stock options is estimated at the date of grant using the Black-Scholes option-pricing model. For purposes of determining the fair value of stock options, we segregate our options into two homogeneous groups, based on exercise and post-vesting employment termination behaviors, resulting in a change in the assumptions used for expected option lives and forfeitures. Expected volatility is based on the historical volatility in our stock price. The following weighted-average assumptions were used for options granted in the years ended December 31, 2012, 2011 and 2010, respectively:

| | Expected Volatility | Risk-free Interest Rate | Expected Term | Dividend Rate |
|-------------------------------------|--------------------------------|------------------------------------|--------------------------|--------------------------|
| December 31, 2012: | | | | |
| Employees | 93% | 0.8% | 5 | 0% |
| Officers and non-employee directors | 81% | 1.5% | 8 | 0% |
| December 31, 2011: | | | | |
| Employees | 88% | 2.2% | 5 | 0% |
| Officers and non-employee directors | 78% | 3.2% | 8 | 0% |
| December 31, 2010: | | | | |
| Employees | 86% | 2.3% | 5 | 0% |
| Officers and non-employee directors | 80% | 3.3% | 8 | 0% |

Impairment of Long-Lived Assets

Our long-lived assets include property, plant and equipment, intangible assets and goodwill. We regularly review long-lived assets for impairment. The recoverability of long-lived assets, other than goodwill, is measured by comparing the assets carrying amount to the expected undiscounted future cash flows that the asset is expected to generate. Determining whether an impairment has occurred typically requires various estimates and assumptions, including determining which cash flows are directly related to the potentially impaired asset, the useful life over which cash flows will occur, their amount, and the asset's residual value, if any. We use internal cash flow estimates, quoted market prices when available and independent appraisals as appropriate to determine fair value. We derive the required cash flow estimates from our historical experience and our internal business plans and apply an appropriate discount rate. During the years ended December 31, 2011 and 2010, we determined that one of our buildings was impaired and therefore recorded impairment losses of \$800,000 and \$900,000, respectively, which were recorded as research and development expense in the accompanying statements of comprehensive loss. In June 2011, we sold this building with an immaterial additional loss on the sale. There were no significant impairments of long-lived assets in 2012.

Goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. We have determined that the reporting unit is the single operating segment disclosed in our current financial statements. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. We determined that the market capitalization approach is the most appropriate method of measuring fair value of the reporting unit. Under this approach, fair value is calculated as the average closing price of our common stock for the 30 days preceding the date that the annual impairment test is performed, multiplied by the number of outstanding shares on that date. A control premium, which is representative of premiums paid in the marketplace to acquire a controlling interest in a company, is then added to the market capitalization to determine the fair value of the reporting unit. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if we encounter events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2012, 2011 and 2010.

Business Combinations

We allocate the purchase price of acquired businesses to the tangible and intangible assets acquired and liabilities assumed based upon their estimated fair values on the acquisition date. The purchase price allocation process requires management to make significant estimates and assumptions, especially at acquisition date with respect to intangible assets and in-process research and development.

These assumptions are based in part on historical experience and are inherently uncertain. Examples of critical estimates in valuing certain of the intangible assets we have acquired or may acquire in the future include but are not limited to: the feasibility and timing of achievement of development, regulatory and commercial milestones; expected costs to develop the in-process research and development into commercially viable products; and future expected cash flows from product sales.

In connection with the purchase price allocations for acquisitions, we estimate the fair value of the contingent payments. The estimated fair value of any contingent payments is determined utilizing a probability-based income approach inclusive of an estimated discount rate.

Unanticipated events and circumstances may occur which may affect the accuracy or validity of such assumptions, estimates or actual results.

Recent Accounting Pronouncements

See Note 3, Recent Accounting Pronouncements, of the Notes to Consolidated Financial Statements, for a discussion of the impact of new accounting standards on our consolidated financial statements.

Results of Operations – Comparison of Years Ended December 31, 2012, 2011 and 2010

Revenues

Total revenues and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

| | Year Ended December 31, | | |
|---------------------|-------------------------|----------|--------|
| | 2012 | 2011 | 2010 |
| Total revenues | \$ 1.1 | \$ 1.8 | \$ 4.9 |
| Dollar decrease | \$ (0.8) | \$ (3.1) | |
| Percentage decrease | (41)% | (62)% | |

Years Ended December 31, 2012 and 2011

- *Collaborative research* – Revenue from collaborative research decreased 52% to \$0.8 million, primarily due to reduced revenues from functional genomics contracts and from the United States Army Medical Research Acquisition Activity.
- *Subscription and license fees* – Revenues from subscriptions and license fees increased 41% to \$0.3 million, primarily due to increases in technology license fees.

Years Ended December 31, 2011 and 2010

- *Collaborative research* – Revenue from collaborative research decreased 61% to \$1.6 million, primarily due to reduced revenues under our alliance with Taconic Farms and from the United States Army Medical Research Acquisition Activity.
- *Subscription and license fees* – Revenue from subscriptions and license fees decreased 70% to \$0.2 million, primarily due to decreases in technology license fees.

In 2012, Taconic Farms, Inc. and Deltagen, Inc. represented 68% and 25% of revenues, respectively. In 2011, Taconic Farms, Texas A&M Institute for Genomic Medicine and United States Army Medical Research Acquisition Activity represented 46%, 20% and 20% of revenues, respectively. In 2010, Taconic Farms and United States Army Medical Research Acquisition Activity represented 35% and 23% of revenues, respectively.

Research and Development Expenses

Research and development expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

| | Year Ended December 31, | | |
|--|-------------------------|---------|---------|
| | 2012 | 2011 | 2010 |
| Total research and development expense | \$ 82.6 | \$ 91.8 | \$ 78.5 |
| Dollar increase (decrease) | \$ (9.3) | \$ 13.3 | |
| Percentage increase (decrease) | (10)% | 17% | |

Research and development expenses consist primarily of third-party and other services principally related to preclinical and clinical development activities, salaries and other personnel-related expenses, facility and equipment costs, laboratory supplies and stock-based compensation expenses.

Years Ended December 31, 2012 and 2011

- *Third-party and other services* – Third-party and other services decreased 6% in 2012 to \$32.9 million, primarily due to a decrease in our external preclinical research and development costs, partially offset by an increase in external clinical research and development costs. Third-party and other services relate principally to our clinical trial and related development activities, such as preclinical and clinical studies and contract manufacturing.
- *Personnel* – Personnel costs decreased 12% in 2012 to \$26.4 million, primarily due to reductions in our personnel in January 2012. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.
- *Facilities and equipment* – Facilities and equipment costs decreased 17% in 2012 to \$11.5 million, primarily due to an impairment of buildings due to excess capacity in 2011 and decreases in depreciation expense and rent costs.
- *Laboratory supplies* – Laboratory supplies expense decreased 33% in 2012 to \$3.5 million primarily due to reductions in early-stage research activities.
- *Stock-based compensation* – Stock-based compensation expense increased 13% in 2012 to \$3.7 million.
- *Other* – Other costs increased 5% to \$4.5 million.

Years Ended December 31, 2011 and 2010

- *Third-party and other services* – Third-party and other services increased 78% in 2011 to \$35.0 million, primarily due to an increase in our external preclinical and clinical research and development costs.
- *Personnel* – Personnel costs decreased 1% in 2011 to \$30.2 million.
- *Facilities and equipment* – Facilities and equipment costs decreased 8% in 2011 to \$13.8 million, primarily due to decreases in depreciation expense and maintenance costs.
- *Laboratory supplies* – Laboratory supplies expense decreased 18% in 2011 to \$5.2 million primarily due to reductions in early-stage research activities.
- *Stock-based compensation* – Stock-based compensation expense was \$3.2 million, consistent with the prior year.
- *Other* – Other costs increased 13% to \$4.3 million.

Increase in Fair Value of Symphony Icon Liability

The increase in fair value of the Symphony Icon purchase liability was \$9.9 million, \$6.8 million and \$2.7 million for the years ended December 31, 2012, 2011 and 2010, respectively (see Note 10, Arrangements with Symphony Icon, Inc., of the Notes to Consolidated Financial Statements, for more information).

General and Administrative Expenses

General and administrative expenses and dollar and percentage changes as compared to the prior year are as follows (dollar amounts are presented in millions):

| | Year Ended December 31, | | |
|--|-------------------------|----------|---------|
| | 2012 | 2011 | 2010 |
| Total general and administrative expense | \$ 17.0 | \$ 17.4 | \$ 19.4 |
| Dollar decrease | \$ (0.3) | \$ (2.0) | |
| Percentage decrease | (2)% | (11)% | |

General and administrative expenses consist primarily of personnel costs to support our research and development activities, stock-based compensation expense, professional fees such as legal fees, and facility and equipment costs.

Years Ended December 31, 2012 and 2011

- *Personnel* – Personnel costs decreased 4% in 2012 to \$8.0 million. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.
- *Stock-based compensation* – Stock-based compensation expense increased 15% in 2012 to \$2.8 million.
- *Professional fees* – Professional fees in 2012 were \$2.8 million, consistent with the prior year.
- *Facilities and equipment* – Facilities and equipment costs decreased 12% in 2012 to \$2.0 million, primarily due to reduced rent costs.
- *Other* – Other costs decreased 8% in 2012 to \$1.4 million.

Years Ended December 31, 2011 and 2010

- *Personnel* – Personnel costs decreased 9% in 2011 to \$8.3 million due to a reduction in our personnel in February 2011.
- *Stock-based compensation* – Stock-based compensation expense increased 6% in 2011 to \$2.5 million.
- *Professional fees* – Professional fees decreased 24% in 2011 to \$2.8 million, primarily due to decreased patent-related, other legal and consulting costs.
- *Facilities and equipment* – Facilities and equipment costs decreased 7% in 2011 to \$2.3 million, primarily due to reduced maintenance costs.
- *Other* – Other costs decreased 19% in 2011 to \$1.5 million.

Interest Income, Interest Expense and Other Income (Expense), Net

Interest Income. Interest income decreased 16% in 2012 to \$0.2 million from \$0.3 million in 2011 and decreased 51% in 2011 from \$0.5 million in 2010, primarily due to lower yields on our investments.

Interest Expense. Interest expense decreased 16% in 2012 to \$2.1 million from \$2.5 million in 2011 and decreased 7% in 2011 from \$2.7 million in 2010.

Other Income (Expense), Net. Other income, net decreased to \$0.1 million in 2012 from \$0.2 million in 2011. Other expense, net decreased to \$0.2 million income in 2011 from \$4.0 million expense in 2010 primarily due to amortization of the Symphony Icon purchase asset in 2010.

Income Tax Benefit

The income tax benefit for the years ended December 31, 2012, 2011 and 2010 was \$0, \$0 and \$26,000, respectively.

Consolidated Net Loss and Consolidated Net Loss per Common Share

Consolidated net loss decreased to \$110.2 million in 2012 from \$116.2 million in 2011 and increased from \$101.8 million in 2010. Net loss per common share was \$0.23 in 2012, a decrease from \$0.34 in 2011 and 2010.

Liquidity and Capital Resources

We have financed our operations from inception primarily through sales of common and preferred stock, contract and milestone payments to us under our drug discovery and development collaborations, target validation, database subscription and technology license agreements, government grants and contracts and financing under debt and lease arrangements. We

have also financed certain of our research and development activities under our agreements with Symphony Icon, Inc. From our inception through December 31, 2012, we had received net proceeds of \$985.8 million from issuances of common and preferred stock. In addition, from our inception through December 31, 2012, we received \$456.1 million in cash payments from drug discovery and development collaborations, target validation, database subscription and technology license agreements, sales of compound libraries and reagents and government grants and contracts, of which \$442.5 million had been recognized as revenues through December 31, 2012.

