LEXICON PHARMACEUTICALS, INC./DE
Form 10-K
March 16, 2011

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

FORM 10-K
(Mark One)

R ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Fiscal Year Ended December 31, 2010

or

£ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Transition Period from _____ to _____

Commission File Number: 000-30111
Lexicon Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	76-0474169
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)
8800 Technology Forest Place The Woodlands, Texas 77381 (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 o No R

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 o No R

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 R No o

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 o No o

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. R

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 o Accelerated filer R Non-accelerated filer o Smaller reporting company o

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 o No R

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 $174.2 million, based on the closing price of the common stock on the Nasdaq Global Market on June 30, 2010 of $1.28 per share. For purposes of the preceding sentence only, all directors, executive officers and beneficial owners of ten percent or more of the registrant's common stock are assumed to be affiliates. As of March 10, 2011, 337,629,760 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2011 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, 2010, are incorporated by reference into Part III of this annual report on Form 10-K.

Lexicon Pharmaceuticals, Inc.

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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," "shou 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.

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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 four drug candidates for which we have completed or are presently conducting Phase 2 clinical trials:

- LX4211, an orally-delivered small molecule compound that we are developing as a treatment for type 2 diabetes;
- LX1031, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome and other gastrointestinal disorders;
- LX1032, an orally-delivered small molecule compound that we are developing as a treatment for the symptoms associated with carcinoid syndrome; and
- LX2931, an orally-delivered small molecule compound that we are developing as a treatment for rheumatoid arthritis and other autoimmune diseases.

We have initiated a Phase 1 clinical trial of LX1033, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome and other gastrointestinal disorders, and we have advanced three other drug candidates into preclinical development: LX7101, a topically-delivered small molecule compound that we are developing as a treatment for glaucoma; LX5061, an orally-delivered small molecule compound that we are developing as a treatment for osteoporosis; and LX2311, an orally-delivered small molecule compound that we are developing as a treatment for autoimmune diseases. We have small molecule compounds from a number of additional drug discovery programs in various stages of preclinical research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline.

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

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.

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Our Drug Development Pipeline

We have four drug candidates for which we have completed or are presently conducting Phase 2 clinical trials. We have initiated a Phase 1 clinical trial of an additional drug candidate, have advanced three other drug candidates into preclinical development and have small molecule compounds from a number of additional programs in various stages of preclinical research:

Drug Program	Potential Indication	Stage of Development					
		Preclinical Research	Preclinical Development	IND	Phase 1	Phase 2	Phase 3
LX4211	Type 2 Diabetes						
LX1031	Irritable Bowel Syndrome						
LX1033	Irritable Bowel Syndrome						
LX1032	Carcinoid Syndrome						
LX2931	Rheumatoid Arthritis						
LX7101	Glaucoma						
LX5061	Osteoporosis						
LX2311	Autoimmune Diseases						

LX4211

LX4211 is an orally-delivered small molecule compound that we are developing for the potential treatment of type 2 diabetes mellitus. We reported top-line data in January 2010 from a Phase 2 clinical trial evaluating the safety and tolerability of LX4211 and its effects on glycemic parameters associated with type 2 diabetes. The Phase 2 trial enrolled 36 patients with non-insulin dependent type 2 diabetes in a double-blind, randomized, placebo-controlled study of 150mg and 300mg doses of LX4211, each administered in a liquid formulation once daily over a four-week treatment period. The efficacy endpoints under evaluation in the trial included urinary glucose excretion, fasting plasma glucose, response to oral glucose tolerance testing, and hemoglobin A1c, also known as HbA1c or A1c, a measure of blood glucose levels over time. Top-line data from the study showed that treatment with 150mg and 300mg of LX4211 provided improvements in glycemic control and demonstrated statistically significant benefits in the primary and multiple secondary efficacy endpoints. A marked and statistically significant decrease in fasting plasma glucose was observed at each measurement point throughout the treatment period in both dose groups relative to placebo. After four weeks of dosing, patients in both dose groups exhibited statistically significant reductions in HbA1c as compared to patients receiving placebo. Patients in both dose groups also exhibited statistically significant improvements in glucose tolerance in response to oral glucose tolerance testing. Consistent with the mechanism of action of LX4211, there was also a significant, dose-dependent increase in 24-hour urinary glucose excretion in both dose groups at each measurement point throughout the study period relative to placebo. Patients in both dose groups also showed positive trends that did not reach statistical significance in broader metabolic and cardiovascular parameters, including weight reduction, decreased blood pressure and lower triglyceride levels. LX4211 demonstrated a favorable safety profile in the trial, with no dose-limiting toxicities observed. Adverse events were

generally mild and equally distributed across all groups, including the placebo group.

We reported top-line data in January 2011 from a mechanistic study comparing a solid oral dose formulation of LX4211 to the liquid dose formulation used in prior clinical trials. The trial enrolled 12 patients with non-insulin dependent type 2 diabetes in a randomized, triple-cross over study in which each patient received three 300mg doses of LX4211 in 5-day intervals over a period of 15 days. Patients were administered two 150mg tablets, six 50mg tablets and a 300mg liquid dose formulation in varying sequences. The endpoints under evaluation in the trial included peptide YY, also known as PYY, and glucagon-like peptide-1, also known as GLP-1, each of which are important mediators of glycemic control, appetite and other

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metabolic parameters. Top-line data from the study showed that treatment with a single 300mg dose of LX4211, administered as two 150mg tablets, significantly increased both GLP-1 and PYY and performed as well as or better than the liquid dose on such measures. We intend to initiate a drug-drug interaction study of LX4211 in patients taking metformin in the first quarter of 2011 and a 12-week Phase 2b clinical trial of the solid oral dose formulation of LX4211 in the second quarter of 2011.

We previously completed a combined Phase 1 single ascending-dose and multiple ascending-dose study of LX4211. 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 discovered that mice lacking SGLT2 have improved glucose tolerance and increased urinary glucose excretion. In preclinical studies, animals treated with LX4211 demonstrated increased urinary glucose excretion and decreased HbA1c levels, with urinary glucose excretion returning to baseline after treatment was discontinued.

LX1031 and LX1033

LX1031 and LX1033 are orally-delivered small molecule compounds that we are developing for the potential treatment of irritable bowel syndrome and other gastrointestinal disorders. We reported top-line data in November 2009 from a Phase 2 clinical trial evaluating the safety and tolerability of LX1031 and its effects on symptoms associated with irritable bowel syndrome. The Phase 2 clinical trial enrolled 155 patients suffering from either diarrhea-predominant or mixed irritable bowel syndrome in a randomized, double-blind, placebo-controlled study of 250mg and 1,000mg doses of LX1031, each administered four times daily over a four-week treatment period. The efficacy endpoints under evaluation in the trial included a global assessment of adequate relief, number of bowel movements, symptom severity evaluation (bloating, urgency and pain), and stool form. Top-line data from the study 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. Improvements in the global assessment were observed in the first week of treatment and were maintained in each of the four weeks of the study, achieving statistical significance relative to placebo at the end of the first and second week and showing an improved trend relative to placebo that did not reach statistical significance at the end of the third and fourth weeks. Improvements in the global assessment of adequate relief corresponded with statistically significant improvements in stool consistency in the same dose group. Increased clinical response correlated with a greater reduction in serotonin synthesis as reflected by measures of urinary 5-HIAA, the primary metabolite of serotonin and a biomarker for serotonin production. LX1031 was well tolerated with no notable differences in adverse events observed between placebo and either treatment group. We are presently seeking to develop an improved formulation of LX1031 with the goal of achieving a lower and less frequent dosing regimen that will provide a similar safety and efficacy profile to that observed with the original formulation.

We previously completed a Phase 1a single ascending-dose study and two Phase 1b multiple ascending-dose studies exploring safety and tolerability and the effects of LX1031 on serotonin synthesis. In Phase 1 clinical trials, all dose levels were well tolerated, no dose-limiting toxicities were observed, and LX1031 was shown to reduce levels of urinary 5-HIAA.

We initiated a Phase 1 clinical trial of LX1033, a back-up compound to LX1031 that preclinical studies indicate has the potential to be as much as 10-fold more potent than LX1031, in March 2011 to evaluate the safety, tolerability and pharmacokinetics of LX1033.

We designed LX1031 and LX1033 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. LX1031 and LX1033 were internally generated by our medicinal chemists and inhibit 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. In preclinical studies, LX1031 and LX1033 demonstrated dose-dependent reductions of serotonin levels in the gastrointestinal tract of multiple species without affecting brain serotonin levels.

LX1032

LX1032 is an orally-delivered small molecule compound that we are developing for the potential treatment of symptoms associated with carcinoid syndrome. We initiated a Phase 2 clinical trial in July 2009 to evaluate the safety and

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tolerability of LX1032 and its effects on symptoms associated with carcinoid syndrome. The Phase 2 trial is expected to enroll up to 24 patients with symptomatic carcinoid syndrome refractory to octreotide therapy in a double-blind, randomized, placebo-controlled study assessing a series of escalating doses of LX1032 against placebo over a 28-day treatment period, given three times daily, followed by cohort expansion at the 500 mg dose. The efficacy endpoints under evaluation in the trial include 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. We also initiated a complementary open-label clinical trial of LX1032 in June 2010, which is expected to enroll up to 16 additional patients. We anticipate reporting results from both trials in the second quarter of 2011.

We previously completed a Phase 1a single ascending-dose study and a Phase 1b multiple ascending-dose study of LX1032. In Phase 1 clinical trials, LX1032 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.

LX1032 was internally generated by our medicinal chemists as an inhibitor of TPH, the same target as LX1031 and LX1033, but LX1032 is chemically distinct and, unlike LX1031 and LX1033, 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, LX1032 was able to reduce peripheral serotonin levels in several different species without affecting serotonin levels in the brain. LX1032 has received Fast Track 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. Fast Track designation provides for an expedited review process that may shorten FDA approval times. LX1032 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.

LX2931

LX2931 is an orally-delivered small molecule compound that we are developing for the potential 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. A reduction in peripheral lymphocyte counts was not observed, 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 intend to initiate a dose-ranging study of LX2931 in patients with rheumatoid arthritis in the first half of 2011 in preparation for a Phase 2 clinical trial of higher doses of LX2931.

We previously completed a drug-drug interaction study of LX2931 in rheumatoid arthritis patients taking methotrexate. We also completed two Phase 1a single ascending-dose studies, a Phase 1b multiple ascending-dose study and a multiple dose study assessing the pharmacokinetics of a solid dose form of LX2931. In the Phase 1 clinical trials, LX2931 demonstrated a dose-dependent reduction in circulating lymphocytes similar to those associated with a beneficial response observed in animal arthritis models after treatment with LX2931. An episode of acute abdominal pain resolving within 24 hours was observed in two out of 24 subjects in the single ascending-dose

trials who received doses above 175 mg. All other doses were well tolerated with 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.

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LX7101

LX7101 is a topically-delivered small molecule compound that we are developing for the potential treatment of glaucoma. We have commenced the preclinical studies of LX7101 that will be required to file an IND.

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

LX5061

LX5061 is an orally-delivered small molecule compound that we are developing for the potential treatment of osteoporosis by enhancing the formation of new bone. We have commenced the preclinical studies of LX5061 that will be required to file an IND.

LX5061 was internally generated by our medicinal chemists to target a protein which plays a key role in regulating cortical bone formation. Our scientists discovered that mice lacking the gene encoding the target of LX5061 exhibited greater cortical bone thickness and strength compared to normal mice. In preclinical studies, LX5061 significantly increased midshaft femur, midshaft humerus and rib cortical thickness and strength in an animal model of osteoporosis.

LX2311

LX2311 is an orally-delivered small molecule compound that we are developing for the potential treatment of autoimmune diseases. We have commenced the preclinical studies of LX2311 that will be required to file an IND.

LX2311 was internally generated by our medicinal chemists to target a protein responsible for regulating the proliferation and activation of lymphocytes and macrophages. Our scientists discovered that T-lymphocytes, B-lymphocytes and macrophages from mice lacking the gene encoding the target of LX2311 exhibited reduced cell activation and produced reduced levels of pro-inflammatory cytokines as compared with cells from normal mice, and that mice lacking the gene encoding the target of LX2311 exhibited an increased level of resistance to experimental autoimmune encephalomyelitis, or EAE, in an animal model of multiple sclerosis, and to inflammation in other models of autoimmune disease as compared to normal mice. In preclinical studies, LX2311 significantly increased resistance to EAE in animal models of multiple sclerosis and to inflammation in other animal models of autoimmune disease.