As of December 31, 2012, we had \$223.2 million in cash, cash equivalents and investments. As of December 31, 2011, we had \$281.7 million in cash, cash equivalents. We used cash of \$94.5 million in operations in 2012. This consisted primarily of the consolidated net loss for the year of \$110.2 million and a net increase in other operating assets net of liabilities of \$4.8 million, partially offset by non-cash charges of \$9.9 million related to the increase in fair value of the Symphony Icon purchase liability, \$6.5 million related to stock-based compensation expense and \$4.2 million related to depreciation expense. Investing activities used cash of \$97.8 million in 2012, primarily due to net purchases of investments of \$97.4 million and purchases of property and equipment of \$0.5 million. Financing activities provided cash of \$36.4 million primarily due to net proceeds from issuance of common stock of \$38.1 million, partially offset by repayment of debt borrowings of \$1.4 million.

Symphony Drug Development Financing Agreements. In June 2007, we entered into a series of related agreements providing for the financing of the clinical development of certain drug programs, including LX1032 and LX1033, along with any other pharmaceutical compositions modulating the same targets as those drug candidates. Under the financing arrangement, we licensed to Symphony Icon, Inc., a then wholly-owned subsidiary of Symphony Icon Holdings LLC, our intellectual property rights related to the programs and Holdings contributed \$45 million to Symphony Icon in order to fund the clinical development of the programs. We also issued and sold to Holdings shares of our common stock in exchange for \$15 million and received an exclusive option to acquire all of the equity of Symphony Icon, thereby allowing us to reacquire the programs.

Upon the recommendation of Symphony Icon's development committee, which was comprised of an equal number of representatives from us and Symphony Icon, Symphony Icon's board of directors had the right to require us to pay Symphony Icon up to \$15 million for Symphony Icon's use in the development of the programs in accordance with a specified development plan and related development budget. Through July 2010, Symphony Icon's board of directors requested us to pay Symphony Icon \$9.3 million under the agreement, all of which was paid prior to the exercise of the purchase option in July 2010.

In July 2010, we entered into an amended and restated purchase option agreement with Symphony Icon and Holdings and simultaneously exercised our purchase option. Pursuant to the amended terms of the purchase option, we paid Holdings \$10 million in July 2010 and issued 13,237,519 shares of common stock to designees of Holdings in July 2012 in satisfaction of an additional \$35 million base payment obligation.

We also agreed to make up to \$45 million in additional contingent payments, which will consist of 50% of any consideration we receive pursuant to any licensing transaction under which we grant a third party rights to commercialize LX1032, LX1033 or other pharmaceutical compositions modulating the same target as those drug candidates, which we refer to as the "LG103 programs," subject to certain exceptions. The contingent payments will be due if and when we receive such consideration from such a licensing transaction. In the event we receive regulatory approval in the United States for the marketing and sale of any product resulting from the LG103 programs prior to entering into such a licensing transaction for the commercialization of such product in the United States, in lieu of any contingent payment from such a licensing transaction, we will pay Holdings the sum of \$15 million and the amount of certain expenses we incurred after our exercise of the purchase option which are attributable to the development of such product, reduced by up to 50% of such sum for the amount of any contingent payments paid prior to such United States regulatory approval attributable to any such licensing transaction outside of the United States with respect to such product. In the event we make any such payment upon United States regulatory approval, we will have no obligation to make subsequent contingent payments attributable to any such licensing transactions for the commercialization of such product outside the United States until the proceeds of such licensing transactions exceed 50% of the payment made as a result of such United States regulatory approval.

The contingent payments may be paid in cash or a combination of cash and common stock, in our discretion, provided that no more than 50% of any contingent payment will be paid in common stock.

Texas Institute for Genomic Medicine. In July 2005, we received an award from the Texas Enterprise Fund for the creation of a knockout mouse embryonic stem cell library containing 350,000 cell lines for the Texas Institute for Genomic Medicine, or TIGM, using our proprietary gene trapping technology, which we completed in 2007. We also equipped TIGM with the bioinformatics software required for the management and analysis of data relating to the library. The Texas Enterprise

Fund made an additional award to the Texas A&M University System for the creation of facilities and infrastructure to house the library.

Under the terms of our award, we are responsible for the creation of a specified number of jobs beginning in 2012, reaching an aggregate of 1,616 new jobs in Texas by December 31, 2016. We will receive credits against those job obligations based on funding received by TIGM and certain related parties from sources other than the State of Texas. We will also receive credits against those jobs obligations for any surplus jobs we create. We may be required to repay the state a portion of the award if we fail to meet those job obligations. Subject to these credits, if we fail to create the specified number of jobs, the State may require us to repay \$2,415 for each job we fall short beginning in 2013. Our maximum aggregate exposure for such payments, if we fail to create any new jobs, is approximately \$14.2 million, without giving effect to any credits to which we may be entitled.

Facilities. In April 2004, we obtained a \$34.0 million mortgage on our facilities in The Woodlands, Texas. The mortgage loan has a ten-year term with a 20-year amortization and bears interest at a fixed rate of 8.23%. The mortgage balance has a principal balance of \$23.5 million as of December 31, 2012. A balloon payment of \$21.4 million is due in April 2014.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. leased a 76,000 square-foot laboratory and office space in Hopewell, New Jersey. Effective December 31, 2012, this lease was amended to decrease the space to approximately 42,000 square feet. The term of the amended lease extends until June 30, 2018. The amended lease provides for escalating yearly base rent payments starting at \$836,000 and increasing to \$941,000 in the final year of the lease. We are the guarantor of the obligations of our subsidiary under the lease.

Including the lease and debt obligations described above, we had incurred the following contractual obligations as of December 31, 2012:

| Contractual Obligations | Payments due by period (in millions) | | | | |
|------------------------------|--------------------------------------|------------------|-----------|-----------|-------------------|
| | Total | Less than 1 year | 2-3 years | 4-5 years | More than 5 years |
| Debt | \$ 23.5 | \$ 1.6 | \$ 21.9 | \$ — | \$ — |
| Interest payment obligations | 2.6 | 1.9 | 0.7 | — | — |
| Operating leases | 5.1 | 0.2 | 2.1 | 2.2 | 0.6 |
| Total | \$ 31.2 | \$ 3.7 | \$ 24.7 | \$ 2.2 | \$ 0.6 |

The foregoing table does not include any potential payments related to the award we received from the Texas Enterprise Fund. Under the terms of the award, we are responsible for the creation of jobs beginning in 2012. Subject to credits, if we fail to create the specified number of jobs, the State of Texas may require us to repay \$2,415 for each job we fall short beginning in 2013 and continuing until 2019. Our maximum aggregate exposure for such payment, if we fail to create any new jobs, is approximately \$14.2 million, without giving effect to any credits to which we may be entitled. See Note 16, Collaboration and License Agreements, of the Notes to Consolidated Financial Statements, for further discussion.

Our future capital requirements will be substantial and will depend on many factors, including our ability to obtain drug discovery and development collaborations and other collaborations and technology license agreements, the amount and timing of payments under such agreements, the level and timing of our research and development expenditures, market acceptance of our products, the resources we devote to developing and supporting our products and other factors. Our capital requirements will also be affected by any expenditures we make in connection with license agreements and acquisitions of and investments in complementary technologies and businesses. We expect to devote substantial capital resources to continue our research and development efforts, to expand our support and product development activities, and for other general corporate activities. We believe that our current unrestricted cash and investment balances and cash and revenues we expect to derive from drug discovery and development collaborations, other collaborations and technology licenses and other sources will be sufficient to fund our operations for at least the next 12 months. During or after this period, if cash generated by operations is insufficient to satisfy our liquidity requirements, we will need to sell additional equity or debt securities or obtain additional credit arrangements. Additional financing may not be available on terms acceptable to us or at all. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders.

Disclosure about Market Risk

We are exposed to limited market and credit risk on our cash equivalents which have maturities of three months or less at the time of purchase. We maintain a short-term investment portfolio which consists of U.S. Treasury bills, money market accounts, and certificates of deposit that mature three to 12 months from the time of purchase, which we believe are subject to limited market and credit risk. We currently do not hedge interest rate exposure or hold any derivative financial instruments in our investment portfolio.

We had approximately \$223.2 million in cash and cash equivalents and short-term investments as of December 31, 2012. We believe that the working capital available to us will be sufficient to meet our cash requirements for at least the next 12 months.

We have operated primarily in the United States and substantially all sales to date have been made in U.S. dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations.

Item 7A. *Quantitative and Qualitative Disclosures About Market Risk*

See “Disclosure about Market Risk” under “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations” for quantitative and qualitative disclosures about market risk.

Item 8. *Financial Statements and Supplementary Data*

The financial statements required by this Item are incorporated under Item 15 in Part IV of this report.

Item 9. *Changes in and Disagreements with Accountants on Accounting and Financial Disclosure*

None.

Item 9A. *Controls and Procedures*

Our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures (as defined in rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) are effective to ensure that the information required to be disclosed by us in the reports we file under the Securities Exchange Act is gathered, analyzed and disclosed with adequate timeliness, accuracy and completeness, based on an evaluation of such controls and procedures as of the end of the period covered by this report.

Subsequent to our evaluation, there were no significant changes in internal controls or other factors that could significantly affect internal controls, including any corrective actions with regard to significant deficiencies and material weaknesses.

Management Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act).

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2012. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework*.

Based on such assessment using those criteria, management believes that, as of December 31, 2012, our internal control over financial reporting is effective.

Our independent auditors have also audited our internal control over financial reporting as of December 31, 2012 as stated in the audit report which appears on page F-2 and is incorporated under Item 15 in Part IV of this report.

Item 9B. *Other Information*

None.

PART III

Item 10. *Directors, Executive Officers and Corporate Governance*

The information required by this Item is hereby incorporated by reference from (a) the information appearing under the captions “Election of Directors,” “Stock Ownership of Certain Beneficial Owners and Management,” “Corporate Governance” and “Executive and Director Compensation” in our definitive proxy statement which involves the election of directors and is to be filed with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2012 and (b) the information appearing under Item 1 in Part I of this report.

Item 11. *Executive Compensation*

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Corporate Governance” and “Executive and Director Compensation” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2012. Notwithstanding the foregoing, in accordance with the instructions to Item 407(e)(5) of Regulation S-K, the information contained in our proxy statement under the sub-heading “Compensation Committee Report” shall not be deemed to be filed as part of or incorporated by reference into this annual report on Form 10-K.

Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Stock Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2012.

Item 13. *Certain Relationships and Related Transactions, and Director Independence*

The information required by this Item is hereby incorporated by reference from the information appearing under the captions “Corporate Governance” and “Transactions with Related Persons” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2012.

Item 14. *Principal Accounting Fees and Services*

The information required by this Item as to the fees we pay our principal accountant is hereby incorporated by reference from the information appearing under the caption “Ratification and Approval of Independent Auditors” in our definitive proxy statement which involves the election of directors and is to be filed with the Commission pursuant to the Securities Exchange Act of 1934 within 120 days of the end of our fiscal year on December 31, 2012.

PART IV

Item 15. Exhibits and Financial Statement Schedules

- (a) Documents filed as a part of this report:
1. Consolidated Financial Statements

| | Page |
|--|-------------|
| <u>Report of Independent Registered Public Accounting Firm</u> | <u>F-1</u> |
| <u>Report of Independent Registered Public Accounting Firm</u> | <u>F-2</u> |
| <u>Consolidated Balance Sheets</u> | <u>F-3</u> |
| <u>Consolidated Statements of Comprehensive Loss</u> | <u>F-4</u> |
| <u>Consolidated Statements of Stockholders' Equity</u> | <u>F-5</u> |
| <u>Consolidated Statements of Cash Flows</u> | <u>F-6</u> |
| <u>Notes to Consolidated Financial Statements</u> | <u>F-7</u> |

2. Financial Statement Schedules

All other financial statement schedules are omitted because they are not applicable or not required, or because the required information is included in the financial statements or notes thereto.

3. Exhibits

| Exhibit No. | Description |
|--------------------|--|
| 3.1 | — Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein). |
| 3.2 | — Second Amended and Restated Bylaws (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein). |
| 4.1 | — Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.2 | — Amendment, dated October 7, 2009, to Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 7, 2009 and incorporated by reference herein). |
| 4.3 | — Registration Rights Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.4 | — Stockholders' Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein). |
| 4.5 | — Supplement to Transaction Agreements, dated March 15, 2010, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated March 15, 2010 and incorporated by reference herein). |
| 4.6 | — Supplement No. 2 to Transaction Agreements, dated February 23, 2012, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated February 23, 2012 and incorporated by reference herein). |
| 4.7 | — Amended and Restated Purchase Option Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC and Symphony Icon, Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |
| 4.8 | — Amended and Restated Registration Rights Agreement, dated July 30, 2010, with Symphony Icon Holdings LLC (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated July 30, 2010 and incorporated by reference herein). |

| Exhibit No. | Description |
|-------------|--|
| 10.1 | — Restated Employment Agreement with Arthur T. Sands, M.D., Ph.D. (filed as Exhibit 10.1 to the Company's Annual Report on Form 10-K for the period ended December 31, 2005 and incorporated by reference herein). |
| 10.2 | — Employment Agreement with Alan Main, Ph.D. (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2001 and incorporated by reference herein). |
| 10.3 | — Employment Agreement with Jeffrey L. Wade, J.D. (filed as Exhibit 10.3 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein). |
| 10.4 | — Employment Agreement with Brian P. Zambrowicz, Ph.D. (filed as Exhibit 10.4 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein). |
| 10.5 | — Offer Letter, dated March 10, 2011, with Pablo Lapuerta, M.D. (filed as Exhibit 10.5 to the Company's Annual Report on Form 10-K for the period ended December 31, 2011 and incorporated by reference herein). |
| 10.6 | — Consulting Agreement with Alan S. Nies, M.D. dated February 19, 2003, as amended (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2010 and incorporated by reference herein). |
| 10.7 | — Consulting Agreement with Robert J. Lefkowitz, M.D. dated March 31, 2003 (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2003 and incorporated by reference herein). |
| 10.8 | — Form of Indemnification Agreement with Officers and Directors (filed as Exhibit 10.7 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein). |
| 10.9 | — Summary of Non-Employee Director Compensation (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein). |
| 10.10 | — Equity Incentive Plan, as amended (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein). |
| 10.11 | — Non-Employee Directors' Equity Incentive Plan, as amended (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein). |
| 10.12 | — Form of Stock Option Agreement with Chairman of Board of Directors under the Equity Incentive Plan (filed as Exhibit 10.17 to the Company's Annual Report on Form 10-K for the period ended December 31, 2005 and incorporated by reference herein). |
| 10.13 | — Form of Stock Option Agreement with Directors under the Non-Employee Directors' Equity Incentive Plan (filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K for the year ended December 31, 2009 and incorporated by reference herein). |
| 10.14 | — Form of Stock Option Agreement with Officers under the Equity Incentive Plan, as amended (filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K for the period ended December 31, 2011 and incorporated by reference herein). |
| *10.15 | — Form of Restricted Stock Unit Agreement with Officers under the Equity Incentive Plan, as amended. |
| †10.16 | — Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company (filed as Exhibit 10.15 to the amendment to the Company's Annual Report on Form 10-K/A for the period ended December 31, 2003, as filed on July 16, 2004, and incorporated by reference herein). |
| †10.17 | — First Amendment, dated May 30, 2006, to Collaboration and License Agreement, dated December 17, 2003, with Bristol-Myers Squibb Company (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2006, and incorporated by reference herein). |
| †10.18 | — Collaboration Agreement, dated July 27, 2004, with Takeda Pharmaceutical Company Limited (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2004 and incorporated by reference herein). |
| †10.19 | — Collaboration and License Agreement, dated February 16, 2010, with N.V. Organon and its affiliates Intervet Inc. and Schering Corporation, acting through its Schering-Plough Research Institute division (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2010 and incorporated by reference herein). |
| †10.20 | — Second Amended and Restated Collaboration and License Agreement, dated November 30, 2005, with Genentech, Inc. (filed as Exhibit 10.22 to the Company's Annual Report on Form 10-K for the period ended December 31, 2005 and incorporated by reference herein). |

| Exhibit No. | Description |
|--------------------|---|
| 10.21 | — Amendment, dated June 8, 2009, to Second Amended and Restated Collaboration and License Agreement, dated November 30, 2005, with Genentech, Inc. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A dated June 8, 2009 and incorporated by reference herein). |
| 10.22 | — Economic Development Agreement dated July 15, 2005, with the State of Texas and the Texas A&M University System (filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2005 and incorporated by reference herein). |
| 10.23 | — Amendment, dated April 30, 2008, to Economic Development Agreement, dated July 15, 2005, with the State of Texas and the Texas A&M University System (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated April 30, 2008 and incorporated by reference herein). |
| 10.24 | — Loan and Security Agreement, dated April 21, 2004, between Lex-Gen Woodlands, L.P. and iStar Financial Inc. (filed as Exhibit 10.18 to the Company's Annual Report on Form 10-K for the period ended December 31, 2004 and incorporated by reference herein). |
| 21.1 | — Subsidiaries (filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the period ended December 31, 2010 and incorporated by reference herein). |
| *23.1 | — Consent of Independent Registered Public Accounting Firm. |
| *24.1 | — Power of Attorney (contained in signature page). |
| *31.1 | — Certification of Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| *31.2 | — Certification of Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| *32.1 | — Certification of Principal Executive and Principal Financial Officers Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| *101.INS | — XBRL Instance Document. |
| *101.SCH | — XBRL Taxonomy Extension Schema Document. |
| *101.CAL | — XBRL Taxonomy Extension Calculation Linkbase Document. |
| *101.DEF | — XBRL Taxonomy Extension Definition Linkbase Document. |
| *101.LAB | — XBRL Taxonomy Extension Label Linkbase Document. |
| *101.PRE | — XBRL Taxonomy Extension Presentation Linkbase Document. |

* Filed herewith.

† Confidential treatment has been requested for a portion of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

| | |
|---------------------|---|
| Date: March 7, 2013 | Lexicon Pharmaceuticals, Inc. By: <u>/s/ ARTHUR T. SANDS</u> Arthur T. Sands, M.D., Ph.D. <i>President and Chief Executive Officer</i> |
| Date: March 7, 2013 | By: <u>/s/ JEFFREY L. WADE</u> Jeffrey L. Wade <i>Executive Vice President, Corporate Development and Chief Financial Officer</i> |

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Arthur T. Sands and Jeffrey L. Wade, or either of them, each with the power of substitution, his or her attorney-in-fact, to sign any amendments to this Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, here ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

| Signature | Title | Date |
|--|---|---------------|
| /s/ ARTHUR T. SANDS Arthur T. Sands, M.D., Ph.D. | President, Chief Executive Officer and Director (Principal Executive Officer) | March 7, 2013 |
| /s/ JEFFREY L. WADE Jeffrey L. Wade | Executive Vice President, Corporate Development and Chief Financial Officer (Principal Financial Officer) | March 7, 2013 |
| /s/ JAMES F. TESSMER James F. Tessmer | Vice President, Finance and Accounting (Principal Accounting Officer) | March 7, 2013 |
| /s/ RAYMOND DEBBANE Raymond Debbane | Chairman of the Board of Directors | March 7, 2013 |
| /s/ PHILIPPE J. AMOUYAL Philippe J. Amouyal | Director | March 7, 2013 |
| /s/ SAMUEL L. BARKER Samuel L. Barker, Ph.D. | Director | March 7, 2013 |
| /s/ ROBERT J. LEFKOWITZ Robert J. Lefkowitz, M.D. | Director | March 7, 2013 |
| /s/ ALAN S. NIES Alan S. Nies, M.D. | Director | March 7, 2013 |
| /s/ FRANK P. PALANTONI Frank P. Palantoni | Director | March 7, 2013 |
| /s/ CHRISTOPHER J. SOBECKI Christopher J. Sobecki | Director | March 7, 2013 |
| /s/ JUDITH L. SWAIN Judith L. Swain, M.D. | Director | March 7, 2013 |

**Report of Independent
Registered Public Accounting Firm**

The Board of Directors and Stockholders
of Lexicon Pharmaceuticals, Inc.:

We have audited the accompanying consolidated balance sheets of Lexicon Pharmaceuticals, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2012. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Lexicon Pharmaceuticals, Inc. as of December 31, 2012 and 2011, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 10 to the consolidated financial statements, in fiscal year 2010 the Company changed its method of accounting for Symphony Icon, Inc., a variable interest entity, with the adoption of the amendments to the Financial Accounting Standards Board Accounting Standards Codification 810, *Consolidation*, effective January 1, 2010.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Lexicon Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 11, 2013 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Houston, Texas
March 11, 2013

**Report of Independent
Registered Public Accounting Firm**

The Board of Directors and Stockholders
of Lexicon Pharmaceuticals, Inc.:

We have audited Lexicon Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Lexicon Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Lexicon Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Lexicon Pharmaceuticals, Inc. and subsidiaries as of December 31, 2012 and 2011, and the related consolidated statements of comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2012 and our report dated March 11, 2013 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Houston, Texas
March 11, 2013

Lexicon Pharmaceuticals, Inc.
Consolidated Balance Sheets
(In thousands, except par value)

| | As of December 31, | |
|---|--------------------|------------|
| | 2012 | 2011 |
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 30,423 | \$ 186,309 |
| Short-term investments, including restricted investments of \$430 | 192,785 | 95,383 |
| Accounts receivable, net of allowances of \$35 | 1,378 | 350 |
| Prepaid expenses and other current assets | 6,349 | 3,748 |
| Total current assets | 230,935 | 285,790 |
| Property and equipment, net of accumulated depreciation and amortization of \$83,416 and \$80,535, respectively | 42,634 | 46,417 |
| Goodwill | 44,543 | 44,543 |
| Other intangible assets | 53,557 | 53,557 |
| Other assets | 109 | 205 |
| Total assets | \$ 371,778 | \$ 430,512 |
| Liabilities and Equity | | |
| Current liabilities: | | |
| Accounts payable | \$ 7,661 | \$ 6,042 |
| Accrued liabilities | 8,922 | 13,786 |
| Current portion of deferred revenue | 128 | 119 |
| Current portion of long-term debt | 1,574 | 1,443 |
| Total current liabilities | 18,285 | 21,390 |
| Deferred revenue, net of current portion | 13,910 | 14,212 |
| Long-term debt | 21,877 | 23,451 |
| Deferred tax liabilities | 18,745 | 18,745 |
| Other long-term liabilities | 32,283 | 55,146 |
| Total liabilities | 105,100 | 132,944 |
| Commitments and contingencies | | |
| Equity: | | |
| Preferred stock, \$.01 par value; 5,000 shares authorized; no shares issued and outstanding | — | — |
| Common stock, \$.001 par value; 900,000 shares authorized; 512,375 and 480,389 shares issued, respectively | 512 | 480 |
| Additional paid-in capital | 1,166,605 | 1,087,033 |
| Accumulated deficit | (899,832) | (789,621) |
| Accumulated other comprehensive gain | 23 | 21 |
| Treasury stock, at cost, 380 and 218 shares, respectively | (630) | (345) |
| Total equity | 266,678 | 297,568 |
| Total liabilities and equity | \$ 371,778 | \$ 430,512 |

The accompanying notes are an integral part of these consolidated financial statements.

Lexicon Pharmaceuticals, Inc.

Consolidated Statements of Comprehensive Loss
(In thousands, except per share amounts)

| | Year Ended December 31, | | |
|--|-------------------------|--------------|--------------|
| | 2012 | 2011 | 2010 |
| Revenues: | | | |
| Collaborative research | \$ 783 | \$ 1,632 | \$ 4,191 |
| Subscription and license fees | 306 | 217 | 717 |
| Total revenues | 1,089 | 1,849 | 4,908 |
| Operating expenses: | | | |
| Research and development, including stock-based compensation of \$3,673, \$3,249 and \$3,170, respectively | 82,574 | 91,828 | 78,520 |
| Increase in fair value of Symphony Icon, Inc. purchase liability | 9,887 | 6,766 | 2,710 |
| General and administrative, including stock-based compensation of \$2,822, \$2,458 and \$2,308, respectively | 17,043 | 17,350 | 19,396 |
| Total operating expenses | 109,504 | 115,944 | 100,626 |
| Loss from operations | (108,415) | (114,095) | (95,718) |
| Gain on investments, net | — | — | 141 |
| Interest income | 213 | 255 | 519 |
| Interest expense | (2,114) | (2,528) | (2,719) |
| Other income (expense), net | 105 | 153 | (4,024) |
| Consolidated net loss before taxes | (110,211) | (116,215) | (101,801) |
| Income tax benefit | — | — | 26 |
| Consolidated net loss | \$ (110,211) | \$ (116,215) | \$ (101,775) |
| Consolidated net loss per common share, basic and diluted | \$ (0.23) | \$ (0.34) | \$ (0.34) |
| Shares used in computing consolidated net loss per common share, basic and diluted | 489,707 | 340,761 | 302,844 |
| Other comprehensive gain (loss): | | | |
| Unrealized gain on investments | 2 | 16 | 5 |
| Comprehensive loss | \$ (110,209) | \$ (116,199) | \$ (101,770) |

The accompanying notes are an integral part of these consolidated financial statements.