Discovery Programs

We have advanced a number of additional drug discovery programs into various stages of preclinical research in preparation for formal preclinical development studies 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

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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 Technology

The core elements of our technology platform include our patented technologies for the generation of knockout mice, our integrated platform of advanced medical technologies for the systematic and comprehensive biological analysis of in vivo behavior and physiology, and our specialized approach to medicinal chemistry and the generation of high-quality, drug-like compound libraries.

Gene Knockout Technologies

Our gene targeting technology, which we have licensed from third parties for the life of the licensed patents, enables us to generate highly-specific alterations in targeted genes. The technology replaces DNA of a gene in a mouse embryonic stem cell through a process known as homologous recombination to disrupt the function of the targeted gene, permitting the generation of knockout mice. By using this technology in combination with one or more additional technologies, we are able to generate alterations that selectively disrupt, or conditionally regulate, the function of the targeted gene for the analysis of the gene’s function in selected tissues, at selected stages in the animal’s development or at selected times in the animal’s life. We can also use this technology to replace the targeted gene with its corresponding human gene for use for preclinical research in our drug programs.

Our gene trapping technology, which we invented and is covered by issued patents that we own, is a high-throughput method of generating knockout mouse clones. The technology uses genetically engineered retroviruses that infect mouse embryonic stem cells in vitro, integrate into the chromosome of the cell and disrupt the function of the gene into which it integrates, permitting the generation of knockout mice. This process also allows us to identify and catalogue each embryonic stem cell clone by DNA sequence from the trapped gene and to select embryonic stem cell clones by DNA sequence for the generation of knockout mice. We have used our gene trapping technology in an automated process to create our OmniBank library of more than 270,000 frozen gene knockout embryonic stem cell clones, each identified by DNA sequence in a relational database.

Physiological Analysis Technologies

We have employed an integrated platform of advanced analytical technologies to rapidly and systematically discover the physiological and behavioral effects resulting from loss of gene function in the knockout mice we have generated using our gene knockout technologies and catalogued those effects in our comprehensive and relational LexVision database. These analyses include many of the most sophisticated diagnostic technologies and tests currently available, many of which might be found in a major medical center. Each of these technologies was adapted specifically for the analysis of mouse physiology. This state-of-the-art technology platform has enabled us to assess the consequences of loss of gene function in a living mammal across a wide variety of parameters relevant to human disease.

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We employ portions of this same physiological analysis technology to analyze the in vivo efficacy and safety profiles of drug candidates in mice. We believe that this approach will allow us, at an early stage, to identify and optimize drug candidates for further preclinical and clinical development that demonstrate in vivo efficacy and to distinguish side effects caused by a specific compound from the target-related side effects that we defined using the same comprehensive series of tests.

Chemistry Technologies

We have used solution-phase chemistry to generate our own diverse libraries of optically pure compounds that are targeted against the same pharmaceutically-relevant gene families that we addressed in our Genome5000 program. These libraries have been built using highly robust and scalable organic reactions that allow us to generate compound collections of great diversity and to specially tailor the compound collections to address various therapeutic target families. We designed these libraries by analyzing the chemical structures of drugs that have been proven safe and effective against human disease and using that knowledge in the design of scaffolds and chemical building blocks for the generation of large numbers of new drug-like compounds. When we identify a hit against one of our in vivo-validated targets, we can rapidly reassemble these building blocks to create hundreds or thousands of variations around the structure of the initial compound, enabling us to accelerate our medicinal chemistry efforts. We have supplemented our internally-generated compound libraries with collections of compounds acquired from third parties. We have also established an alliance with Nuevolution A/S providing us with access to Nuevolution's Chemetics® platform chemistry technology, allowing us to screen our targets against ultra-large libraries of fragment-based chemical compounds.

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 of our small molecule programs by developing drug candidates from those programs internally and to collaborate with third parties with respect to the discovery, development and commercialization of small molecule and biotherapeutic drug candidates for other targets, particularly when the collaboration provides us with access to expertise and resources that we do not possess internally or are complementary to our own.

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.

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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

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, but will receive credits against those job obligations based on funding received by TIGM and certain related parties. We may be required to repay the state a portion of the award if we fail to meet those job obligations.

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.

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Technology Licenses. We have granted non-exclusive, internal research-use sublicenses under certain gene targeting patent rights to a number of leading pharmaceutical and biotechnology companies. Many of these agreements extend for the life of the patents. Others have terms of one to three years, in some cases with provisions for subsequent renewals. We have typically received up-front license fees and, in some cases, received additional license fees or milestone payments on products that the sublicensee discovers or developed using our technology.

Our Executive Officers

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

Name	Age	Position with the Company
Arthur T. Sands, M.D., Ph.D.	49	President and Chief Executive Officer and Director
Alan J. Main, Ph.D.	57	Executive Vice President of Pharmaceutical Research
Jeffrey L. Wade, J.D.	46	Executive Vice President, Corporate Development and Chief Financial Officer
Brian P. Zambrowicz, Ph.D.	48	Executive Vice President and Chief Scientific Officer
James F. Tessmer	51	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.

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 boards of directors of the Texas Healthcare and Bioscience Institute and the Texas Life Science Center for Innovation and Commercialization. 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.

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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 two in the United States.

- worldwide patent applications that claim LX1031 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 LX1033 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including six in the United States.

- worldwide patent applications that claim LX1032 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use, from which patents have granted in multiple jurisdictions, including six 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 three in the United States.

- worldwide patent applications that claim LX7101 and associated crystalline forms, pharmaceutical compositions, and methods of manufacture and use.

- a provisional United States patent application, upon which worldwide patent applications may be based, that claims LX5061 and associated pharmaceutical compositions and methods of manufacture and use.

- a provisional United States patent application, upon which worldwide patent applications may be based, that claims LX2311 and associated pharmaceutical compositions and methods of manufacture and use.

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.

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

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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;

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- 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.

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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 2010, 2009 and 2008, respectively, we incurred expenses of $78.5 million, $81.2 million and $107.2 million in company-sponsored as well as collaborative research and development activities, including $3.2 million, $3.0 million and $3.9 million of stock-based compensation expense in 2010, 2009 and 2008, 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, 2011, we employed 290 persons, of whom 77 hold M.D., Ph.D. or D.V.M. degrees and another 47 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.

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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, 2010, we had $211.1 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;
- 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, LX1031, LX1033, LX1032 and LX2931;
- future results from clinical trials of our drug candidates;
- the cost and timing of regulatory approvals of drug candidates that we successfully develop;
- market acceptance of products that we successfully develop and commercially launch;
- the effect of competing programs and products, and of technological and market developments;
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights; and
- the cost and timing of establishing or contracting for sales, marketing and distribution capabilities.

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

If our capital resources are insufficient to meet future capital requirements, we will need to raise additional funds to continue our currently planned operations. If we raise additional capital by issuing equity securities, our then-existing stockholders will experience dilution and the terms of any new equity securities may have preferences over our common stock. We cannot be certain that additional financing, whether debt or equity, will be available in amounts or

on terms acceptable to us, if at all. We may be unable to raise sufficient additional capital on reasonable terms, and if so, we will be forced to significantly curtail or cease our operations or obtain funds by entering into financing agreements on unattractive terms.

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

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment of approximately $205.5 million to purchase 50,824,986 shares of our common stock in August 2007. Under the securities purchase agreement, as amended and supplemented, and after accounting for the $181.5 million in net proceeds from

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our public offering and concurrent private placement of common stock in March 2010, Invus, L.P. and its affiliate Invus C.V., which we collectively refer to as Invus, have the right to require us to initiate a pro rata rights offering to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount to be designated by Invus of up to approximately $163.0 million. The price per share of the rights offering would be designated by Invus in a range between $4.50 and a then-current average market price of our common stock. All stockholders would have oversubscription rights with respect to the rights offering and Invus would be required to purchase its pro rata portion of the offering. Invus may exercise its right to require us to conduct the rights offering by giving us notice within a period of one year beginning on February 28, 2011, which will be extended by the number of days during such period that Invus is not permitted by the securities purchase agreement to initiate the rights offering as a result of any "blackout period" in connection with certain public offerings of our common stock.

Under the securities purchase agreement, until the later of the completion of the rights offering or the expiration of the period during which Invus may require us to initiate the rights offering, we have agreed not to issue any of our common stock for a per share price of less than $4.50 without the prior written consent of Invus, except pursuant to an employee or director stock option, incentive compensation or similar plan or to persons involved in the pharmaceutical industry in connection with simultaneous strategic transactions involving such persons in the ordinary course. In addition, if we notify Invus of a proposed public offering for an offering above $4.50 per share during the period in which Invus may require us to initiate the rights offering, Invus will have a period of 10 business days in which to exercise its right to require us to conduct the rights offering, in which case we would be required to forego the proposed public offering and proceed with the rights offering. If we are not able to issue common stock at prices equal to or greater than $4.50 per share in the future, due to market conditions or otherwise, this obligation will limit our ability to raise capital by issuing additional equity securities without the consent of Invus. In the event Invus declines to grant such consent and, in addition, elects not to exercise its right to require us to initiate the rights offering, or elects to limit the size of the rights offering, our ability during this period to satisfy our future capital requirements by issuing equity securities will be limited if we are unable to do so by issuing common stock at prices equal to or greater than $4.50 per share.

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

We have incurred net losses since our inception, including net losses of $101.8 million for the year ended December 31, 2010, $82.8 million for the year ended December 31, 2009 and $76.9 million for the year ended December 31, 2008. As of December 31, 2010, we had an accumulated deficit of $673.4 million. We are unsure when we will become profitable, if ever. The size of our net losses will depend, in part, on the rate of decline or growth in our revenues and on the level of our expenses.

We derive substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses, and will continue to do so for the foreseeable future. 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 to date with respect to our four most advanced clinical drug candidates, that our interests are better served by retaining rights to our discoveries and advancing our therapeutic programs to a later stage, which could limit our near-term revenues. Given the early-stage nature of our operations, we do not currently derive any revenues from sales of pharmaceutical products.

A large portion of our expenses is fixed, including expenses related to facilities, equipment and personnel. In addition, we expect to spend significant amounts to fund our research and development activities, including the conduct of clinical trials and the advancement of additional potential therapeutics into clinical development. As a result, we expect that our operating expenses will continue to increase significantly as our drug programs progress into and through human clinical trials and, consequently, we will need to generate significant additional revenues to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

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;

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- the expiration or other termination of collaborations and technology licenses, which may not be renewed or replaced;
- the success rate of our discovery and development efforts leading to opportunities for new collaborations and licenses, as well as milestone payments and royalties;
- the timing and willingness of our collaborators to commercialize pharmaceutical products that would result in milestone payments and royalties; and
- general and industry-specific economic conditions, which may affect our and our collaborators' research and development expenditures.

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

Risks Related to Discovery and Development of Our Drug Candidates

We are an early-stage company, and have not proven our ability to successfully develop and commercialize drug candidates based on our drug target discoveries.

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

We have not proven our ability to develop or commercialize drug candidates based on our drug target discoveries. The generation and selection of potential drug candidates for a target is a difficult, expensive and time-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

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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. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in

regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our drug candidates may cause delays in the approval or rejection of an application. Even if the FDA or a comparable authority in another country approves a drug candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

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

If we or our collaborators obtain initial regulatory approvals from the FDA or foreign regulatory authorities for any products that we may develop, we or our collaborators will be subject to extensive and rigorous ongoing domestic and foreign

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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.

A primary trend in the United States health care industry is toward reform and cost containment. Current and future prescription drug benefit programs, including any programs that may become effective as a result of such trend, may have the effect of reducing the prices that we are able to charge for products we develop and sell through plans under the

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programs. These prescription drug programs may also cause third-party payors other than the federal government, including the states under the Medicaid program, to discontinue coverage for products we develop or to lower the price that they will pay.

Proponents of drug reimportation may attempt to pass 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.

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 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. 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

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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.

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Risks Related to Our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, 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 technologies and products. 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 technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products 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, unknown to us, 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 many of the genes and encoded drug targets that are the focus of our drug discovery programs. In some cases, patents have

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issued from these applications. In addition, many companies and institutions have well-established patent portfolios directed to common techniques, methods and means of developing, producing and manufacturing pharmaceutical products. Other companies or institutions could bring legal actions against us or our collaborators for damages or to stop us or our collaborators from engaging in certain discovery or development activities or from manufacturing and marketing any resulting therapeutic products. If any of these actions are successful, in addition to our potential liability for damages, these entities would likely require us or our collaborators to obtain a license in order to continue engaging in the infringing activities or to manufacture or market the resulting therapeutic products or may force us to terminate such activities or manufacturing and marketing efforts.