Lexicon Pharmaceuticals, Inc.

**Consolidated Statements of Stockholders' Equity
(In thousands)**

Lexicon Pharmaceuticals, Inc. Stockholders

| | <u>Common Stock</u> | | <u>Additional Paid-In Capital</u> | <u>Accumulated Deficit</u> | <u>Accumulated Other Comprehensive Gain</u> | <u>Treasury Stock</u> | <u>Total</u> | <u>Noncontrolling Interest</u> | <u>Total Equity</u> |
|---|---------------------|------------------|---|--------------------------------|---|---------------------------|--------------|------------------------------------|-------------------------|
| | <u>Shares</u> | <u>Par Value</u> | | | | | | | |
| Balance at December 31, 2009 | 175,785 | \$ 176 | \$ 733,874 | \$ (570,175) | \$ — | \$ (88) | \$ 163,787 | \$ (290) | \$ 163,497 |
| Deconsolidation of Symphony Icon, Inc. | — | — | — | — | — | — | — | 290 | 290 |
| Cumulative-effect adjustment for adoption of new accounting principle | — | — | — | (1,456) | — | — | (1,456) | — | (1,456) |
| Stock-based compensation | — | — | 5,116 | — | — | — | 5,116 | — | 5,116 |
| Issuance of common stock, net of fees | 161,770 | 162 | 181,312 | — | — | — | 181,474 | — | 181,474 |
| Issuance of common stock under Equity Incentive Plans | 11 | — | 22 | — | — | — | 22 | — | 22 |
| Repurchase of common stock | — | — | — | — | — | (149) | (149) | — | (149) |
| Net loss | — | — | — | (101,775) | — | — | (101,775) | — | (101,775) |
| Unrealized gain on investments | — | — | — | — | 5 | — | 5 | — | 5 |
| Balance at December 31, 2010 | 337,566 | 338 | 920,324 | (673,406) | 5 | (237) | 247,024 | — | 247,024 |
| Stock-based compensation | — | — | 5,707 | — | — | — | 5,707 | — | 5,707 |
| Issuance of common stock under Equity Incentive Plans | 330 | — | 552 | — | — | — | 552 | — | 552 |
| Issuance of common stock, net of fees | 142,493 | 142 | 160,450 | — | — | — | 160,592 | — | 160,592 |
| Repurchase of common stock | — | — | — | — | — | (108) | (108) | — | (108) |
| Net loss | — | — | — | (116,215) | — | — | (116,215) | — | (116,215) |
| Unrealized gain on investments | — | — | — | — | 16 | — | 16 | — | 16 |
| Balance at December 31, 2011 | 480,389 | 480 | 1,087,033 | (789,621) | 21 | (345) | 297,568 | — | 297,568 |
| Stock-based compensation | — | — | 6,495 | — | — | — | 6,495 | — | 6,495 |
| Issuance of common stock to designees of Symphony Icon Holdings LLC | 13,238 | 13 | 34,987 | — | — | — | 35,000 | — | 35,000 |
| Issuance of common stock under Equity Incentive Plans | 1,248 | 1 | 1,053 | — | — | — | 1,054 | — | 1,054 |
| Issuance of common stock, net of fees | 17,500 | 18 | 37,037 | — | — | — | 37,055 | — | 37,055 |
| Repurchase of common stock | — | — | — | — | — | (285) | (285) | — | (285) |
| Net loss | — | — | — | (110,211) | — | — | (110,211) | — | (110,211) |
| Unrealized gain on investments | — | — | — | — | 2 | — | 2 | — | 2 |
| Balance at December 31, 2012 | 512,375 | \$ 512 | \$ 1,166,605 | \$ (899,832) | \$ 23 | \$ (630) | \$ 266,678 | \$ — | \$ 266,678 |

The accompanying notes are an integral part of these consolidated financial statements.

Lexicon Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(In thousands)

| | Year Ended December 31, | | |
|--|--------------------------------|-------------------|------------------|
| | 2012 | 2011 | 2010 |
| Cash flows from operating activities: | | | |
| Consolidated net loss | \$ (110,211) | \$ (116,215) | \$ (101,775) |
| Adjustments to reconcile consolidated net loss to net cash used in operating activities: | | | |
| Depreciation | 4,190 | 4,887 | 5,394 |
| Impairment of fixed assets | — | 704 | 1,001 |
| Amortization of Symphony Icon, Inc. purchase option | — | — | 3,957 |
| Increase in fair value of Symphony Icon, Inc. purchase liability | 9,887 | 6,766 | 2,710 |
| Stock-based compensation | 6,495 | 5,707 | 5,478 |
| Net gain on auction rate securities ("ARS") and ARS Rights | — | — | (141) |
| Changes in operating assets and liabilities: | | | |
| (Increase) decrease in accounts receivable | (1,028) | 394 | 488 |
| (Increase) decrease in prepaid expenses and other current assets | (2,601) | (865) | 6,704 |
| (Increase) decrease in other assets | 96 | 414 | (218) |
| Increase (decrease) in accounts payable and other liabilities | (995) | 10,365 | (5,238) |
| Decrease in deferred revenue | (293) | (95) | (728) |
| Net cash used in operating activities | <u>(94,460)</u> | <u>(87,938)</u> | <u>(82,368)</u> |
| Cash flows from investing activities: | | | |
| Purchases of property and equipment | (492) | (1,206) | (1,132) |
| Proceeds from disposal of property and equipment | 85 | 2,625 | 64 |
| Acquisition of Symphony Icon, Inc., net of cash acquired | — | — | (5,561) |
| Purchases of investments | (233,250) | (108,092) | (155,856) |
| Maturities of investments | 135,850 | 176,628 | 48,641 |
| Net cash provided by (used in) investing activities | <u>(97,807)</u> | <u>69,955</u> | <u>(113,844)</u> |
| Cash flows from financing activities: | | | |
| Proceeds from issuance of common stock, net of fees | 38,109 | 160,781 | 181,496 |
| Repurchase of common stock | (285) | (108) | (149) |
| Proceeds from debt borrowings | — | — | 11,377 |
| Repayment of debt borrowings | (1,443) | (3,589) | (49,858) |
| Net cash provided by financing activities | <u>36,381</u> | <u>157,084</u> | <u>142,866</u> |
| Net increase (decrease) in cash and cash equivalents | <u>(155,886)</u> | <u>139,101</u> | <u>(53,346)</u> |
| Cash and cash equivalents at beginning of year | 186,309 | 47,208 | 100,554 |
| Cash and cash equivalents at end of year | <u>\$ 30,423</u> | <u>\$ 186,309</u> | <u>\$ 47,208</u> |
| Supplemental disclosure of cash flow information: | | | |
| Cash paid for interest | \$ 2,028 | \$ 2,447 | \$ 2,424 |
| Cash received related to income taxes | \$ — | \$ — | \$ 26 |
| Supplemental disclosure of noncash investing and financing activities: | | | |
| Unrealized gain on investments | \$ 2 | \$ 16 | \$ 5 |
| Common stock issued in satisfaction of Symphony Icon base payment obligation | \$ 35,000 | \$ — | \$ — |
| Intangible assets acquired with long-term liabilities | \$ — | \$ — | \$ 43,557 |

The accompanying notes are an integral part of these consolidated financial statements.

Lexicon Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

December 31, 2012

1. Organization and Operations

Lexicon Pharmaceuticals, Inc. (“Lexicon” or the “Company”) is a Delaware corporation incorporated on July 7, 1995. Lexicon was organized to discover the functions and pharmaceutical utility of genes and use those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease.

Lexicon has financed its operations from inception primarily through sales of common and preferred stock, contract and milestone payments to it under drug discovery and development collaborations, target validation, database subscription and technology license agreements, government grants and contracts and financing under debt and lease arrangements. The Company’s future success is dependent upon many factors, including, but not limited to, its ability to discover and develop pharmaceutical products for the treatment of human disease, establish new collaboration and license agreements, achieve milestones under such agreements, obtain and enforce patents and other proprietary rights in its discoveries, comply with federal and state regulations, and maintain sufficient capital to fund its activities. As a result of the aforementioned factors and the related uncertainties, there can be no assurance of the Company’s future success.

2. Summary of Significant Accounting Policies

Basis of Presentation: The accompanying consolidated financial statements include the accounts of Lexicon and its wholly-owned subsidiaries. Intercompany transactions and balances are eliminated in consolidation.

Use of Estimates: The preparation of financial statements in conformity with U. S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the period. Actual results could differ from those estimates.

Cash, Cash Equivalents and Short-Term Investments: Lexicon considers all highly-liquid investments with original maturities of three months or less to be cash equivalents. As of December 31, 2012 and 2011, short-term investments consist of U.S. treasury bills and certificates of deposit. The certificates of deposits are classified as available-for-sale securities and are carried at fair value, based on quoted market prices of the securities. The Company views its available-for-sale securities as available for use in current operations regardless of the stated maturity date of the security. Unrealized gains and losses on such securities are reported as a separate component of stockholders’ equity. Net realized gains and losses, interest and dividends are included in interest income. The cost of securities sold is based on the specific identification method.

Restricted Cash and Investments: Lexicon is required to maintain restricted cash or investments to collateralize standby letters of credit for the lease on its office and laboratory facilities in Hopewell, New Jersey (see Note 11). As of December 31, 2012 and 2011, restricted cash and investments were \$0.4 million and \$0.4 million, respectively.

Accounts Receivable: Lexicon records trade accounts receivable in the normal course of business related to the sale of products or services. The allowance for doubtful accounts takes into consideration such factors as historical write-offs, the economic climate and other factors that could affect collectibility. Write-offs are evaluated on a case by case basis.

Concentration of Credit Risk: Lexicon's cash equivalents, investments and accounts receivable represent potential concentrations of credit risk. The Company attempts to minimize potential concentrations of risk in cash equivalents and investments by placing investments in high-quality financial instruments. The Company’s accounts receivable are unsecured and are concentrated in pharmaceutical and biotechnology companies located in the United States and Europe. The Company has not experienced any significant credit losses to date. In 2012, customers in the United States represented 100% of revenue. In 2011, customers in the United States represented 100% of revenue. In 2010, customers in the United States and Europe represented 94% and 6% of revenue, respectively. At December 31, 2012, management believes that the Company has no significant concentrations of credit risk.

Segment Information and Significant Customers: Lexicon operates in one business segment, which primarily focuses on the discovery of the functions and pharmaceutical utility of genes and the use of those gene function discoveries in the discovery and development of pharmaceutical products for the treatment of human disease. Substantially all of the Company’s

revenues have been derived from drug discovery alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, technology licenses, subscriptions to its databases, government grants and contracts and compound library sales. In 2012, Taconic Farms, Inc. and Deltagen, Inc. represented 68% and 25% of revenues, respectively. In 2011, Taconic Farms, Texas A&M Institute for Genomic Medicine and United States Army Medical Research Acquisition Activity represented 46%, 20% and 20% of revenues, respectively. In 2010, Taconic Farms and United States Army Medical Research Acquisition Activity represented 35% and 23% of revenues, respectively.

Property and Equipment: Property and equipment are carried at cost and depreciated using the straight-line method over the estimated useful life of the assets which ranges from three to 40 years. Maintenance, repairs and minor replacements are charged to expense as incurred. Leasehold improvements are amortized over the shorter of the estimated useful life or the remaining lease term. Significant renewals and betterments are capitalized.