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

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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

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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

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.

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Invus' ownership of our common stock and its other rights under our stockholders' agreement we entered into in connection with Invus, L.P.'s $205.5 million initial investment in our common stock provide Invus with substantial influence over matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions, as well as other corporate matters.

Under the stockholders' agreement we entered into in connection with Invus, L.P.'s $205.5 million initial investment in our common stock, Invus currently has the right to designate the greater of three members or 30% (or the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, if less than 30%) of all members of our board of directors, rounded up to the nearest whole number of directors, pursuant to which Invus has designated Raymond Debbane, president and chief executive officer of The Invus Group, LLC, an affiliate of Invus, and Philippe J. Amouyal and Christopher J. Sobecki, each of whom are managing directors of The Invus Group, LLC. In the event that the number of shares of our common stock owned by Invus and its affiliates ever exceeds 50% of the total number of shares of our common stock then outstanding (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), from and after that time, Invus will have the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, rounded up to the nearest whole number of directors. The directors appointed by Invus have proportionate representation on the compensation and corporate governance committees of our board of directors.

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

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

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

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

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

- solicit proxies to vote any of our voting securities or any voting securities of our subsidiaries;
- submit to our board of directors a written proposal for any merger, recapitalization, reorganization, business combination or other extraordinary transaction involving an acquisition of us or any of our subsidiaries or any of our or our subsidiaries' securities or assets by Invus and its affiliates;
- enter into discussions, negotiations, arrangements or understandings with any third party with respect to any of the foregoing; or
- request us or any of our representatives, directly or indirectly, to amend or waive any of these standstill provisions.

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The standstill provisions of the stockholders' agreement will terminate on the earliest to occur of (a) August 28, 2017, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all of the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), (d) the date on which any third party makes a public proposal to acquire (by purchase, exchange, merger or otherwise) assets or business constituting 50% or more of our revenues, net income or assets or 50% of any class of our equity securities our board of directors recommends or approves, or proposes to recommend or approve, any such transaction or (e) the date on which any third party acquires beneficial ownership (by purchase, exchange, merger or otherwise) of assets or business constituting 20% or more of our revenues, net income or assets or 20% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction.

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

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

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

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

Invus is entitled to certain minority protections, including consent rights over (a) the creation or issuance of any new class or series of shares of our capital stock (or securities convertible into or exercisable for shares of our capital stock) having rights, preferences or privileges senior to or on parity with our common stock, (b) any amendment to our certificate of incorporation or bylaws, or amendment to the certificate of incorporation or bylaws of any of our

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

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

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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 300,000 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 76,000 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 $28.5 million as of December 31, 2010.

In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. entered into a lease for our facility in Hopewell, New Jersey. The term of the lease extends until June 30, 2013. The lease provides for an escalating yearly base rent payment of $1.3 million in the first year, $2.1 million in years two and three, $2.2 million in years four to six, $2.3 million in years seven to nine and $2.4 million in years ten and eleven. 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.

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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]

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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, and previously on The Nasdaq Global Market.

	High	Low
2009		
First Quarter	$1.75	$0.81
Second Quarter	$1.63	$0.94
Third Quarter	$3.78	$1.11
Fourth Quarter	$2.13	$1.30
2010		
First Quarter	$2.87	$1.20
Second Quarter	$1.69	$1.19
Third Quarter	$1.63	$1.17
Fourth Quarter	$1.91	$1.22

As of February 28, 2011, there were approximately 230 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, 2005 and ending December 31, 2010. The graph assumes that the value of the investment in our common stock and each index was $100 at December 31, 2005, and that all dividends were reinvested.

	December 31,					
	2005	2006	2007	2008	2009	2010
Lexicon Pharmaceuticals, Inc.	100	99	83	38	47	39
Nasdaq Composite Index	100	110	120	72	103	120
Nasdaq Biotechnology Index	100	101	106	92	107	123

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.

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Item 6. Selected Financial Data

The statement of operations data for the years ended December 31, 2010, 2009 and 2008 and the balance sheet data as of December 31, 2010 and 2009 have been derived from our audited financial statements included elsewhere in this annual report on Form 10-K. The statements of operations data for the years ended December 31, 2007 and 2006, and the balance sheet data as of December 31, 2008, 2007 and 2006 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,				
	2010	2009	2008	2007	2006
Statements of Operations Data:		(in thousands, except per share data)			
Revenues	$4,908	$10,700	$32,321	$50,118	$72,798
Operating expenses:					
Research and development, including stock-based compensation of $3,170 in 2010, $3,022 in 2009, $3,941 in 2008, $5,150 in 2007 and $4,394 in 2006	78,520	81,238	107,232	103,237	105,494
Increase in fair value of Symphony Icon, Inc. purchase liability	2,710	—	—	—	—
General and administrative, including stock-based compensation of $2,308 in 2010, $2,252 in 2009, $2,559 in 2008, $2,776 in 2007 and $2,636 in 2006	19,396	19,418	21,624	21,835	22,535
Total operating expenses	100,626	100,656	128,856	125,072	128,029
Loss from operations	(95,718)	(89,956)	(96,535)	(74,954)	(55,231)
Interest and other income (expense), net	(6,083)	(3,463)	(349)	3,721	801
Consolidated net loss before taxes	(101,801)	(93,419)	(96,884)	(71,233)	(54,430)
Income tax benefit	26	102	—	—	119
Consolidated net loss	(101,775)	(93,317)	(96,884)	(71,233)	(54,311)
Less: net loss attributable to noncontrolling interest in Symphony Icon, Inc.	—	10,537	20,024	12,439	—
Net loss attributable to Lexicon Pharmaceuticals, Inc.	$(101,775)	$(82,780)	$(76,860)	$(58,794)	$(54,311)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	$(0.34)	$(0.57)	$(0.56)	$(0.59)	$(0.81)
Shares used in computing net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	302,844	145,465	136,797	99,798	66,876

	As of December 31,				
	2010	2009	2008	2007	2006
Balance Sheet Data:		(in thousands)			
Cash, cash equivalents and short-term investments, including restricted cash and investments of $430	$211,111	$157,096	$86,502	$222,109	$79,999
Short-term investments held by Symphony Icon, Inc.	—	5,417	16,610	36,666	—
Long-term investments	—	—	55,686	—	—
Working capital	203,963	118,730	87,991	229,303	39,586
Total assets	366,884	257,761	261,508	369,296	190,266

Long-term debt, net of current portion	27,345	28,482	29,529	30,493	31,372
Accumulated deficit	(673,406)	(570,175)	(487,395)	(410,535)	(351,741)
Lexicon Pharmaceuticals, Inc. stockholders' equity	247,024	163,787	185,580	256,300	85,501

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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 four drug candidates for which we have completed or are presently conducting Phase 2 clinical trials. We have initiated a Phase 1 clinical trial of an additional drug candidate, have advanced three other drug candidates into preclinical development and have small molecule compounds from a number of additional drug discovery programs in various stages of preclinical 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 of our small molecule drug programs by developing drug candidates from such programs internally and to collaborate with third parties with respect to the discovery, development and commercialization of small molecule and biotherapeutic drug candidates for other targets, particularly when the collaboration provides us with access to expertise and resources that we do not possess internally or are complementary to our own. We have established drug discovery and development collaborations with a number of leading pharmaceutical and biotechnology companies which have enabled us to generate near-term cash while offering us the potential to retain economic participation in products our collaborators develop through the collaboration. In addition, we have established collaborations and license agreements with other leading pharmaceutical and biotechnology companies, research institutes and academic institutions under which we received fees and, in some cases, are eligible to receive milestone and royalty payments, in return for granting access to some of our technologies and discoveries.

We derive substantially all of our revenues from drug discovery and development collaborations and other collaborations and technology licenses. 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 technology licenses, 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 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 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 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 our four most advanced 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, 2010, we had an accumulated deficit of $673.4 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. In connection with the continued expansion of our drug discovery and development programs, we expect to continue to incur significant research and development costs. As a result, we will need to generate significantly higher revenues to achieve profitability.

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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 four drug candidates for which we have completed or are presently conducting Phase 2 clinical trials:

- LX4211, an orally-delivered small molecule compound that we are developing as a treatment for type 2 diabetes;
- LX1031, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome and other gastrointestinal disorders;

- LX2931, an orally-delivered small molecule compound that we are developing as a treatment for rheumatoid arthritis and other autoimmune diseases; and
- LX1032, an orally-delivered small molecule compound that we are developing as a treatment for the symptoms associated with carcinoid syndrome.

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We have initiated a Phase 1 clinical trial of LX1033, an orally-delivered small molecule compound that we are developing as a treatment for irritable bowel syndrome and other gastrointestinal disorders, and we have advanced three other drug candidates into preclinical development: LX7101, a topically-delivered small molecule compound that we are developing as a treatment for glaucoma; LX5061, an orally-delivered small molecule compound that we are developing as a treatment for osteoporosis; and LX2311, an orally-delivered small molecule compound that we are developing as a treatment for autoimmune diseases. We have small molecule compounds from a number of additional drug discovery programs in various stages of preclinical research and believe that our systematic, target biology-driven approach to drug discovery will enable us to continue to expand our clinical pipeline. 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:

Phase	Estimated Completion Period
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. We update our estimates for these accruals on a monthly basis. 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 operations 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 $5.5 million for the year ended December 31, 2010, or $0.02 per share. As of December 31, 2010, stock-based compensation cost for all outstanding unvested options was $7.9

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, 2010, 2009 and 2008, respectively:

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	Expected Volatility	Risk-free Interest Rate	Expected Term	Dividend Rate
December 31, 2010:				
Employees	86%	2.3%	5	0%
Officers and non-employee directors	80%	3.3%	8	0%
December 31, 2009:				
Employees	78%	1.9%	5	0%
Officers and non-employee directors	77%	2.7%	8	0%
December 31, 2008:				
Employees	66%	2.9%	6	0%
Officers and non-employee directors	66%	3.8%	9	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 year ended December 31, 2010, we determined that one of our buildings was excess capacity and therefore recorded an impairment loss of $900,000, which was recorded as research and development expense in the accompanying statement of operations. There were no other significant impairments of long-lived assets in 2010.

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 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.

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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, 2010, 2009 and 2008

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,		
	2010	2009	2008
Total revenues	$4.9	$10.7	$32.3
Dollar decrease	$(5.8)	$(21.6)	
Percentage decrease	(54)%	(67)%	

Years Ended December 31, 2010 and 2009

- Collaborative research – Revenue from collaborative research decreased 55% to $4.2 million, primarily due to reduced revenues under our alliances with N.V. Organon and Bristol-Myers Squibb Company due to the completion in 2009 of the target discovery portion of these alliances.

- Subscription and license fees – Revenues from subscriptions and license fees decreased 48% to $0.7 million, primarily due to decreases in technology license fees.

Years Ended December 31, 2009 and 2008

- Collaborative research – Revenue from collaborative research decreased 66% to $9.3 million, primarily due to reduced revenues under our alliances with Bristol-Myers Squibb and N.V. Organon due to the completion in 2009 of the target discovery portion of these alliances, and completion in 2008 of the target discovery portion of our alliance with Genentech, Inc., partially offset by increases in revenue from our collaboration with Taconic Farms, Inc.

- Subscription and license fees – Revenue from subscriptions and license fees decreased 73% to $1.4 million, primarily due to a decrease in technology license fees.

In 2010, Taconic Farms, Inc. and United States Army Medical Research Acquisition Activity represented 35% and 23% of revenues, respectively. In 2009, Bristol-Myers Squibb Company, N.V. Organon and Taconic Farms represented 31%, 23% and 21% of revenues, respectively. In 2008, Bristol-Myers Squibb, Organon and Genentech, Inc. represented 32%, 29% and 13% 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,		
	2010	2009	2008
Total research and development expense	$78.5	$81.2	$107.2
Dollar decrease	$(2.7)	$(26.0)	
Percentage decrease	(3)%	(24)%	

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

Years Ended December 31, 2010 and 2009

- Personnel – Personnel costs decreased 7% in 2010 to $30.6 million, primarily due to reductions in our personnel in January 2009 and associated severance costs. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.

- Third-party and other services – Third-party and other services decreased 3% in 2010 to $19.6 million, primarily due to a decrease in our external clinical research and development costs. Third-party and other services include third-party research services, technology licenses and subscriptions to third-party databases.

- Facilities and equipment – Facilities and equipment costs decreased 2% in 2010 to $15.0 million, primarily due to decreases in depreciation and utilities expenses, partially offset by an impairment of buildings due to excess capacity.

- Laboratory supplies – Laboratory supplies expense increased 3% in 2010 to $6.4 million.

- Stock-based compensation – Stock-based compensation expense increased 5% in 2010 to $3.2 million.

- Other – Other costs were $3.8 million, consistent with the prior year.

Years Ended December 31, 2009 and 2008

- Personnel – Personnel costs decreased 21% in 2009 to $32.7 million, primarily due to reductions in our personnel in May 2008 and January 2009.

- Third-party and other services – Third-party and other services decreased 33% in 2009 to $20.2 million, primarily due to a decrease in external preclinical research and development costs.

- Facilities and equipment – Facilities and equipment costs decreased 17% in 2009 to $15.3 million, primarily due to decreases in depreciation expense and utilities expense.

- Laboratory supplies – Laboratory supplies expense decreased 28% in 2009 to $6.2 million, primarily due to reductions in our genetics research activities.

- Stock-based compensation – Stock-based compensation expense decreased 23% in 2009 to $3.0 million, primarily as a result of the reduction in our personnel.

- Other – Other costs decreased 22% in 2009 to $3.8 million, primarily due to a decrease in computer software expense.

Increase in Fair Value of Symphony Icon Liability

The increase in fair value of the Symphony Icon purchase liability was $2.7 million for the year ended December 31, 2010 (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):

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	Year Ended December 31,		
	2010	2009	2008
Total general and administrative expense	$19.4	$19.4	$21.6
Dollar decrease	$(0.0)	$(2.2)	
Percentage decrease	(0)%	(10)%	

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

Years Ended December 31, 2010 and 2009

- Personnel – Personnel costs increased 1% in 2010 to $9.2 million. Salaries, bonuses, employee benefits, payroll taxes, recruiting and relocation costs are included in personnel costs.
- Professional fees – Professional fees decreased 9% in 2010 to $3.6 million, primarily due to decreased legal and consulting fees.
- Facilities and equipment – Facilities and equipment costs decreased 4% in 2010 to $2.4 million.
- Stock-based compensation – Stock-based compensation expense increased 2% in 2010 to $2.3 million.
- Other – Other costs increased 16% in 2010 to $1.9 million.

Years Ended December 31, 2009 and 2008

- Personnel – Personnel costs decreased 13% in 2009 to $9.0 million, primarily due to reductions in our personnel in May 2008 and January 2009.
- Professional fees – Professional fees decreased 7% in 2009 to $4.0 million, primarily due to decreased consulting fees.
- Facilities and equipment – Facilities and equipment costs were $2.5 million, consistent with the prior year.
- Stock-based compensation – Stock-based compensation expense decreased 12% in 2009 to $2.3 million, primarily as a result of the reduction in our personnel.
- Other – Other costs decreased 16% in 2009 to $1.6 million.

Gain (Loss) on Investments, Net, Interest Income, Interest Expense and Other (Expense) Income, Net

Gain (Loss) on Investments, Net. Gain on investments was $9.9 million for the year ended December 31, 2010, representing the increase in fair value of our student loan auction rate securities. These gains were partially offset by a loss on investments of $9.7 million for the year ended December 31, 2010, representing the decline in fair value of the rights obtained from UBS AG, the investment bank that sold us our auction rate securities. Gain on investments was $3.5 million for the year ended December 31, 2009, representing the increase in fair value of our student loan auction rate securities. This gain was partially offset by a loss on investments of $2.3 million for the year ended December 31, 2009, representing the decline in fair value of the rights obtained from UBS AG. Loss on investments was $13.4 million for the year ended December 31, 2008, representing the decline in fair value of our student loan

auction rate securities. This loss was partially offset by a gain on investments of $12.1 million for the year ended December 31, 2008, representing the increase in fair value of the rights obtained from UBS AG.

Interest Income. Interest income decreased 41% in 2010 to $0.5 million from $0.9 million in 2009 primarily due to lower yields on our investments. Interest income decreased 85% in 2009 from $5.8 million in 2008, primarily due to lower average cash and investment balances as well as lower yields on our investments.

Interest Expense. Interest expense decreased 8% in 2010 to $2.7 million from $3.0 million in 2009 and increased 10% in 2009 from $2.7 million in 2008.

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Other (Expense) Income, Net. Other expense, net increased 58% in 2010 to $4.0 million from 2009 primarily due to amortization of the remaining Symphony Icon purchase asset. Other expense, net increased 21% in 2009 to $2.6 million from 2008 primarily due to an impairment of surplus equipment as a result of our reduction of personnel in January 2009.

Income Tax Benefit

The income tax benefit for the years ended December 31, 2010 and 2009 was $26,000 and $102,000, respectively.

Noncontrolling Interest in Symphony Icon, Inc.

The loss attributed to the noncontrolling interest holders of Symphony Icon decreased 47% to $10.5 million in 2009 from $20.0 million in 2008, due to the timing of expenditures related to clinical development of the drug candidates licensed to Symphony Icon. As discussed in Note 3, Recent Accounting Pronouncements, of the Notes to Consolidated Financial Statements, we have determined that upon the adoption of a new accounting pronouncement regarding variable interest entities on January 1, 2010, we are no longer the primary beneficiary of Symphony Icon, and therefore, we did not include the financial condition and results of operations of Symphony Icon in our consolidated financial statements for the period from January 1, 2010 through the exercise of the Purchase Option (as defined in Note 10, Arrangements with Symphony Icon, Inc., of the Notes to Consolidated Financial Statements) on July 30, 2010.

Net Loss Attributable to Lexicon Pharmaceuticals, Inc. and Net Loss Attributable to Lexicon Pharmaceuticals, Inc. per Common Share

Net loss attributable to Lexicon Pharmaceuticals, Inc. increased to $101.8 million in 2010 from $82.8 million in 2009 and $76.9 million in 2008. Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share decreased to $0.34 in 2010 from $0.57 in 2009 and increased from $0.56 in 2008.

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, 2010, we had received net proceeds of $786.9 million from issuances of common and preferred stock. In addition, from our inception through December 31, 2010, we received $453.0 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 $439.6 million had been recognized as revenues through December 31, 2010.

As of December 31, 2010, we had $211.1 million in cash, cash equivalents and investments. As of December 31, 2009, we had $157.1 million in cash, cash equivalents and investments and $5.4 million in investments held by Symphony Icon. We used cash of $82.4 million in operations in 2010. This consisted primarily of the consolidated net loss for the year of $101.8 million and a net gain on investments and auction rate securities of $0.1 million, partially offset by non-cash charges of $5.5 million related to stock-based compensation expense, $5.4 million related to depreciation expense, $4.0 million related to the amortization of the Symphony Icon purchase option, a non-cash charge of $2.7 million related to the increase in fair value of the Symphony Icon purchase liability, and a net decrease in other operating assets net of liabilities of $1.0 million. Investing activities used cash of $113.8 million in 2010, primarily due to net purchases of investments of $107.2 million, the acquisition of Symphony Icon of $5.6 million, net

of cash acquired, and purchases of property and equipment of $1.1 million. Financing activities provided cash of $142.9 million due to net proceeds from issuance of common stock of $181.5 million, partially offset by net repayment of debt borrowings of $38.5 million.

Invus Securities Purchase Agreement. In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment of approximately $205.5 million to purchase 50,824,986 shares of our common stock in August 2007. Under the securities purchase agreement, as amended and supplemented, and after accounting for the $181.5 million in net proceeds from our public offering and concurrent private placement of common stock in March 2010, Invus, L.P. and its affiliate Invus C.V., which we collectively refer to as Invus, have the right to require us to initiate a pro rata rights offering to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount of up to approximately $163.0 million. The price per share of the rights offering would be designated by Invus in a range between $4.50 and a then-current average market price of our common stock. All stockholders would have oversubscription rights with respect to the rights offering and Invus would be required to purchase its

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pro rata portion of the offering. Invus may exercise its right to require us to conduct such a rights offering by giving us notice within a period of one year beginning on February 28, 2011, which will be extended by the number of days during such period that Invus is not permitted under the securities purchase agreement to initiate the rights offering as a result of any "blackout period" in connection with certain public offerings of our common stock.

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

In connection with the securities purchase agreement, we entered into a stockholders' agreement with Invus, L.P. under which Invus (a) has specified rights with respect to designation of directors and participation in future equity issuances by us, (b) is subject to certain standstill restrictions, as well as restrictions on transfer and the voting of the shares of common stock held by it and its affiliates, and (c), as long as Invus holds at least 15% of the total number of outstanding shares of our common stock, is entitled to certain minority protections.

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 LX1031, 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 and agreed to make up to $80 million in additional base and contingent payments.

The base payments will be in an amount equal to $50 million, less 50% of the expenses we incur after our exercise of the purchase option for the development of LX1031, LX1032, LX1033 and other pharmaceutical compositions modulating the same target as those drug candidates, which we refer to as the "LG103 programs," subject to certain exceptions and up to an aggregate reduction of $15 million. The base payments are payable in our discretion at any time before July 30, 2013.

The contingent payments will consist of 50% of any consideration we receive pursuant to any licensing transaction under which we grant a third party rights to commercialize a drug candidate from the LG103 programs, subject to certain exceptions and up to a maximum of $30 million plus the amount of any reduction in the base payments for our development expenses for the LG103 programs, which we refer to as the "recapture eligible amount." 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 any recapture eligible amount 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.

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The base payments and the contingent payments may be paid in cash, common stock, or a combination of cash and common stock, in our discretion, provided that at least 50% of any payment made on or prior to July 30, 2012 will be paid in common stock and no more than 50% of any payment made after such date will be paid in common stock.
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 $28.5 million as of December 31, 2010. In May 2002, our subsidiary Lexicon Pharmaceuticals (New Jersey), Inc. leased a 76,000 square-foot laboratory and office space in Hopewell, New Jersey. The term of the lease extends until June 30, 2013. The lease provides for an escalating yearly base rent payment of $1.3 million in the first year, $2.1 million in years two and three, $2.2 million in years four to six, $2.3 million in years seven to nine and $2.4 million in years ten and eleven. 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, 2010:

	Payments due by period (in millions)				
Contractual Obligations	Total	Less than 1 year	2-3 years	4-5 years	More than 5 years
Debt	$28.5	$1.1	$2.6	$24.8	$—
Interest payment obligations	7.4	2.3	4.4	0.7	—
Operating leases	6.5	2.6	3.9	—	—
Symphony Icon payment obligations [1]	35.0	—	35.0	—	—
Total	$77.4	$6.0	$45.9	$25.5	$—

[1] Represents expected base payments under Symphony Icon purchase option, which may be paid in cash, common stock, or a combination of cash and common stock, in our discretion, provided that at least 50% of any payment made on or prior to July 30, 2012 will be paid in common stock and no more than 50% of any payment made after such date will be paid in common stock.

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 $211.1 million in cash and cash equivalents and short-term investments as of December 31, 2010. 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.

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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, 2010. 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, 2010, our internal control over financial reporting is effective.

Our independent auditors have also audited our internal control over financial reporting as of December 31, 2010 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.

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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, 2010 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, 2010. 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, 2010.

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, 2010.

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, 2010.

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PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) Documents filed as a part of this report:

1. Consolidated Financial Statements

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	—	Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Registration Statement on Form S-1 (Registration No. 333-96469) and incorporated by reference herein).
3.2	—	First Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.2 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein).
3.3	—	Second Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.3 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated by reference herein).
3.4	—	Third Certificate of Amendment to Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2009 and incorporated by reference herein).
3.5	—	Amended and Restated Bylaws (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated October 24, 2007 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	—	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).
4.5	—	

		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).
4.6	—	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).