Impairment of Long-Lived Assets: Long-lived assets and certain identifiable intangible assets to be held and used are reviewed for impairment when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values.

Goodwill Impairment: Goodwill is not amortized, but is tested at least annually for impairment at the reporting unit level. The Company has determined that the reporting unit is the single operating segment disclosed in its current financial statements. Impairment is the condition that exists when the carrying amount of goodwill exceeds its implied fair value. The first step in the impairment process is to determine the fair value of the reporting unit and then compare it to the carrying value, including goodwill. If the fair value exceeds the carrying value, no further action is required and no impairment loss is recognized. Additional impairment assessments may be performed on an interim basis if the Company encounters events or changes in circumstances that would indicate that, more likely than not, the carrying value of goodwill has been impaired. There was no impairment of goodwill in 2012, 2011 or 2010.

Revenue Recognition: Revenues are recognized when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable and collectibility is reasonably assured. Payments received in advance under these arrangements are recorded as deferred revenue until earned. Revenues are earned from drug discovery and development collaborations, target validation collaborations, database subscriptions, technology licenses, and government grants and contracts. Revenues generated from third parties under collaborative arrangements are recorded on a gross basis on the consolidated statements of comprehensive loss as Lexicon is the principal participant for these transactions for the purpose of accounting for these arrangements.

Upfront fees under drug discovery and development collaborations are recognized as revenue on a straight-line basis over the estimated period of service, generally the contractual research term, as this period is Lexicon's best estimate of the period over which the services will be rendered, to the extent they are non-refundable. Lexicon has determined that the level of effort it performs to meet its obligations is fairly constant throughout the estimated periods of service. As a result, Lexicon has determined that it is appropriate to recognize revenue from such agreements on a straight-line basis, as management believes this reflects how the research is provided during the initial period of the agreement. When it becomes probable that a collaborator will extend the research period, Lexicon adjusts the revenue recognition method as necessary based on the level of effort required under the agreement for the extension period.

Research funding under these alliances is recognized as services are performed to the extent they are non-refundable, either on a straight-line basis over the estimated service period, generally the contractual research term, or as contract research costs are incurred. Milestone-based fees are recognized upon completion of specified milestones according to contract terms. Payments received under target validation collaborations and government grants and contracts are recognized as revenue as Lexicon performs its obligations related to such research to the extent such fees are non-refundable. Non-refundable technology license fees are recognized as revenue upon the grant of the license when performance is complete and there is no continuing involvement.

The Company analyzes its multiple element arrangements to determine whether the elements can be separated and accounted for individually as separate units of accounting. An element of a contract can be accounted for separately if the delivered elements have standalone value to the collaborator and the fair value of any undelivered elements is determinable through objective and reliable evidence. If an element is considered to have standalone value but the fair value of any of the undelivered items cannot be determined, all elements of the arrangement are recognized as revenue over the period of performance for such undelivered items or services.

Research and Development Expenses: Research and development expenses consist of costs incurred for company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses and are expensed as incurred. Technology license fees for technologies that are utilized in research and development and have no alternative future use are expensed when incurred. Substantial portions of the Company's preclinical and clinical trials are performed by third-party laboratories, medical centers, contract research organizations and other vendors. For preclinical studies, the Company accrues expenses based upon estimated percentage of work completed and the contract milestones remaining. For clinical studies, expenses are accrued based upon the number of patients enrolled and the duration of the study. The Company monitors patient enrollment, the progress of clinical studies and related activities to the extent possible through internal reviews of data reported to the Company by the vendors and clinical site visits. The Company's estimates depend on the timeliness and accuracy of the data provided by the vendors regarding the status of each program and total program spending. The Company periodically evaluates the estimates to determine if adjustments are necessary or appropriate based on information it receives.

Stock-Based Compensation: The Company recognizes compensation expense in its statements of comprehensive loss for share-based payments, including stock options and restricted stock units issued to employees, based on their fair values on the date of the grant, with the compensation expense recognized over the period in which an employee is required to provide service in exchange for the stock award. Stock-based compensation expense for awards without performance conditions is recognized on a straight-line basis. Stock-based compensation expense for awards with performance conditions is recognized over the period from the date the performance condition is determined to be probable of occurring through the time the applicable condition is met. As of December 31, 2012, stock-based compensation cost for all outstanding unvested options and restricted stock units was \$10.2 million, which is expected to be recognized over a weighted-average period of 1.3 years.

The fair value of stock options is estimated at the date of grant using the Black-Scholes method. The Black-Scholes option-pricing model requires the input of subjective assumptions. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options. For purposes of determining the fair value of stock options, the Company segregates its options into two homogeneous groups, based on exercise and post-vesting employment termination behaviors, resulting in a change in the assumptions used for expected option lives and forfeitures. Expected volatility is based on the historical volatility in the Company's stock price. The following weighted-average assumptions were used for options granted in the years ended December 31, 2012, 2011 and 2010, respectively:

| | Expected Volatility | Risk-free Interest Rate | Expected Term | Dividend Rate |
|-------------------------------------|------------------------|----------------------------|------------------|------------------|
| December 31, 2012: | | | | |
| Employees | 93% | 0.8% | 5 | 0% |
| Officers and non-employee directors | 81% | 1.5% | 8 | 0% |
| December 31, 2011: | | | | |
| Employees | 88% | 2.2% | 5 | 0% |
| Officers and non-employee directors | 78% | 3.2% | 8 | 0% |
| December 31, 2010: | | | | |
| Employees | 86% | 2.3% | 5 | 0% |
| Officers and non-employee directors | 80% | 3.3% | 8 | 0% |

Net Loss per Common Share: Net loss per common share is computed using the weighted average number of shares of common stock outstanding. Shares associated with stock options, restricted stock units and warrants are not included because they are antidilutive.

3. Recent Accounting Pronouncements

In June 2011, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2011-05, "Presentation of Comprehensive Income", which improves the comparability, consistency, and transparency of financial reporting and increases the prominence of items reported in other comprehensive income ("OCI") by eliminating the option to present components of OCI as part of the statement of stockholders' equity. The amendments in this standard require that all non-owner changes in stockholders' equity be presented either in a single continuous statement of comprehensive

income or in two separate but consecutive statements. Under either method, adjustments must be displayed for items that are reclassified from OCI to net income, in both net income and OCI. The standard does not change the current option for presenting components of OCI gross or net of the effect of income taxes, provided that such tax effects are presented in the statement in which OCI is presented or disclosed in the notes to the financial statements. Additionally, the standard does not affect the calculation or reporting of earnings per share. This pronouncement should be applied retrospectively for fiscal years beginning after December 15, 2011, with early adoption permitted. Lexicon adopted this pronouncement in 2012 and there was no material impact to its consolidated results of operations and financial condition.

In July 2012, the FASB issued ASU No. 2012-02, "Testing Indefinite-Lived Intangible Assets for Impairment", which amends FASB ASC Topic 350. ASU 2012-02 gives companies the option to perform a qualitative assessment to determine whether it is more likely than not that an indefinite-lived intangible asset is impaired. If the qualitative assessment supports the conclusion that it is more likely than not that the fair value of the asset exceeds its carrying amount, the entity would not need to perform the two-step quantitative impairment test. ASU 2012-02 is effective for annual and interim impairment tests performed for fiscal years beginning after September 15, 2012, with early adoption permitted. Lexicon adopted this pronouncement in 2012 and there was no material impact to its consolidated results of operations and financial condition.

4. Cash and Cash Equivalents and Investments

The fair value of cash and cash equivalents and investments held at December 31, 2012 and 2011 are as follows:

| | As of December 31, 2012 | | | |
|---|-------------------------|------------------------|-------------------------|----------------------|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
| | (in thousands) | | | |
| Cash and cash equivalents | \$ 30,423 | \$ — | \$ — | \$ 30,423 |
| Securities maturing within one year: | | | | |
| Certificates of deposit | 551 | — | — | 551 |
| U.S. treasury securities | 192,211 | 24 | (1) | 192,234 |
| Total short-term investments | \$ 192,762 | \$ 24 | \$ (1) | \$ 192,785 |
| Total cash and cash equivalents and investments | \$ 223,185 | \$ 24 | \$ (1) | \$ 223,208 |

| | As of December 31, 2011 | | | |
|---|-------------------------|------------------------|-------------------------|----------------------|
| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Estimated Fair Value |
| | (in thousands) | | | |
| Cash and cash equivalents | \$ 186,309 | \$ — | \$ — | \$ 186,309 |
| Securities maturing within one year: | | | | |
| Certificates of deposit | 548 | — | — | 548 |
| U.S. treasury securities | 94,814 | 24 | (3) | 94,835 |
| Total short-term investments | \$ 95,362 | \$ 24 | \$ (3) | \$ 95,383 |
| Total cash and cash equivalents and investments | \$ 281,671 | \$ 24 | \$ (3) | \$ 281,692 |

There were no realized gains or losses for the year ended December 31, 2012, no realized gains or losses for the year ended December 31, 2011, and no realized gains or losses for the year ended December 31, 2010.

5. Fair Value Measurements

The Company uses various inputs in determining the fair value of its investments and measures these assets on a recurring basis. Assets and liabilities recorded at fair value in the consolidated balance sheets are categorized by the level of

objectivity associated with the inputs used to measure their fair value. The following levels are directly related to the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities:

- Level 1 – quoted prices in active markets for identical assets
- Level 2 – other significant observable inputs (including quoted prices for similar investments, market corroborated inputs, etc.)
- Level 3 – significant unobservable inputs (including the Company’s own assumptions in determining the fair value of assets and liabilities)

The inputs or methodology used for valuing securities are not necessarily an indication of the credit risk associated with investing in those securities. The following tables provide the fair value measurements of applicable Company assets and liabilities that are measured at fair value on a recurring basis according to the fair value levels defined above as of December 31, 2012 and 2011.

| Assets and Liabilities at Fair Value | | | | |
|---|-------------------|----------------|------------------|-------------------|
| As of December 31, 2012 | | | | |
| | Level 1 | Level 2 | Level 3 | Total |
| (in thousands) | | | | |
| Assets | | | | |
| Cash and cash equivalents | \$ 30,423 | \$ — | \$ — | \$ 30,423 |
| Short-term investments | 192,785 | — | — | 192,785 |
| Total cash and cash equivalents and investments | <u>\$ 223,208</u> | <u>\$ —</u> | <u>\$ —</u> | <u>\$ 223,208</u> |
| Liabilities | | | | |
| Other long-term liabilities | \$ — | \$ — | \$ 29,920 | \$ 29,920 |
| Total liabilities | <u>\$ —</u> | <u>\$ —</u> | <u>\$ 29,920</u> | <u>\$ 29,920</u> |

| Assets and Liabilities at Fair Value | | | | |
|---|-------------------|----------------|------------------|-------------------|
| As of December 31, 2011 | | | | |
| | Level 1 | Level 2 | Level 3 | Total |
| (in thousands) | | | | |
| Assets | | | | |
| Cash and cash equivalents | \$ 186,309 | \$ — | \$ — | \$ 186,309 |
| Short-term investments | 95,383 | — | — | 95,383 |
| Total cash and cash equivalents and investments | <u>\$ 281,692</u> | <u>\$ —</u> | <u>\$ —</u> | <u>\$ 281,692</u> |
| Liabilities | | | | |
| Other long-term liabilities | \$ — | \$ — | \$ 55,033 | \$ 55,033 |
| Total liabilities | <u>\$ —</u> | <u>\$ —</u> | <u>\$ 55,033</u> | <u>\$ 55,033</u> |

The Company did not have any Level 3 financial assets during the years ended December 31, 2012 and 2011. In 2010, Lexicon held auction rate securities and related rights that permitted Lexicon to require the investment bank that sold Lexicon the auction rate securities to purchase its auction rate securities at par value. On June 30, 2010, Lexicon exercised the rights and the investment bank purchased Lexicon's remaining auction rate securities at par value on July 1, 2010. The table presented below summarizes the change in consolidated balance sheet carrying value associated with Level 3 financial assets for the year ended December 31, 2010.