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Exhibit No.		Description
4.7	—	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).
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 May 4, 2009, with Ajay Bansal (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated May 4, 2009 and incorporated by reference herein).
*10.6	—	Consulting Agreement with Philip M. Brown, M.D., J.D., dated October 16, 2010, as amended.
10.7	—	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).
10.8	—	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).
10.9	—	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).
10.10	—	Summary of Non-Employee Director Compensation (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated April 23, 2009 and incorporated by reference herein).
10.11	—	Summary of 2011 Named Executive Officer Cash Compensation (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated February 25, 2011 and incorporated by reference herein).
10.12	—	Equity Incentive Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated April 23, 2009 and incorporated by reference herein).
10.13	—	Non-Employee Directors' Stock Option Plan (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated April 23, 2009 and incorporated by reference herein).
10.14	—	Coelacanth Corporation 1999 Stock Option Plan (filed as Exhibit 99.1 to the Company's Registration Statement on Form S-8 (Registration No. 333-66380) and incorporated by reference herein).
10.15	—	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).
10.16	—	Form of Stock Option Agreement with Directors under the Non-Employee Directors' Stock Option 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).
10.17	—	Form of Stock Option Agreement with Officers under the Equity Incentive Plan (filed as Exhibit 10.16 to the Company's Annual Report on Form 10-K for the year ended December 31, 2009 and incorporated by reference herein).
10.18	—	

		Form of Stock Bonus Agreement with Officers under the Equity Incentive Plan (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated February 23, 2011 and incorporated by reference herein).
10.19	—	Form of 2010 Restricted Stock Unit Agreement with Officers under the Equity Incentive Plan (filed as Exhibit 10.2 to the Company's Current Report on Form 8-K dated February 15, 2010 and incorporated by reference herein).
10.20	—	Form of 2011 Restricted Stock Unit Agreement with Officers under the Equity Incentive Plan (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated February 23, 2011 and incorporated by reference herein).
†10.21	—	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).

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Exhibit No.		Description
†10.22	—	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).
†10.23	—	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).
†10.24	—	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).
†10.25	—	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).
10.26	—	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).
10.27	—	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).
10.28	—	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).
10.29	—	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).
10.30	—	Lease Agreement, dated May 23, 2002, between Lexicon Pharmaceuticals (New Jersey), Inc. and Townsend Property Trust Limited Partnership (filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2002 and incorporated by reference herein).
*21.1	—	Subsidiaries.
*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.

* 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.

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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.

Lexicon Pharmaceuticals, Inc.

Date: March 15, 2011 By: /s/ ARTHUR T. SANDS
Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

Date: March 15, 2011 By: /s/ JEFFREY L. WADE
Jeffrey L. Wade
Executive Vice President, Corporate Development and Chief Financial Officer

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 and Chief Executive Officer (Principal Executive Officer)	March 15, 2011
/s/ JEFFREY L. WADE Jeffrey L. Wade	Executive Vice President, Corporate Development and Chief Financial Officer (Principal Financial Officer)	March 15, 2011
/s/ JAMES F. TESSMER James F. Tessmer	Vice President, Finance and Accounting (Principal Accounting Officer)	March 15, 2011
/s/ SAMUEL L. BARKER Samuel L. Barker, Ph.D.	Chairman of the Board of Directors	March 15, 2011
/s/ PHILIPPE J. AMOUYAL Philippe J. Amouyal	Director	March 15, 2011
/s/ RAYMOND DEBBANE Raymond Debbane	Director	March 15, 2011
/s/ ROBERT J. LEFKOWITZ Robert J. Lefkowitz, M.D.	Director	March 15, 2011
/s/ ALAN S. NIES Alan S. Nies, M.D.	Director	March 15, 2011
/s/ FRANK P. PALANTONI Frank P. Palantoni	Director	March 15, 2011

/s/ CHRISTOPHER J. SOBECKI Christopher J. Sobecki	Director	March 15, 2011
/s/ JUDITH L. SWAIN Judith L. Swain, M.D.	Director	March 15, 2011

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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, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010. 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, 2010 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2010, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 3 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, 2010, 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 15, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Houston, Texas
March 15, 2011

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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, 2010, 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, 2010, 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, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010 and our report dated March 15, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Houston, Texas
March 15, 2011

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

	As of December 31,	
	2010	2009
Assets		
Current assets:		
Cash and cash equivalents	$47,208	$100,554
Short-term investments, including restricted investments of $430	163,903	56,542
Short-term investments held by Symphony Icon, Inc. (Note 3)	—	5,417
Accounts receivable, net of allowances of $35	744	815
Prepaid expenses and other current assets	2,883	6,356
Total current assets	214,738	169,684
Property and equipment, net of accumulated depreciation and amortization of $80,323 and $75,795, respectively	53,427	58,754
Goodwill	44,543	25,798
Other intangible assets	53,557	—
Other assets	619	3,525
Total assets	$366,884	$257,761
Liabilities and Equity		
Current liabilities:		
Accounts payable	$3,159	$5,919
Accrued liabilities	6,264	5,611
Current portion of deferred revenue	214	942
Current portion of long-term debt	1,138	38,482
Total current liabilities	10,775	50,954
Deferred revenue, net of current portion	14,212	14,212
Long-term debt	27,345	28,482
Deferred tax liabilities	18,745	—
Other long-term liabilities	48,783	616
Total liabilities	119,860	94,264
Commitments and contingencies		
Equity:		
Lexicon Pharmaceuticals, Inc. stockholders' equity:		
Preferred stock, $.01 par value; 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $.001 par value; 900,000 shares authorized; 337,566 and 175,785 shares issued, respectively	338	176
Additional paid-in capital	920,324	733,874
Accumulated deficit	(673,406)	(570,175)
Accumulated other comprehensive gain	5	—
Treasury stock, at cost, 158 and 80 shares, respectively	(237)	(88)
Total Lexicon Pharmaceuticals, Inc. stockholders' equity	247,024	163,787
Noncontrolling interest in Symphony Icon, Inc. (Note 3)	—	(290)
Total equity	247,024	163,497
Total liabilities and equity	$366,884	$257,761

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

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Lexicon Pharmaceuticals, Inc.

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

	Year Ended December 31,		
	2010	2009	2008
Revenues:			
Collaborative research	$4,191	$9,334	$27,177
Subscription and license fees	717	1,366	5,144
Total revenues	4,908	10,700	32,321
Operating expenses:			
Research and development, including stock-based compensation of $3,170, $3,022 and $3,941, respectively	78,520	81,238	107,232
Increase in fair value of Symphony Icon, Inc. purchase liability	2,710	—	—
General and administrative, including stock-based compensation of $2,308, $2,252 and $2,559, respectively	19,396	19,418	21,624
Total operating expenses	100,626	100,656	128,856
Loss from operations	(95,718)	(89,956)	(96,535)
Gain (loss) on investments, net	141	1,173	(1,314)
Interest income	519	880	5,762
Interest expense	(2,719)	(2,966)	(2,691)
Other expense, net	(4,024)	(2,550)	(2,106)
Consolidated net loss before taxes	(101,801)	(93,419)	(96,884)
Income tax benefit	26	102	—
Consolidated net loss	(101,775)	(93,317)	(96,884)
Less: net loss attributable to Symphony Icon, Inc. (Note 3)	—	10,537	20,024
Net loss attributable to Lexicon Pharmaceuticals, Inc.	$(101,775)	$(82,780)	$(76,860)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	$(0.34)	$(0.57)	$(0.56)
Shares used in computing net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	302,844	145,465	136,797

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

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Lexicon Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity
(In thousands)

	Lexicon Pharmaceuticals, Inc. Stockholders								
	Common Stock Shares	Common Stock Par Value	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Gain (Loss)	Treasury Stock	Total	Noncontrolling Interest	Total Equity
Balance at December 31, 2007	136,796	$137	$666,702	$ (410,535)	$ (4)	$—	$256,300	$ 30,271	$286,571
Stock-based compensation	—	—	6,135	—	—	—	6,135	—	6,135
Exercise of common stock options	1	—	1	—	—	—	1	—	1
Net loss	—	—	—	(76,860)	—	—	(76,860)	(20,024)	(96,884)
Unrealized gain on investments	—	—	—	—	4	—	4	—	4
Comprehensive loss							(76,856)		(96,880)
Balance at December 31, 2008	136,797	137	672,838	(487,395)	—	—	185,580	10,247	195,827
Stock-based compensation	—	—	5,639	—	—	—	5,639	—	5,639
Grant of restricted stock	534	—	—	—	—	—	—	—	—
Issuance of common stock, net of fees	38,333	39	55,133	—	—	—	55,172	—	55,172
Exercise of common stock options	121	—	264	—	—	—	264	—	264
Repurchase of common stock	—	—	—	—	—	(88)	(88)	—	(88)
Net loss	—	—	—	(82,780)	—	—	(82,780)	(10,537)	(93,317)
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	—	—	—	(1,456)	—	—	(1,456)	—	(1,456)

accounting principle									
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
Exercise of common stock options	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
Comprehensive loss							(101,770)		(101,770)
Balance at December 31, 2010	337,566	$338	$920,324	$(673,406)	$5	$(237)	$247,024	$—	$247,024

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

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Lexicon Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2010	2009	2008
Cash flows from operating activities:			
Consolidated net loss	$(101,775)	$(93,317)	$(96,884)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	5,394	6,159	7,929
Impairment of fixed assets	1,001	436	—
Amortization of Symphony Icon, Inc. purchase option	3,957	2,141	2,141
Increase in fair value of Symphony Icon, Inc. purchase liability	2,710	—	—
Stock-based compensation	5,478	5,274	6,500
(Gain) loss on auction rate securities (“ARS”)	(9,866)	(3,508)	13,374
(Gain) loss on ARS Rights	9,725	2,335	(12,060)
Changes in operating assets and liabilities:			
(Increase) decrease in receivables	488	(247)	1,195
(Increase) decrease in prepaid expenses and other current assets	6,704	(869)	(1,375)
(Increase) decrease in other assets	(218)	104	108
Decrease in accounts payable and other liabilities	(5,238)	(2,794)	(2,256)
Decrease in deferred revenue	(728)	(4,730)	(14,272)
Net cash used in operating activities	(82,368)	(89,016)	(95,600)
Cash flows from investing activities:			
Purchases of property and equipment	(1,132)	(369)	(2,187)
Proceeds from disposal of property and equipment	64	107	—
Purchases of investments held by Symphony Icon, Inc.	—	(4,250)	—
Maturities of investments held by Symphony Icon, Inc.	—	15,443	20,056
Acquisition of Symphony Icon, Inc., net of cash acquired	(5,561)	—	—
Purchases of investments	(155,856)	(59,955)	(39,847)
Maturities of investments	48,641	60,901	181,393
Net cash provided by (used in) investing activities	(113,844)	11,877	159,415
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of fees	181,496	55,436	1
Repurchase of common stock	(149)	(88)	—
Proceeds from debt borrowings	11,377	38,592	—
Repayment of debt borrowings	(49,858)	(2,120)	(881)
Net cash provided by (used in) financing activities	142,866	91,820	(880)
Net increase (decrease) in cash and cash equivalents	(53,346)	14,681	62,935
Cash and cash equivalents at beginning of year	100,554	85,873	22,938
Cash and cash equivalents at end of year	$47,208	$100,554	$85,873
Supplemental disclosure of cash flow information:			
Cash paid for interest	$2,424	$2,519	$2,599

Cash received related to income taxes	$26	$102	$—
Supplemental disclosure of noncash investing and financing activities:			
Unrealized gain on investments	$5	$—	$4
Intangible assets acquired with long-term liabilities	$43,557	$—	$—

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

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Lexicon Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

December 31, 2010

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, payments received under collaboration and alliance agreements, database subscription agreements, government grants and contracts and technology licenses, and financing obtained 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 additional 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. In 2009 and 2008, the consolidated financial statements also include the accounts of one variable interest entity, Symphony Icon, Inc. ("Symphony Icon"), for which the Company was the primary beneficiary and therefore had consolidated the financial condition and results of operations of Symphony Icon. Upon the adoption of a new accounting pronouncement regarding variable interest entities on January 1, 2010, Lexicon determined that it was no longer the primary beneficiary of Symphony Icon, and therefore did not include the financial condition and results of operations of Symphony Icon in its consolidated financial statements for the period from January 1, 2010 through the exercise of the Purchase Option (as defined in Note 10) on July 30, 2010.

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, 2010, short-term investments consist of U.S. treasury bills and certificates of deposit. As of December 31, 2009, short-term investments consisted of certificates of deposit, auction rate securities and auction rate security rights (“ARS Rights”) obtained from UBS AG, the investment bank that sold Lexicon the auction rate securities it held prior to July 1, 2010 (see Note 4). 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. Lexicon has elected to classify its auction rate securities and ARS Rights as trading securities, which requires recording these securities at fair value. 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, 2010 and 2009, restricted cash and investments were $0.4 million.

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

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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 2010, customers in the United States and Europe represented 94% and 6% of revenue, respectively. In 2009, customers in the United States and Europe represented 75% and 25% of revenue, respectively. In 2008, customers in the United States and Europe represented 68% and 32% of revenue, respectively. At December 31, 2010, 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 2010, Taconic Farms, Inc. and United States Army Medical Research Acquisition Activity represented 35% and 23% of revenues, respectively. In 2009, Bristol-Myers Squibb Company, N.V. Organon and Taconic Farms represented 31%, 23% and 21% of revenues, respectively. In 2008, Bristol-Myers Squibb, Organon and Genentech, Inc. represented 32%, 29% and 13% 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 2010, 2009 or 2008.

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 operations 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-

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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.

Stock-Based Compensation: The Company recognizes compensation expense in its statement of operations for share-based payments, including stock options and restricted stock 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, 2010, stock-based compensation cost for all outstanding unvested options and restricted stock units was $7.9 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, 2010, 2009 and 2008, respectively:

	Expected Volatility	Risk-free Interest Rate	Expected Term	Dividend Rate
December 31, 2010:				
Employees	86%	2.3%	5	0%
Officers and non-employee directors	80%	3.3%	8	0%
December 31, 2009:				
Employees	78%	1.9%	5	0%
Officers and non-employee directors	77%	2.7%	8	0%
December 31, 2008:				
Employees	66%	2.9%	6	0%
Officers and non-employee directors	66%	3.8%	9	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 and warrants are not included because they are

antidilutive.

Comprehensive Loss: Comprehensive loss is comprised of net loss and unrealized gains and losses on available-for-sale securities. Comprehensive loss is reflected in the consolidated statements of stockholders' equity. There were unrealized gains of $5,000, none and $4,000 in the years ended December 31, 2010, 2009 and 2008, respectively.

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3. Recent Accounting Pronouncements

In June 2009, the Financial Accounting Standards Board (“FASB”) issued a new accounting pronouncement regarding variable interest entities which changes how a company determines when an entity that is insufficiently capitalized or is not controlled through voting (or similar rights) should be consolidated. The determination of whether a company is required to consolidate an entity is based on, among other things, an entity's purpose and design and a company's ability to direct the activities that most significantly impacts the entity's economic performance. The impact of the adoption of this pronouncement may be applied retrospectively with a cumulative-effect adjustment to retained earnings as of the beginning of the first year restated, or through a cumulative-effect adjustment on the date of adoption. This pronouncement, found under FASB ASC Topic 810, is effective for fiscal years, and interim periods within those fiscal years, beginning on or after November 15, 2009. The Company determined that upon adoption of this pronouncement on January 1, 2010, Lexicon was no longer the primary beneficiary of Symphony Icon, and therefore did not include the financial condition and results of operations of Symphony Icon in its consolidated financial statements for the period from January 1, 2010 through the exercise of the Purchase Option (as defined in Note 10) on July 30, 2010. As of December 31, 2009, Symphony Icon had $6.2 million in current assets, $5.4 million of which was short-term investments, and $4.2 million in current liabilities. On January 1, 2010, Lexicon recorded a cumulative-effect adjustment to retained earnings (accumulated deficit) as a result of adopting this pronouncement, which increased the accumulated deficit balance by $1.5 million.

In October 2009, the FASB issued Accounting Standards Update (“ASU”) No. 2009-13, “Multiple-Deliverable Revenue Arrangements”, which amends FASB ASC Topic 605. ASU No. 2009-13 addresses how to determine whether an arrangement involving multiple deliverables contain more than one unit of accounting and how to allocate consideration to each unit of accounting in the arrangement. This pronouncement replaces all references to fair value as the measurement criteria with the term selling price and establishes a hierarchy for determining the selling price of a deliverable. The pronouncement also eliminates the use of the residual value method for determining the allocation of arrangement consideration, and requires additional disclosures. This pronouncement should be applied prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010, with early adoption permitted. This pronouncement's impact on accounting for revenue arrangements is dependent upon arrangements entered into on or after that time.

In April 2010, the FASB issued ASU No. 2010-17, “Milestone Method of Revenue Recognition”, which amends FASB ASC Topic 605. ASU No. 2010-17 provides guidance on defining a milestone and determining when it may be appropriate to apply the milestone method of revenue recognition for research or development transactions. Research or development arrangements frequently include payment provisions whereby a portion or all of the consideration is contingent upon milestone events such as successful completion of phases in a study or achieving a specific result from the research or development efforts. The amendments in this ASU provide guidance on the criteria that should be met for determining whether the milestone method of revenue recognition is appropriate. ASU 2010-17 is effective for fiscal years and interim periods within those years beginning on or after June 15, 2010, with early adoption permitted. This pronouncement's impact on accounting for revenue arrangements with milestones is dependent upon milestones achieved on or after that time.

4. Cash and Cash Equivalents and Investments

The fair value of cash and cash equivalents and investments held at December 31, 2010 and 2009 are as follows:

	As of December 31, 2010			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		

Cash and cash equivalents	$47,207	$1	$—	$47,208
Securities maturing within one year:				
Certificates of deposit	545	—	—	545
U.S. treasury securities	163,354	10	(6)	163,358
Total short-term investments	$163,899	$10	$(6)	$163,903
Total cash and cash equivalents and investments	$211,106	$11	$(6)	$211,111

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	As of December 31, 2009			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		
Cash and cash equivalents	$100,554	$—	$—	$100,554
Securities maturing within one year:				
Certificates of deposit	508	—	—	508
ARS rights	—	9,725	—	9,725
Securities maturing after ten years:				
Auction rate securities	56,175	—	(9,866)	46,309
Total short-term investments	$56,683	$9,725	$(9,866)	$56,542
Short-term investments held by Symphony Icon, Inc.:				
Cash and cash equivalents	5,417	—	—	5,417
Total short-term investments held by Symphony Icon, Inc.	$5,417	$—	$—	$5,417
Total cash and cash equivalents and investments	$162,654	$9,725	$(9,866)	$162,513

There were no realized gains or losses for the years ended December 31, 2010 and 2009. There were realized gains of $123,000 for the year ended December 31, 2008.

At December 31, 2009, Lexicon held $56.2 million (par value), with an estimated fair value of $46.3 million, of auction rate securities. On July 1, 2010, Lexicon sold all of its remaining auction rate securities and received the total par value amount of such auction rate securities in cash. These notes were issued by various state agencies for the purpose of financing student loans. The securities have historically traded at par and were redeemable at par plus accrued interest at the option of the issuer. Interest was typically paid at the end of each auction period or semiannually. Until February 2008, the market for Lexicon’s auction rate securities was highly liquid. However, starting in February 2008, a substantial number of auctions “failed,” meaning that there was not enough demand to sell all of the securities that holders desired to sell at auction. The immediate effect of a failed auction was that such holders could not sell the securities at auction and the interest rate on the security generally reset to a maximum interest rate. In the case of funds invested by Lexicon in auction rate securities which were the subject of a failed auction, Lexicon was not able to access the funds without a loss of principal unless a future auction on these investments was successful or the issuer redeemed the security. Lexicon has modified its current investment strategy to reallocate its investments more into U.S. treasury securities and U.S. treasury-backed money market investments.

At December 31, 2009, observable auction rate securities market information was not available to determine the fair value of Lexicon’s investments. Lexicon estimated the fair value of these securities at $46.3 million as of December 31, 2009 using models of the expected future cash flows related to the securities and taking into account assumptions about the cash flows of the underlying student loans, as well as secondary market trading data. The assumptions used in preparing the discounted cash flow model include estimates of interest rates, timing and amount of cash flows, liquidity premiums and expected holding periods of the auction rate securities, based on data available as of December 31, 2009. The underlying assumptions are volatile and are subject to change.

In November 2008, Lexicon accepted an offer from UBS AG, the investment bank that sold Lexicon the auction rate securities, providing Lexicon with the ARS Rights. The ARS Rights permitted Lexicon to require UBS to purchase its auction rate securities at par value during the period from June 30, 2010 through July 2, 2012. Conversely, UBS had the right, in its discretion, to purchase or sell the securities at any time by paying Lexicon the par value of such securities. On June 30, 2010, Lexicon exercised the ARS Rights and UBS purchased Lexicon's remaining $23.6

million of auction rate securities at par value on July 1, 2010. Lexicon was also eligible to borrow from UBS Bank USA, an affiliate of UBS, at no net cost up to 75% of the market value of the securities, as determined by UBS Bank USA, which loans became payable upon the purchase or sale of the securities by UBS (see note 9). On July 1, 2010, Lexicon paid the remaining $16.0 million outstanding under this credit line.

The enforceability of the ARS Rights resulted in a separate asset that was measured at its fair value. Lexicon elected to measure the ARS Rights under a fair value option, which permits entities to choose, at certain election dates, to measure eligible items at fair value. As a result of accepting the ARS Rights, Lexicon elected to classify the ARS Rights and reclassify its investments in auction rate securities as trading securities from available-for-sale securities. As a result, Lexicon was required to assess the fair

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value of these two individual assets and record changes each period until the ARS Rights were exercised and the auction rate securities were redeemed.

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, 2010 and 2009.

	Assets and Liabilities at Fair Value As of December 31, 2010			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Assets				
Cash and cash equivalents	$47,208	$—	$—	$47,208
Short-term investments	163,903	—	—	163,903
Total cash and cash equivalents and investments	$211,111	$—	$—	$211,111
Liabilities				
Other long-term liabilities	$—	$—	$48,458	$48,458
Total liabilities	$—	$—	$48,458	$48,458

	Financial Assets at Fair Value As of December 31, 2009			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Assets				
Cash and cash equivalents	$100,554	$—	$—	$100,554
Short-term investments	508	—	56,034	56,542
Short-term investments held by Symphony Icon, Inc.	5,417	—	—	5,417
Total cash and cash equivalents and investments	$106,479	$—	$56,034	$162,513

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The table presented below summarizes the change in consolidated balance sheet carrying value associated with Level 3 financial assets for the years ended December 31, 2008, 2009 and 2010.

	Short-term Investments	Long-term Investments	Total
	(in thousands)		
Balance at December 31, 2007	$—	$—	$—
Unrealized losses included in earnings as loss on investments	—	(13,374)	(13,374)
Unrealized gains included in earnings as gain on investments	—	12,060	12,060
Net sales and settlements	—	(21,050)	(21,050)
Transfers into Level 3	—	78,050	78,050
Balance at December 31, 2008	—	55,686	55,686
Unrealized gains included in earnings as gain on investments	350	823	1,173
Net sales and settlements	(725)	(100)	(825)
Reclassification from long-term to short-term investments	56,409	(56,409)	—
Balance at December 31, 2009	56,034	—	56,034
Unrealized gains included in earnings as gain on investments, net	141	—	141
Net sales and settlements	(56,175)	—	(56,175)
Balance at December 31, 2010	$—	$—	$—

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 in Symphony Icon purchase liability in the accompanying consolidated statements of operations. During the year ended December 31, 2010, the fair value of the Symphony Icon purchase consideration liability increased by $2.7 million. The following table summarizes the change in consolidated balance sheet carrying value associated with Level 3 liabilities for the year ended December 31, 2010.

	Other Long-term Liabilities
	(in thousands)
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	$48,267

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.

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6. Property and Equipment

Property and equipment at December 31, 2010 and 2009 are as follows:

	Estimated Useful Lives In Years	As of December 31, 2010	2009
		(in thousands)	
Computers and software	3-5	$10,989	$10,986
Furniture and fixtures	5-7	7,634	7,634
Laboratory equipment	3-7	38,135	39,047
Leasehold improvements	7-10	9,896	9,786
Buildings	15-40	63,532	63,532
Land	—	3,564	3,564
Total property and equipment		133,750	134,549
Less: Accumulated depreciation and amortization		(80,323)	(75,795)
Net property and equipment		$53,427	$58,754

During the year ended December 31, 2010, the Company determined that one of its buildings was excess capacity and therefore recorded an impairment loss of $900,000, which was recorded as research and development expense in the accompanying statement of operations. The fair value of the impaired building was estimated using sales prices in similar real estate sales.