| | <u>Short-term Investments</u> |
|---|-----------------------------------|
| | <u>(in thousands)</u> |
| Balance at December 31, 2009 | \$ 56,034 |
| Unrealized gains included in earnings as gain on investments, net | 141 |
| Net sales and settlements | (56,175) |
| Balance at December 31, 2010 | <u>\$ —</u> |

Transfers between levels are recognized at the actual date of circumstance that caused the transfer. The Company's Level 3 liabilities are estimated using a probability-based income approach utilizing an appropriate discount rate. Subsequent changes in the fair value of the Symphony Icon purchase consideration liability are recorded as an increase or decrease in Symphony Icon purchase liability in the accompanying consolidated statements of comprehensive loss. During the years ended December 31, 2012, 2011 and 2010, the fair value of the Symphony Icon ("Symphony Icon") purchase consideration liability increased by \$9.9 million, \$6.8 million and \$2.7 million, respectively. The following table summarizes the change in consolidated balance sheet carrying value associated with Level 3 liabilities for the years ended December 31, 2010, 2011 and 2012.

| | <u>Other Long-term Liabilities</u> |
|--|--|
| | <u>(in thousands)</u> |
| Balance at December 31, 2009 | \$ — |
| Purchase consideration liability resulting from the Symphony Icon acquisition | 45,557 |
| Change in valuation of purchase consideration payable to former Symphony Icon stockholders | 2,710 |
| Balance at December 31, 2010 | <u>48,267</u> |
| Change in valuation of purchase consideration payable to former Symphony Icon stockholders | 6,766 |
| Balance at December 31, 2011 | <u>55,033</u> |
| Change in valuation of purchase consideration payable to former Symphony Icon stockholders | 9,887 |
| Payment of base payment obligation with common stock | (35,000) |
| Balance at December 31, 2012 | <u>\$ 29,920</u> |

The Company also has assets that under certain conditions are subject to measurement at fair value on a non-recurring basis. These assets include goodwill associated with the acquisitions of Coelacanth Corporation in 2001 and Symphony Icon on July 30, 2010 and intangible assets associated with the acquisition of Symphony Icon on July 30, 2010. For these assets, measurement at fair value in periods subsequent to their initial recognition is applicable if one or more is determined to be impaired.

6. Property and Equipment

Property and equipment at December 31, 2012 and 2011 are as follows:

| | Estimated Useful Lives In Years | As of December 31, | |
|---|---------------------------------------|--------------------|-----------|
| | | 2012 | 2011 |
| | | (in thousands) | |
| Computers and software | 3-5 | \$ 11,042 | \$ 10,986 |
| Furniture and fixtures | 5-7 | 7,343 | 7,391 |
| Laboratory equipment | 3-7 | 36,065 | 37,030 |
| Leasehold improvements | 7-10 | 9,991 | 9,934 |
| Buildings | 15-40 | 58,945 | 58,947 |
| Land | — | 2,664 | 2,664 |
| Total property and equipment | | 126,050 | 126,952 |
| Less: Accumulated depreciation and amortization | | (83,416) | (80,535) |
| Net property and equipment | | \$ 42,634 | \$ 46,417 |

During the years ended December 31, 2011 and 2010, the Company determined that one of its buildings was impaired and therefore recorded impairment losses of \$800,000 and \$900,000, respectively, which were recorded as research and development expense in the accompanying statements of comprehensive loss. The fair value of the impaired building was estimated using sales prices in similar real estate sales and offers received from potential purchasers of the building. In June 2011, the Company sold this building with an immaterial additional loss on the sale.

7. Income Taxes

Lexicon recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently in the financial statements and tax returns. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax bases of liabilities and assets using enacted tax rates and laws in effect in the years in which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on a more-likely-than-not criteria in determining if a valuation allowance should be provided.

The components of Lexicon's deferred tax assets (liabilities) at December 31, 2012 and 2011 are as follows:

| | As of December 31, | |
|--|--------------------|-------------|
| | 2012 | 2011 |
| | (in thousands) | |
| Deferred tax assets: | | |
| Net operating loss carryforwards | \$ 216,579 | \$ 195,810 |
| Research and development tax credits | 32,066 | 34,611 |
| Capitalized research and development | 71,839 | 60,938 |
| Stock-based compensation | 12,972 | 11,843 |
| Deferred revenue | 4,906 | 5,008 |
| Other | 10,429 | 7,126 |
| Total deferred tax assets | 348,791 | 315,336 |
| Deferred tax liabilities: | | |
| Deferred tax liability related to acquisition of Symphony Icon | (18,745) | (18,745) |
| Other | (340) | (343) |
| Total deferred tax liabilities | (19,085) | (19,088) |
| Less: valuation allowance | (348,451) | (314,993) |
| Net deferred tax liabilities | \$ (18,745) | \$ (18,745) |

The \$18.7 million deferred tax liability relates to the tax impact of future amortization or possible impairments associated with intangible assets acquired with Symphony Icon, which are not deductible for tax purposes. Lexicon does not believe it can estimate the reversal of the temporary difference related to the assets acquired with sufficient certainty such that the related deferred tax liability could be considered as a source of taxable income in assessing the Company's need for a valuation allowance.

At December 31, 2012, Lexicon had both federal and state NOL carryforwards of approximately \$602.5 million and \$394.3 million, respectively. The federal and state NOL carryforwards began to expire in 2011 and continued to expire in 2012. The Company has R&D tax credit carryforwards of approximately \$32.1 million expiring beginning in 2012. Utilization of the NOL and R&D credit carryforwards may be subject to a significant annual limitation due to ownership changes that have occurred previously or could occur in the future provided by Section 382 of the Internal Revenue Code. Based on the federal tax law limits and the Company's cumulative loss position, Lexicon concluded it was appropriate to establish a full valuation allowance for its net deferred tax assets until an appropriate level of profitability is sustained. During the year ended December 31, 2012, the valuation allowance increased \$33.5 million, primarily due to the Company's current year net loss. Lexicon recorded income tax benefits of \$0, \$0 and \$26,000 in the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012 and 2011, the Company did not have any unrecognized tax benefits.

The Company is primarily subject to U.S. federal and New Jersey and Texas state income taxes. The tax years 1995 to current remain open to examination by U.S. federal authorities and 2004 to current remain open to examination by state authorities. The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2012 and 2011, the Company had no accruals for interest or penalties related to income tax matters.

8. Goodwill

On July 12, 2001, Lexicon completed the acquisition of Coelacanth Corporation in a merger. Coelacanth, now Lexicon Pharmaceuticals (New Jersey), Inc., forms the core of the Company's division responsible for small molecule compound discovery. The results of Lexicon Pharmaceuticals (New Jersey), Inc. are included in the Company's results of operations for the period subsequent to the acquisition. Goodwill associated with the acquisition of \$25.8 million, which represents the excess of the \$36.0 million purchase price over the fair value of the underlying net identifiable assets, was assigned to the consolidated entity, Lexicon.

On July 30, 2010, Lexicon exercised its Purchase Option (as defined in Note 10) and completed the acquisition of Symphony Icon. Goodwill associated with the acquisition of \$18.7 million, which represents the assets recognized in connection with the deferred tax liability acquired and did not result from excess purchase price, was assigned to the consolidated entity, Lexicon.

Goodwill is not subject to amortization, but is tested at least annually for impairment at the reporting unit level, which is the Company's single operating segment. The Company performed an impairment test of goodwill on its annual impairment assessment date. This test did not result in an impairment of goodwill.

9. Debt Obligations

In April 2004, Lexicon purchased its existing laboratory and office buildings and animal facilities in The Woodlands, Texas with proceeds from a \$34.0 million third-party mortgage financing and \$20.8 million in cash. The mortgage loan has a ten-year term with a 20-year amortization and bears interest at a fixed rate of 8.23%. The mortgage had a principal balance of \$23.5 million as of December 31, 2012. A balloon payment of \$21.4 million is due in April 2014. Net proceeds from the sale of the building as discussed in Note 6, "Property and Equipment," were used to pay down the mortgage principal in June 2011 in the amount of \$2.4 million. The buildings and land that serve as collateral for the mortgage loan are included in property and equipment at \$58.9 million and \$2.7 million, respectively, before accumulated depreciation, as of December 31, 2012. The fair value of Lexicon's mortgage loan approximates its carrying value. The fair value of Lexicon's mortgage loan is estimated using discounted cash flow analysis, based on the Company's estimated current incremental borrowing rate.

The following table includes the aggregate future principal payments of the Company's long-term debt as of December 31, 2012:

| | For the Year Ending December 31 |
|-----------------------------|--|
| | (in thousands) |
| 2013 | \$ 1,574 |
| 2014 | 21,877 |
| Total debt | 23,451 |
| Less current portion | (1,574) |
| Total long-term debt | \$ 21,877 |

10. Arrangements with Symphony Icon, Inc.

On June 15, 2007, Lexicon entered into a series of related agreements providing for the financing of the clinical development of certain of its drug candidates, including LX1032 and LX1033, along with any other pharmaceutical compositions modulating the same targets as those drug candidates (the "Programs"). The agreements included a Novated and Restated Technology License Agreement pursuant to which the Company licensed to Symphony Icon, a then wholly-owned subsidiary of Symphony Icon Holdings LLC ("Holdings"), the Company's intellectual property rights related to the Programs. Holdings contributed \$45 million to Symphony Icon in order to fund the clinical development of the Programs.

Under a Share Purchase Agreement, dated June 15, 2007, between the Company and Holdings, the Company issued and sold to Holdings 7,650,622 shares of its common stock on June 15, 2007 in exchange for \$15 million and an exclusive purchase option (the "Purchase Option") that gave the Company the right to acquire all of the equity of Symphony Icon, thereby allowing the Company to reacquire all of the Programs. On July 30, 2010, Lexicon entered into an Amended and Restated Purchase Option Agreement with Symphony Icon and Holdings and simultaneously exercised the Purchase Option, thereby reacquiring the Programs. Pursuant to the amended terms of the Purchase Option, Lexicon paid Holdings \$10 million on July 30, 2010 and issued 13,237,519 shares of common stock to designees of Holdings on July 30, 2012 in satisfaction of an additional \$35.0 million base payment obligation.

Lexicon also agreed to make up to \$45 million in additional contingent payments, which will consist of 50% of any consideration Lexicon receives pursuant to any licensing transaction (a "Licensing Transaction") under which Lexicon grants a third party rights to commercialize LX1032, LX1033 or other pharmaceutical compositions modulating the same target as those drug candidates (the "LG103 Programs"), subject to certain exceptions. The contingent payments will be due if and when Lexicon receives such consideration from a Licensing Transaction. In the event Lexicon receives regulatory approval in the United States for the marketing and sale of any product resulting from the LG103 Programs prior to entering into a Licensing Transaction for the commercialization of such product in the United States, in lieu of any contingent payment from such a Licensing Transaction, Lexicon will pay Holdings the sum of \$15 million and the amount of certain expenses Lexicon incurred after its exercise of the Purchase Option which are attributable to the development of such product, reduced by up to 50% of such sum for the amount of any contingent payments paid prior to such United States regulatory approval attributable to any such Licensing Transaction outside of the United States with respect to such product. In the event Lexicon makes any such payment upon United States regulatory approval, Lexicon will have no obligation to make subsequent contingent payments attributable to any such Licensing Transactions for the commercialization of such product outside the United States until the proceeds of such Licensing Transactions exceed 50% of the payment made as a result of such United States regulatory approval. The contingent payments may be paid in cash or a combination of cash and common stock, in Lexicon's discretion, provided that no more than 50% of any contingent payment will be paid in common stock.