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, 2010 and 2009 are as follows:

	As of December 31, 2010	2009
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$180,543	$161,020
Research and development tax credits	31,399	29,440
Capitalized research and development	42,208	29,870
Stock-based compensation	10,730	9,778
Deferred revenue	5,041	5,296
Other	2,825	1,699
Total deferred tax assets	272,746	237,103
Deferred tax liabilities:		
Deferred tax liability related to acquisition of Symphony Icon	(18,745)	—
Other	(412)	(413)

Total deferred tax liabilities	(19,157)	(413)
Less: valuation allowance	(272,334)	(236,690)
Net deferred tax liabilities	$(18,745)	$—

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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, 2010, Lexicon had both federal and state NOL carryforwards of approximately $498.3 million and $67.0 million, respectively. The federal and state NOL carryforwards begin to expire in 2011. The Company has R&D tax credit carryforwards of approximately $31.4 million expiring beginning in 2011. 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, 2010, the valuation allowance increased $35.6 million, primarily due to the Company's current year net loss. Lexicon recorded income tax benefits of $26,000 and $102,000 in the years ended December 31, 2010 and 2009, respectively. As of December 31, 2010 and 2009, 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, 2010 and 2009, 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. The following table represents the changes in goodwill for the year ended December 31, 2010:

Balance at December 31, 2009	$25,798
Additional goodwill related to the acquisition of Symphony Icon	18,745
Balance at December 31, 2010	$44,543

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

Mortgage Loan: 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 buildings and land that serve as collateral for the mortgage loan are included in property and equipment at $63.5 million and $3.6 million, respectively, before accumulated depreciation, as of December 31, 2010.

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.

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UBS Credit Line: In January 2009, Lexicon entered into a credit line agreement with UBS Bank USA that provided an uncommitted, demand, revolving line of credit. Lexicon entered into the credit line in connection with its acceptance of an offer from UBS AG, the investment bank that sold Lexicon its auction rate securities, providing Lexicon with rights to require UBS to purchase its auction rate securities at par value during the period from June 30, 2010 through July 2, 2012. On June 30, 2010, Lexicon exercised its rights and UBS purchased Lexicon's remaining $23.6 million of auction rate securities at par value on July 1, 2010. The credit line was secured only by these auction rate securities and advances under the credit line were made on a “no net cost” basis, meaning that the interest paid by Lexicon on advances did not exceed the interest or dividends paid to Lexicon by the issuer of the auction rate securities. The interest rate paid on the line of credit was less than the Company's estimated current incremental borrowing rate. On July 1, 2010, Lexicon repaid its remaining $16.0 million outstanding under this credit line with the proceeds from the UBS purchase of Lexicon's auction rate securities.

The following table includes the aggregate future principal payments of the Company’s long-term debt as of December 31, 2010:

	For the Year Ending December 31 (in thousands)
2011	$1,138
2012	1,230
2013	1,343
2014	24,772
Total debt	28,483
Less current portion	(1,138)
Total long-term debt	$27,345

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 LX1031, 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, Inc. 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 the Purchase Option (as defined below).

Under a Purchase Option Agreement, dated June 15, 2007, among the Company, Symphony Icon and Holdings, the Company received from Holdings 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. 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 in the accompanying consolidated balance sheet 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, $2.1 million and $2.1 million is recorded in other expense, net in the accompanying consolidated statements of operations for the years ended December 31, 2010, 2009 and 2008, respectively.

Under an Amended and Restated Research and Development Agreement, dated June 15, 2007, among the Company, Symphony Icon and Holdings (the "R&D Agreement"), Symphony Icon and the Company were developing the Programs in accordance with a specified development plan and related development budget. The R&D Agreement provided that the

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Company would continue to be primarily responsible for the development of the Programs. The Company's development activities were supervised by Symphony Icon's development committee, which was comprised of an equal number of representatives from the Company and Symphony Icon. The development committee reported to Symphony Icon's board of directors, which was comprised of five members, including one member designated by the Company and two independent directors.

Under a Research Cost Sharing, Payment and Extension Agreement, dated June 15, 2007, among the Company, Symphony Icon and Holdings, upon the recommendation of the development committee, Symphony Icon's board of directors had the right to require the Company to pay Symphony Icon up to $15 million for Symphony Icon's use in the development of the Programs in accordance with the specified development plan and related development budget. Through July 2010, Symphony Icon's board of directors requested the Company to pay Symphony Icon $9.3 million under this agreement, all of which was paid prior to the exercise of the Purchase Option on July 30, 2010.

Prior to January 1, 2010, Lexicon had determined that Symphony Icon was a variable interest entity for which it was the primary beneficiary. This determination was based on Holdings' lack of controlling rights with respect to Symphony Icon's activities and the limitation on the amount of expected residual returns Holdings could expect from Symphony Icon if Lexicon exercised its Purchase Option. Lexicon had determined it was a variable interest holder of Symphony Icon due to its contribution of the intellectual property relating to the Programs and its issuance of shares of its common stock in exchange for the Purchase Option. Lexicon had determined that it was a primary beneficiary as a result of certain factors, including its primary responsibility for the development of the Programs and its contribution of the intellectual property relating to the Programs. As a result, Lexicon included the financial condition and results of operations of Symphony Icon in its consolidated financial statements through December 31, 2009. Symphony Icon's cash and cash equivalents have been recorded on Lexicon's consolidated financial statements as short-term investments held by Symphony Icon as of December 31, 2009. The noncontrolling interest in Symphony Icon on Lexicon's consolidated balance sheet initially reflected the $45 million proceeds contributed into Symphony Icon less $2.3 million of structuring and legal fees. As the collaboration progressed, this line item was reduced by Symphony Icon's losses, which were $10.5 million and $20.0 millions for the years ended December 31, 2009 and 2008, respectively. The reductions to the noncontrolling interest in Symphony Icon were reflected in Lexicon's consolidated statements of operations using a similar caption and reduced the amount of Lexicon's reported net loss.

Upon the adoption of a new accounting pronouncement regarding variable interest entities on January 1, 2010, Lexicon determined that it was no longer the primary beneficiary of Symphony Icon. Under the new accounting guidance, neither Lexicon nor Holdings has the power to direct the activities that most significantly impact the economic performance of Symphony Icon; therefore, there was no primary beneficiary. As a result, Lexicon deconsolidated Symphony Icon as of January 1, 2010, and did not include the financial condition and results of operations of Symphony Icon in its consolidated financial statements for the period from January 1, 2010 through the exercise of the Purchase Option on July 30, 2010. Through the exercise of the Purchase Option on July 30, 2010, Lexicon did not charge any license fees and did not record any revenue from Symphony Icon.

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 and agreed to make up to $80 million in additional base and contingent payments.

The base payments will be in an amount equal to $50 million, less 50% of the expenses Lexicon incurs after its exercise of the Purchase Option for the development of LX1031, LX1032, LX1033 and other pharmaceutical compositions modulating the same target as those drug candidates (the “LG103 Programs”), subject to certain exceptions and up to an aggregate reduction of $15 million. The base payments are payable in Lexicon's discretion at any time before July 30, 2013.

The contingent payments will consist of 50% of any consideration Lexicon receives pursuant to any licensing transaction under which Lexicon grants a third party rights to commercialize a drug candidate from the LG103 Programs (a “Licensing Transaction”), subject to certain exceptions and up to a maximum of $30 million plus the amount of any reduction in the base payments for Lexicon's development expenses for the LG103 Programs (the “Recapture Eligible Amount”). 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 any Recapture Eligible Amount 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

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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 base payments and the contingent payments may be paid in cash, common stock, or a combination of cash and common stock, in Lexicon's discretion, provided that at least 50% of any payment made on or prior to July 30, 2012 will be paid in common stock and no more than 50% of any payment made after such date will be paid in common stock.

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. Subsequent changes in the fair value of the Symphony Icon purchase consideration liability are recorded as increase in fair value of Symphony Icon purchase liability expense in the accompanying consolidated statements of operations. During the year ended December 31, 2010, the fair value of the Symphony Icon purchase consideration liability increased by $2.7 million.

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	58,541
Accounts payable and accrued liabilities	(2,984)
Deferred tax liability	(18,745)
Total liabilities assumed	(21,729)
Net identifiable assets acquired	36,812
Goodwill	18,745
Net assets acquired	$55,557

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. 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.

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The following represents the pro forma consolidated statements of operations as if Symphony Icon had been included in the consolidated results of Lexicon for the entire years ending December 31, 2010 and 2009 (in thousands):

	Year Ended December 31,	
	2010	2009
Revenues	$4,908	$10,700
Net loss attributable to Lexicon Pharmaceuticals, Inc.	(97,818)	(91,176)

These amounts have been calculated by removing the amortization of the Purchase Option for the years ended December 31, 2010 and 2009 and removing any amounts allocated to noncontrolling interest for the year ended December 31, 2009. There are no revenue or earnings of Symphony Icon included in Lexicon's consolidated income statement 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 expires in June 2013. The lease provides for two five-year renewal options at 95% of the fair market rent and includes escalating lease payments. Rent expense is recognized on a straight-line basis over the original 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 in restricted investments as collateral as of December 31, 2010 and 2009. Additionally, Lexicon leases certain equipment under operating leases.

Rent expense for all operating leases was approximately $2.5 million, $2.4 million and $2.5 million for the years ended December 31, 2010, 2009 and 2008, respectively. The following table includes non-cancelable, escalating future lease payments for the facility in New Jersey:

	For the Year Ending December 31 (in thousands)
2011	$2,579
2012	2,633
2013	1,316
Total	$6,528

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. made an initial investment of approximately $205.5 million to purchase 50,824,986 shares of the Company’s common stock in August 2007. Under the Securities Purchase Agreement, as amended and supplemented, and after accounting for the $181.5 million in net proceeds from the Company's public offering and concurrent private placement of common stock in March 2010, Invus, L.P. and its affiliate Invus C.V. (collectively, "Invus") have the right to require the Company to initiate a pro rata rights offering to the Company’s stockholders, which would provide all stockholders

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with non-transferable rights to acquire shares of the Company's common stock, in an aggregate amount to be designated by Invus of up to approximately $163.0 million. The price per share of the rights offering would be designated by Invus in a range between $4.50 and a then-current average market price of the Company's common stock. All stockholders would have oversubscription rights with respect to the rights offering and Invus would be required to purchase its pro rata portion of the offering. Invus may exercise its right to require the Company to conduct such a rights offering by giving the Company notice within a period of one year beginning on February 28, 2011, which will be extended by the number of days during such period that Invus is not permitted under the Securities Purchase Agreement to initiate the rights offering as a result of any "blackout period" in connection with certain public offerings of the Company's common stock. Lexicon has determined that the rights offering should be treated as an equity instrument, and accordingly has not recorded a liability for the future settlement of such rights offering.

Until the later of the completion of the rights offering or the expiration of the period during which Invus may require the Company to initiate the rights offering, the Company will not, without Invus' prior consent, issue any shares of its common stock at a price below $4.50 per share, subject to certain exceptions. If the Company notifies Invus of a proposed public offering for an offering above $4.50 per share during the period in which Invus may require the Company to initiate the rights offering, Invus will have a period of 10 business days in which to exercise its right to require the Company to conduct the rights offering, in which case the Company would be required to forego the proposed public offering and proceed with the rights offering.

In connection with the Securities Purchase Agreement, Lexicon entered into a Stockholders' Agreement with Invus, L.P. under which Invus (a) has specified rights with respect to designation of directors and to participate in future equity issuances by the Company, (b) is subject to certain standstill restrictions, as well as restrictions on transfer and the voting of the shares of common stock held by it and its affiliates, and (c), as long as Invus holds at least 15% of the total number of outstanding shares of the Company's common stock, is entitled to certain minority protections.

13. Other Capital Stock Agreements

Common Stock: In October 2009, Lexicon completed the public offering and sale of 38,333,332 shares of its common stock at a price of $1.50 per share, resulting in net proceeds of $55.2 million, after deducting underwriting discounts and commissions of $1.9 million and offering expenses of $0.4 million. Invus purchased 15,455,145 of these shares. All of the net proceeds of this offering are reflected as issuance of common stock in the accompanying financial statements.

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.

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 as the 2000 Equity Incentive Plan, and later amended and restated in April 2009 as the Equity Incentive Plan (the "Equity Incentive Plan").

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 35,000,000 shares. No more than 3,500,000 shares may be issued pursuant to awards other than stock options and stock appreciation rights. As of December 31, 2010, an aggregate of 35,000,000 shares of common stock had been reserved for issuance, options to purchase 18,952,653 shares and 360,800 restricted stock units were

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outstanding, 4,321,426 shares had been issued upon the exercise of stock options and 540,023 shares had been issued pursuant to stock bonus awards or restricted stock awards granted under the Equity Incentive Plan.