Lexicon originally calculated the value of the Purchase Option as the difference between the fair value of the common stock issued to Holdings of \$23.6 million (calculated at the time of issuance) and the \$15.0 million in cash received from Holdings for the issuance of the common stock. Lexicon recorded the value of the Purchase Option as an asset, and was amortizing this asset over the four-year option period. Upon the adoption of a new accounting pronouncement regarding variable interest entities (formerly SFAS No. 167) on January 1, 2010, \$2.3 million of structuring and legal fees originally allocated to noncontrolling interest was allocated to the value of the Purchase Option. This resulted in a cumulative-effect adjustment to retained earnings of \$1.5 million, representing the additional amortization expense that would have been recorded through December 31, 2009. The unamortized balance of \$3.1 million was recorded in prepaid expenses and other current assets as of December 31, 2009. Upon the exercise of the Purchase Option on July 30, 2010 as discussed below, the

remaining balance was amortized immediately. The amortization expense of \$4.0 million is recorded in other expense, net in the accompanying consolidated statement of comprehensive loss for the year ended December 31, 2010.

Lexicon accounted for the exercise of the Purchase Option and acquisition of Symphony Icon as a business combination. In connection with its acquisition of Symphony Icon, Lexicon paid \$10.0 million in cash, and has also agreed to pay Holdings additional base and contingent payments as discussed above. The fair value of the base and contingent consideration payments was \$45.6 million and was estimated by applying a probability-based income approach utilizing an appropriate discount rate. This estimation was based on significant inputs that are not observable in the market, referred to as Level 3 inputs. Key assumptions include: (1) a discount rate of 14% for the base payments; (2) a discount rate of 18% for the contingent payments; and (3) a probability adjusted contingency. The discount rate assumptions have not changed through December 31, 2012, and as programs progress, the probability adjusted contingency is adjusted as necessary. Subsequent changes in the fair value of the Symphony Icon purchase consideration liability are recorded as increase or decrease in fair value of Symphony Icon purchase liability expense in the accompanying consolidated statements of comprehensive loss. During the years ended December 31, 2012, 2011 and 2010, the fair value of the Symphony Icon purchase consideration liability increased by \$9.9 million, \$6.8 million and \$2.7 million, respectively.

The following table presents the allocation of the purchase consideration, including the upfront, base and contingent payments, based on fair value (in thousands):

| | | |
|---|----|----------------------|
| Cash and cash equivalents | \$ | 4,439 |
| Prepaid expenses | | 545 |
| Intangible assets - in-process research and development | | 53,557 |
| Total identifiable assets | | <u>58,541</u> |
| Accounts payable and accrued liabilities | | (2,984) |
| Deferred tax liability | | (18,745) |
| Total liabilities assumed | | <u>(21,729)</u> |
| Net identifiable assets acquired | | 36,812 |
| Goodwill | | 18,745 |
| Net assets acquired | \$ | <u><u>55,557</u></u> |

The deferred tax liability relates to the tax impact of future amortization or possible impairments associated with the identified intangible assets, which are not deductible for tax purposes. Intangible assets related to in-process research and development ("IPR&D") assets are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. During the period the assets are considered indefinite-lived, they will not be amortized but will be tested for impairment on an annual basis and between annual tests if Lexicon becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D assets below their respective carrying amounts. Lexicon performed an impairment test of indefinite-lived intangible assets on its annual impairment assessment date. This test did not result in an impairment of intangible assets. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time. In estimating fair value of the IPR&D assets, Lexicon compensated for the differing phases of development of each asset by probability-adjusting its estimation of the expected future cash flows associated with each asset. Lexicon then determined the present value of the expected future cash flows. The projected cash flows from the IPR&D assets were based on key assumptions such as estimates of revenues and operating profits related to the feasibility and timing of achievement of development, regulatory and commercial milestones, expected costs to develop the IPR&D assets into commercially viable products and future expected cash flows from product sales.

The following represents the pro forma consolidated statement of comprehensive loss as if Symphony Icon had been included in the consolidated results of Lexicon for the entire year ending December 31, 2010 (in thousands):

| | | |
|--|----|----------|
| Revenues | \$ | 4,908 |
| Net loss attributable to Lexicon Pharmaceuticals, Inc. | | (97,818) |

These amounts have been calculated by removing the amortization of the Purchase Option for the year ended December 31, 2010. There are no revenue or earnings of Symphony Icon included in Lexicon's consolidated statement of comprehensive loss for the period from the acquisition date of July 30, 2010 through December 31, 2010.

11. Commitments and Contingencies

Operating Lease Obligations: A Lexicon subsidiary leases laboratory and office space in Hopewell, New Jersey under an agreement that was scheduled to expire in June 2013. Effective December 31, 2012, this lease was amended, and the amended lease expires in June 2018. The amended lease includes escalating lease payments. Rent expense is recognized on a straight-line basis over the amended lease term. Lexicon is the guarantor of the obligation of its subsidiary under this lease. The Company is required to maintain restricted investments to collateralize a standby letter of credit for this lease. The Company had \$0.4 million and \$0.4 million in restricted investments as collateral as of December 31, 2012 and 2011, respectively. Additionally, Lexicon leases certain equipment under operating leases.

Rent expense for all operating leases was approximately \$2.2 million, \$2.5 million and \$2.5 million for the years ended December 31, 2012, 2011 and 2010, respectively. The following table includes non-cancelable, escalating future lease payments for the facility in New Jersey:

| | <u>For the Year Ending December 31</u> |
|------------|--|
| | <u>(in thousands)</u> |
| 2013 | \$ 230 |
| 2014 | 1,052 |
| 2015 | 1,078 |
| 2016 | 1,103 |
| 2017 | 1,129 |
| Thereafter | 572 |
| Total | <u>\$ 5,164</u> |

Employment Agreements: Lexicon has entered into employment agreements with certain of its corporate officers. Under the agreements, each officer receives a base salary, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreements are at-will and contain non-competition agreements. The agreements also provide for a termination clause, which requires either a six or 12-month payment based on the officer's salary and payment of a specified portion of the officer's bonus target for such year, in the event of termination.

Legal Proceedings: Lexicon is from time to time party to claims and legal proceedings that arise in the normal course of its business and that it believes will not have, individually or in the aggregate, a material adverse effect on its results of operations, financial condition or liquidity.

12. Agreements with Invus, L.P. and Its Affiliates

In June 2007, Lexicon entered into a Securities Purchase Agreement (the "Securities Purchase Agreement") with Invus, L.P. under which Invus, L.P. purchased 50,824,986 shares of the Company's common stock in August 2007. In November 2011, Invus, L.P. and its affiliate Invus C.V. (collectively "Invus") exercised their rights under the Securities Purchase Agreement to require Lexicon to conduct a pro rata rights offering to its stockholders. In December 2011, Lexicon completed the rights offering of 142,492,883 shares of its common stock at a price of \$1.13 per share, resulting in net proceeds of \$160.6 million, after offering expenses of \$0.4 million. Invus and its affiliates purchased 115,044,247 of these shares, resulting in Invus and its affiliates owning greater than 50% of Lexicon's outstanding common stock. All of the net proceeds of this rights offering are reflected as issuance of common stock in the accompanying financial statements. The rights offering exercise price of \$1.13 was less than the closing price of Lexicon's common stock on the last day of the offering period of \$1.14; however, if considered a bonus element, this difference in price did not result in a change in earnings per share from what was originally reported in previous periods.

In connection with the Securities Purchase Agreement, Lexicon also entered into a Stockholders' Agreement with Invus, L.P. under which Invus has specified rights with respect to designation of directors, participation in future equity issuances by the Company and certain consent rights.

13. Other Capital Stock Agreements

Common Stock: In March 2010, Lexicon completed the public offering and concurrent private placement of 161,770,206 shares of its common stock at a price of \$1.15 per share, resulting in net proceeds of \$181.5 million, after deducting underwriting discounts and commissions of \$4.3 million and offering expenses of \$0.3 million. Invus purchased 94,270,206 of these shares. All of the net proceeds of this offering are reflected as issuance of common stock in the accompanying financial statements.

In October 2012, Lexicon sold 17,500,000 shares of its common stock at a price of \$2.25 per share in a public offering, resulting in net proceeds of \$37.1 million, after deducting underwriting discounts and commissions of \$2.0 million and offering expenses of \$0.2 million. Invus, L.P. purchased 3,000,000 of these shares. All of the net proceeds of this offering are reflected as issuance of common stock in the accompanying financial statements.

14. Equity Incentive Awards and Warrants

Equity Incentive Plans

Equity Incentive Plan: In September 1995, Lexicon adopted the 1995 Stock Option Plan, which was subsequently amended and restated in February 2000 and renamed the 2000 Equity Incentive Plan, subsequently amended and restated in April 2009 and renamed the Equity Incentive Plan (the “Equity Incentive Plan”), and subsequently amended in April 2012.

The Equity Incentive Plan provides for the grant of incentive stock options to employees and nonstatutory stock options to employees, directors and consultants of the Company. The plan also permits the grant of stock bonus awards, restricted stock awards, restricted stock unit (phantom stock) awards and stock appreciation rights. Incentive and nonstatutory stock options have an exercise price of 100% or more of the fair market value of our common stock on the date of grant. The purchase price of restricted stock awards may not be less than 85% of fair market value. However, the plan administrator may award stock bonus awards in consideration of past services or phantom stock awards without a purchase payment. Shares may be subject to a repurchase option in the discretion of the plan administrator. Most options granted under the Equity Incentive Plan become vested and exercisable over a period of four years; however some have been granted with different vesting schedules. Options granted under the Equity Incentive Plan have a term of ten years from the date of grant.

The total number of shares of common stock that may be issued pursuant to stock awards under the Equity Incentive Plan shall not exceed in the aggregate 50,000,000 shares. No more than 15,000,000 shares may be issued pursuant to awards other than stock options and stock appreciation rights. As of December 31, 2012, an aggregate of 50,000,000 shares of common stock had been reserved for issuance, options to purchase 20,679,439 shares and 3,871,975 restricted stock units were outstanding, 5,087,155 shares had been issued upon the exercise of stock options, 518,250 shares had been issued pursuant to restricted stock units and 740,300 shares had been issued pursuant to stock bonus awards or restricted stock awards granted under the Equity Incentive Plan.

Non-Employee Directors' Equity Incentive Plan: In February 2000, Lexicon adopted the 2000 Non-Employee Directors' Stock Option Plan, which was subsequently amended and restated in April 2009 and renamed the Non-Employee Directors' Stock Option Plan, and subsequently amended in April 2012 and renamed the Non-Employee Directors' Equity Incentive Plan (the “Directors' Plan”). Under the Directors' Plan, non-employee directors receive an initial option to purchase 30,000 shares of common stock. In addition, on the day following each of the Company's annual meetings of stockholders, each non-employee director who has been a director for at least six months is automatically granted an option to purchase 20,000 shares of common stock and a restricted stock award of the number of shares of common stock having a fair market value on the date of grant of \$20,000, rounded down to the nearest whole share number. Initial option grants become vested and exercisable over a period of five years and annual option grants become vested over a period of 12 months from the date of grant. Options granted under the Directors' Plan have an exercise price equal to the fair market value of the Company's common stock on the date of grant and a term of ten years from the date of grant.

The total number of shares of common stock that may be issued pursuant to stock awards under the Directors' Plan shall not exceed in the aggregate 1,500,000 shares. As of December 31, 2012, an aggregate of 1,500,000 shares of common stock had been reserved for issuance, options to purchase 846,000 shares were outstanding, none had been issued upon the exercise of stock options and 94,112 shares had been issued pursuant to restricted stock awards granted under the Directors' Plan.

Stock Option Activity: The following is a summary of option activity under Lexicon's equity incentive plans:

| (in thousands, except exercise price data) | 2012 | | 2011 | | 2010 | |
|--|---------------|---------------------------------|---------------|---------------------------------|---------------|---------------------------------|
| | Options | Weighted Average Exercise Price | Options | Weighted Average Exercise Price | Options | Weighted Average Exercise Price |
| Outstanding at beginning of year | 20,476 | \$ 2.84 | 19,598 | \$ 3.46 | 17,346 | \$ 4.16 |
| Granted | 3,441 | 1.84 | 2,974 | 1.80 | 4,928 | 1.87 |
| Exercised | (636) | 1.66 | (130) | 1.46 | (11) | 2.15 |
| Expired | (1,231) | 6.93 | (1,662) | 8.50 | (1,912) | 6.40 |
| Forfeited | (525) | 1.78 | (304) | 1.76 | (753) | 1.76 |
| Outstanding at end of year | <u>21,525</u> | 2.51 | <u>20,476</u> | 2.84 | <u>19,598</u> | 3.46 |
| Exercisable at end of year | <u>15,582</u> | \$ 2.77 | <u>13,940</u> | \$ 3.34 | <u>11,845</u> | \$ 4.54 |

The weighted average estimated grant date fair value of options granted during the years ended December 31, 2012, 2011 and 2010 were \$1.37, \$1.36 and \$1.40, respectively. The total intrinsic value of options exercised during the years ended December 31, 2012, 2011 and 2010 were \$462,000, \$63,000 and \$1,100, respectively. The weighted average remaining contractual term of options outstanding and exercisable was 6.0 and 5.1 years, respectively, as of December 31, 2012. At December 31, 2012, the aggregate intrinsic value of the outstanding options and the exercisable options was \$2.5 million and \$1.9 million, respectively.

The following is a summary of the nonvested options as of December 31, 2012, and changes during the year then ended, under Lexicon's equity incentive plans:

| | Options | Weighted Average Grant Date Fair Value |
|--------------------------------|----------------|--|
| | (in thousands) | |
| Nonvested at beginning of year | 6,536 | \$ 1.33 |
| Granted | 3,441 | 1.37 |
| Vested | (3,509) | 1.30 |
| Forfeited | (525) | 1.26 |
| Nonvested at end of year | <u>5,943</u> | \$ 1.37 |

Stock Bonus and Restricted Stock Unit Activity:

During the year ended December 31, 2011, Lexicon granted its officers 200,277 shares of stock bonus awards in lieu of cash bonus awards. The stock bonus awards had a weighted average grant date fair value of \$1.81 per share and vested immediately. During the year ended December 31, 2012, Lexicon granted its non-employee directors 94,112 shares of restricted stock awards. The restricted stock awards had a weighed average grant date fair value of \$1.70 per share and vested immediately.

During the years ended December 31, 2012 and 2011, Lexicon granted its employees restricted stock units in lieu of or in addition to annual stock option awards. These restricted stock units vest in four annual installments. The following is a summary of restricted stock units activity under Lexicon's stock-based compensation plans for the year ended December 31, 2012:

| | Shares | Weighted Average Grant Date Fair Value |
|----------------------------------|----------------|--|
| | (in thousands) | |
| Outstanding at December 31, 2011 | 2,127 | \$ 1.81 |
| Granted | 2,390 | 1.80 |
| Vested | (518) | 1.81 |
| Forfeited | (456) | 1.81 |
| Nonvested at December 31, 2012 | 3,543 | \$ 1.80 |

During the year ended December 31, 2010, Lexicon granted certain employees restricted stock units with a performance condition. The shares subject to the restricted stock units granted in 2010 vest upon the dosing of the first patient in a pivotal human clinical trial in any country, the results of which could be used to establish safety and efficacy of a pharmaceutical product discovered or developed by Lexicon as a basis for a New Drug Application. Stock-based compensation expense for awards with performance conditions is recognized over the period from the date the performance condition is determined to be probable of occurring through the time the applicable condition is met. The following is a summary of performance-based restricted stock units activity under Lexicon's stock-based compensation plans for the year ended December 31, 2012:

| | Shares | Weighted Average Grant Date Fair Value |
|----------------------------------|----------------|--|
| | (in thousands) | |
| Outstanding at December 31, 2011 | 350 | \$ 1.90 |
| Forfeited | (21) | 1.90 |
| Nonvested at December 31, 2012 | 329 | \$ 1.90 |

Aggregate Shares Reserved for Issuance

As of December 31, 2012, an aggregate of 25,397,414 shares of common stock were reserved for issuance upon exercise of outstanding stock options and vesting of outstanding restricted stock units and 19,662,769 additional shares were available for future grants under Lexicon's equity incentive plans. The Company has a policy of using either authorized and unissued shares or treasury shares, including shares acquired by purchase in the open market or in private transactions, to satisfy equity award exercises.

15. Benefit Plan

Lexicon maintains a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all full-time employees. Participating employees may defer a portion of their pretax earnings, up to the Internal Revenue Service annual contribution limit. Beginning in 2000, the Company was required to match employee contributions according to a specified formula. The matching contributions totaled \$490,000, \$583,000 and \$642,000 in the years ended December 31, 2012, 2011 and 2010, respectively. Company contributions are vested based on the employee's years of service, with full vesting after four years of service.

16. Collaboration and License Agreements

Lexicon has derived substantially all of its revenues from drug discovery and development alliances, target validation collaborations for the development and, in some cases, analysis of the physiological effects of genes altered in knockout mice, government grants and contracts, technology licenses, subscriptions to its databases and compound library sales.

Texas Institute for Genomic Medicine. In July 2005, Lexicon received a \$35.0 million award from the Texas Enterprise Fund for the creation of a knockout mouse embryonic stem cell library containing 350,000 cell lines for the Texas Institute for Genomic Medicine ("TIGM") using Lexicon's proprietary gene trapping technology, which Lexicon completed in 2007. Lexicon also equipped TIGM with the bioinformatics software required for the management and analysis of data relating to the library. The Texas Enterprise Fund also awarded \$15.0 million to the Texas A&M University System for the creation of facilities and infrastructure to house the library.

Under the terms of the award, Lexicon is responsible for the creation of a specified number of jobs beginning in 2012, reaching an aggregate of 1,616 new jobs in Texas by December 31, 2016. Lexicon will obtain credits based on funding received by TIGM and certain related parties from sources other than the State of Texas that it may offset against its potential liability for any job creation shortfalls. Lexicon will also obtain credits against future jobs commitment liabilities for any surplus jobs it creates. Subject to these credits, if Lexicon fails to create the specified number of jobs, the state may require Lexicon to repay \$2,415 for each job Lexicon falls short beginning in 2013. Lexicon's maximum aggregate exposure for such payments, if Lexicon fails to create any new jobs, is approximately \$14.2 million, without giving effect to any credits to which Lexicon may be entitled. Lexicon has recorded this obligation as deferred revenue and accounts payable in the accompanying consolidated balance sheets. The Texas A&M University System, together with TIGM, has independent job creation obligations and is obligated for an additional period to maintain an aggregate of 5,000 jobs, inclusive of those Lexicon creates.

Taconic Farms. Lexicon established a collaboration with Taconic Farms, Inc. in November 2005 for the marketing, distribution and licensing of certain lines of knockout mice and entered into an expanded collaboration with Taconic in July 2009 that expired in July 2010. Under the terms of the collaboration, Lexicon is presently making available through Taconic more than 3,600 distinct lines of knockout mice, and in some cases, phenotypic data relating to such lines of knockout mice, for use by pharmaceutical and biotechnology companies, academic and non-profit institutions and other researchers. Lexicon receives license fees and royalties from payments received by Taconic from customers obtaining access to knockout mice and any related phenotypic data. The Company received payments totaling \$6.7 million through December 31, 2012. Revenue recognized under these agreements was \$0.7 million, \$0.8 million and \$1.7 million for the years ended December 31, 2012, 2011 and 2010, respectively.

17. Selected Quarterly Financial Data

The table below sets forth certain unaudited statements of comprehensive loss data, and net loss per common share data, for each quarter of 2012 and 2011:

(in thousands, except per share data)

| | Quarter Ended | | | |
|---|---------------|-------------|--------------|-------------|
| | March 31 | June 30 | September 30 | December 31 |
| | (Unaudited) | | | |
| 2012 | | | | |
| Revenues | \$ 300 | \$ 199 | \$ 372 | \$ 218 |
| Loss from operations | \$ (29,383) | \$ (25,480) | \$ (29,060) | \$ (24,492) |
| Consolidated net loss | \$ (29,868) | \$ (25,931) | \$ (29,539) | \$ (24,873) |
| Consolidated net loss per common share, basic and diluted | \$ (0.06) | \$ (0.05) | \$ (0.06) | \$ (0.05) |
| Shares used in computing consolidated net loss per common share | 480,324 | 480,634 | 490,049 | 507,619 |
| 2011 | | | | |
| Revenues | \$ 596 | \$ 555 | \$ 355 | \$ 343 |
| Loss from operations | \$ (29,136) | \$ (25,926) | \$ (25,691) | \$ (33,342) |
| Consolidated net loss | \$ (29,629) | \$ (26,638) | \$ (26,103) | \$ (33,845) |
| Consolidated net loss per common share, basic and diluted | \$ (0.09) | \$ (0.08) | \$ (0.08) | \$ (0.10) |
| Shares used in computing consolidated net loss per common share | 337,527 | 337,668 | 337,678 | 350,069 |

Corporate Information

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Transfer Agent

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877-854-4583

www-us.computershare.com/investor

Annual Report

Our 2012 annual report on Form 10-K is available, without charge, upon request by contacting our Investor Relations Department at 281-863-3000.

Annual Meeting

Our annual meeting of shareholders will be held at 8:00 a.m. CDT on May 9, 2013 at Lexicon's corporate headquarters, 8800 Technology Forest Place, The Woodlands, Texas 77381.

This annual report to shareholders contains forward-looking statements, including statements relating to Lexicon's regulatory filings, clinical and preclinical development programs and the potential therapeutic and commercial potential of the drug candidates in those programs. These statements involve risks, uncertainties and other important factors that may cause the actual results of Lexicon to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such risks, uncertainties and other important factors is contained in the sections entitled "Factors Affecting Forward-Looking Statements" and "Risk Factors" in our annual report on Form 10-K for the year ended December 31, 2012, as filed with the Securities and Exchange Commission and included as part of this annual report to shareholders.

Executive Officers

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

Pablo Lapuerta, M.D.
Executive Vice President of Clinical Development and Chief Medical Officer

Alan J. Main, Ph.D.
Executive Vice President, Pharmaceutical Research

Jeffrey L. Wade, J.D.
Executive Vice President, Corporate Development and Chief Financial Officer

Brian P. Zambrowicz, Ph.D.
Executive Vice President and Chief Scientific Officer

James F. Tessmer
Vice President, Finance and Accounting

Board of Directors

Raymond Debbane, Chairman
President and Chief Executive Officer, The Invus Group, LLC

Philippe J. Amouyal
Managing Director, The Invus Group, LLC

Samuel L. Barker, Ph.D.
Founder and Principal, Clearview Projects, Inc.; Former President, U.S. Pharmaceutical Group, Bristol-Myers Squibb Company

Robert J. Lefkowitz, M.D.
Investigator, Howard Hughes Medical Institute and James B. Duke Professor of Medicine and Professor of Biochemistry, Duke University Medical Center; Recipient of 2012 Nobel Prize in Chemistry

Alan S. Nies, M.D.
Chairman, Lexicon Pharmaceuticals Medical Advisory Board; Former Senior Vice President, Clinical Sciences, Merck & Co., Inc.

Frank P. Palantoni
President, Pet and Animal Health Division of Central Garden and Pet Company

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

Christopher J. Sobbecki
Managing Director, The Invus Group, LLC

Judith L. Swain, M.D.
Executive Director, Singapore Institute for Clinical Sciences and Lien Chow Professor of Medicine at the National University of Singapore

ON THE COVER:
WR124, a Wolf-Rayet star

Lexicon employees' depiction of WR124, a Wolf-Rayet star, a class of star characterized by its high energy and state of rapid transition.* Like WR124, Lexicon is in the process of undergoing a rapid transition as our clinical programs enter Phase 3 trials. Lexicon has made numerous transitions over the years, but we have pursued a consistent strategy:

- identifying new targets with promising mechanisms of action,
- discovering new small molecule drug candidates addressing those targets, and
- advancing those drug candidates through preclinical and clinical development towards the market

all in service of our mission of discovering breakthrough treatments for human disease. In 2012, we advanced our first drug candidate into Phase 3 development, with more poised to follow.

* Based on the original picture by Yves Grosdidier, Anthony Moffat, Gilles Joncas, Agnes Acker, STScI, and NASA, November 1998.
www.cfa.harvard.edu/~pberlind/atlas/htmls/wrstars.html



Corporate Headquarters

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