Non-Employee Directors' Stock Option Plan: In February 2000, Lexicon adopted the 2000 Non-Employee Directors' Stock Option Plan, which was subsequently amended and restated in April 2009 as the Non-Employee Directors' Stock Option Plan, (the "Directors' Plan") to provide for the automatic grant of nonstatutory stock options to non-employee directors of the Company. 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 10,000 shares of common stock, and the non-employee chairman of the board of directors is automatically granted an option to purchase 20,000 shares of common stock. 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 1,200,000 shares. As of December 31, 2010, an aggregate of 1,200,000 shares of common stock had been reserved for issuance, options to purchase 644,000 shares were outstanding, and none had been exercised under the Directors' Plan.

Coelacanth Corporation 1999 Stock Option Plan: Lexicon assumed the Coelacanth Corporation 1999 Stock Option Plan (the "Coelacanth Plan") and the outstanding stock options under the plan in connection with its July 2001 acquisition of Coelacanth Corporation. The Company will not grant any further options under the plan. As outstanding options under the plan expire or terminate, the number of shares authorized for issuance under the plan will be correspondingly reduced.

The purpose of the plan was to provide an opportunity for employees, directors and consultants of Coelacanth to acquire a proprietary interest, or otherwise increase their proprietary interest, in Coelacanth as an incentive to continue their employment or service. Both incentive and nonstatutory options are outstanding under the plan. Most outstanding options vest over time and expire ten years from the date of grant. The exercise price of options awarded under the plan was determined by the plan administrator at the time of grant. In general, incentive stock options have an exercise price of 100% or more of the fair market value of Coelacanth common stock on the date of grant and nonstatutory stock options have an exercise price as low as 85% of fair market value on the date of grant.

As of December 31, 2010, an aggregate of 28,910 shares of common stock had been reserved for issuance, options to purchase 993 shares of common stock were outstanding and 27,917 shares of common stock had been issued upon the exercise of stock options issued under the Coelacanth Plan.

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

	2010		2009		2008	
(in thousands, except exercise price data)	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price
Outstanding at beginning of year	17,346	$4.16	16,898	$5.13	16,351	$5.65
Granted	4,928	1.87	4,864	1.44	4,077	2.08
Exercised	(11)	2.15	(121)	2.18	(1)	1.89
Expired	(1,912)	6.40	(3,372)	5.66	(2,663)	4.32
Forfeited	(753)	1.76	(923)	2.46	(866)	3.03

Outstanding at end of year	19,598	3.46	17,346	4.16	16,898	5.13
Exercisable at end of year	11,845	$4.54	10,462	$5.69	11,410	$6.28

The weighted average estimated grant date fair value of options granted during the years ended December 31, 2010, 2009 and 2008 were $1.40, $1.04 and $1.43, respectively. The total intrinsic value of options exercised during the years ended December 31, 2010, 2009 and 2008 were $1,100, $600 and $300, respectively. The weighted average remaining contractual term of options outstanding and exercisable was 6.4 and 5.0 years, respectively, as of December 31, 2010. At December 31, 2010, the aggregate intrinsic value of the outstanding options and the exercisable options was $230,000 and $127,000, respectively.

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The following is a summary of the nonvested options as of December 31, 2010, and changes during the year then ended, under Lexicon's stock option plans:

	Options	Weighted Average Grant Date Fair Value
	(in thousands)	
Nonvested at beginning of year	6,883	$1.30
Granted	4,928	1.40
Vested	(3,305)	1.40
Forfeited	(753)	1.30
Nonvested at end of year	7,753	$1.32

Restricted Stock Activity:

During the year ended December 31, 2009, Lexicon granted its officers restricted stock bonus awards under the Equity Incentive Plan in lieu of cash bonus awards. The shares subject to the awards vested in two installments over the one-year period following the date of grant. The following is a summary of restricted stock activity under Lexicon's stock option plans for the year ended December 31, 2010:

	Shares	Weighted Average Grant Date Fair Value
	(in thousands)	
Outstanding at December 31, 2009	255	$1.45
Vested	(255)	1.45
Nonvested at December 31, 2010	—	$—

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 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 restricted stock units activity under Lexicon's stock option plans for the year ended December 31, 2010:

	Shares	Weighted Average Grant Date Fair Value
	(in thousands)	
Outstanding at December 31, 2009	—	$—
Granted	387	1.90
Forfeited	(26)	1.90
Nonvested at December 31, 2010	361	$1.90

Warrants

In connection with the acquisition of Coelacanth in July 2001, Lexicon assumed Coelacanth's outstanding warrants to purchase 25,169 shares of common stock. The warrants expired on March 31, 2009. The fair value of the warrants was included in the total purchase price for the acquisition.

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Aggregate Shares Reserved for Issuance

As of December 31, 2010, an aggregate of 19,958,446 shares of common stock were reserved for issuance upon exercise of outstanding stock options and vesting of outstanding restricted stock units and 11,381,098 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 Plans

Lexicon has established an Annual Profit Sharing Incentive Plan (the "Profit Sharing Plan"). The purpose of the Profit Sharing Plan is to provide for the payment of incentive compensation out of the profits of the Company to certain of its employees. Participants in the Profit Sharing Plan are entitled to an annual cash bonus equal to their proportionate share (based on salary) of 15 percent of the Company's annual pretax income, if any.

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 $642,000, $614,000 and $828,000 in the years ended December 31, 2010, 2009 and 2008, 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.

Drug Discovery and Development Alliances

Bristol-Myers Squibb. Lexicon established an alliance with Bristol-Myers Squibb Company in December 2003 to discover, develop and commercialize small molecule drugs in the neuroscience field. Lexicon initiated the alliance with a number of neuroscience drug discovery programs at various stages of development and used its gene knockout technology to identify additional drug targets with promise in the neuroscience field. For those targets that were selected for the alliance, Lexicon 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 collaboration enter clinical trials, Bristol-Myers Squibb will have the first option to assume full responsibility for clinical development and commercialization.

Lexicon received an upfront payment of $36.0 million and research funding of $30.0 million in the initial three years of the agreement, or the target function discovery term. This funding was in consideration for access to Lexicon's technology and infrastructure and for Lexicon's production and specified phenotypic analysis of knockout mice in support of the target function discovery portion of the alliance. Bristol-Myers Squibb extended the target discovery term of the alliance in May 2006 in exchange for $20.0 million in additional research funding over the extension period, which expired in October 2009. This additional funding was in consideration for additional research and phenotypic analysis of knockout mice which supplemented the phenotypic analysis conducted in the initial target

function discovery term. Lexicon will also receive clinical and regulatory milestone payments ranging, depending on the timing and extent of its efforts in the alliance, up to $76.0 million for each drug developed by Bristol-Myers Squibb under the alliance. Lexicon will earn royalties on sales of drugs commercialized by Bristol-Myers Squibb. The party with responsibility for the clinical development and commercialization of drugs resulting from the alliance will bear the costs of those efforts. The original upfront payment of $36.0 million and research funding of $30.0 million was recognized over the initial estimated period of service of three years. The additional research funding of $20.0 million was recognized over the estimated performance period of two and one-half additional years subject to the extension, beginning in January 2007. Lexicon recorded a change in estimate that increased net loss and net loss per share by $1.7 million and $0.01 per share, respectively, in the year ended December 31, 2008 due to an increase in estimated performance period of this extension.

The upfront payment of $36.0 million was not related to a deliverable with standalone value at inception, and Lexicon accounted for the entire agreement with Bristol-Myers Squibb as a single unit of accounting. Milestone payments received are

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in consideration for additional performance. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $1.7 million and $9.3 million for the years ended December 31, 2009 and 2008, respectively.

Genentech. Lexicon established an alliance with Genentech, Inc. in December 2002 to discover novel therapeutic proteins and antibody targets. Lexicon used its target validation technologies to discover the functions of secreted proteins and potential antibody targets identified through Genentech's internal drug discovery research. Lexicon received an upfront payment of $9.0 million and funding under a $4.0 million loan in 2002. In addition, Lexicon received $24.0 million in performance payments for its work in the collaboration as it was completed. The upfront payment of $9.0 million was recognized over the initial estimated period of service of three years, which was subsequently extended to three and one-half years.

In November 2005, Lexicon and Genentech expanded the alliance to include additional research, as well as the development and commercialization of new biotherapeutic drugs. Lexicon received a total of $25.0 million in upfront and milestone payments and research funding for the three-year advanced research portion of the expanded alliance. In the expanded alliance, Lexicon conducted advanced research on a broad subset of targets validated in the original collaboration using Lexicon's proprietary gene knockout technology. The upfront payment under the expanded agreement was recognized over the estimated period of service of three years.

Lexicon has exclusive rights to develop and commercialize biotherapeutic drugs for two of the targets included in the alliance, while Genentech has exclusive rights to develop and commercialize biotherapeutic drugs for the other targets. Lexicon retains 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. Lexicon will receive clinical and regulatory milestone payments ranging, depending on the extent of Lexicon's efforts in the alliance, up to $25 million for each drug target for which Genentech develops a biotherapeutic drug under the alliance. Lexicon 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 Lexicon develops or commercializes under the alliance. The research collaboration term under the agreement expired in November 2008.

The upfront payment was not related to a deliverable with standalone value at inception and Lexicon accounted for the entire agreement with Genentech as a single unit of accounting. Milestone payments received are in consideration for additional performance. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $4.0 million for the year ended December 31, 2008.

Schering-Plough/Organon. Lexicon established a drug discovery alliance with N.V. Organon in May 2005 to discover, develop and commercialize novel biotherapeutic drugs. In the alliance, Lexicon created and analyzed knockout mice for 300 genes selected by the parties that encode secreted proteins or potential antibody targets, including two of Lexicon's preexisting drug discovery programs. Lexicon 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, Lexicon 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.

Lexicon received an upfront payment of $22.5 million from Organon in exchange for access to Lexicon's drug target discovery capabilities and the exclusive right to co-develop biotherapeutic drugs for the 300 genes selected for the alliance. Organon has also provided Lexicon with annual research funding totaling $30.0 million for its 50% share of the alliance's costs during this same period. The target discovery portion of the alliance expired in December 2009.

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The upfront payment of $22.5 million was not related to a deliverable with standalone value at inception, and Lexicon accounted for the entire agreement with Organon as a single unit of accounting. Revenue from the upfront payment was recognized on a straight-line basis over the four-year period that Lexicon performed its obligations under the target function discovery portion of the alliance. Revenue from the research funding fees was recognized as Lexicon performed its obligations under the target function discovery portion of the alliance, reflecting the gross amount billed to Organon on the basis of shared costs during the period. Milestone payments received are in consideration for additional performance. Therefore, Lexicon recognizes revenue from such milestone payments upon achievement of the milestones.

Revenue recognized under this agreement was $0.2 million, $2.3 million and $9.2 million for the years ended December 31, 2010, 2009 and 2008, respectively.

Other Collaborations and Licenses

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. Revenue recognized under this agreement was $0.1 million for the year ended December 31, 2008.

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. 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 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 $5.0 million through December 31, 2010. Revenue recognized under these agreements was $1.7 million, $2.2 million and $747,000 for the years ended December 31, 2010, 2009 and 2008, respectively.

Bristol-Myers Squibb. Lexicon entered into drug target validation agreements with Bristol-Myers Squibb Company in December 2004, January 2006, October 2006, November 2007 and February 2009, under which Lexicon is developing mice and phenotypic data for certain genes requested by Bristol-Myers Squibb under those agreements. The collaboration term under each of these agreements will expire after the final phenotypic data set has been delivered by Lexicon under that agreement. The Company received payments totaling $10.6 million under these

agreements through December 31, 2010. Revenue recognized under these agreements was $0.4 million, $1.1 million and $1.1 million for the years ended December 31, 2010, 2009 and 2008, respectively.

Genentech. Lexicon entered into a drug target validation agreement with Genentech, Inc. in February 2007. Under this agreement, Lexicon developed mice with mutations requested by Genentech. The collaboration term under the agreement has expired as the final delivery of the selected mice was performed by Lexicon in 2009. The Company received payments totaling $1.1 million under the agreement through December 31, 2009. Revenue recognized under this agreement was $26,000 and $0.1 million for the years ended December 31, 2009 and 2008, respectively.

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17. Selected Quarterly Financial Data

The table below sets forth certain unaudited statements of operations data, and net loss per common share data, for each quarter of 2010 and 2009:

(in thousands, except per share data)

	Quarter Ended March 31	June 30 (Unaudited)	September 30	December 31
2010				
Revenues	$1,641	$1,233	$781	1,253
Loss from operations	$(24,966)	$(24,074)	$(24,253)	(22,425)
Net loss attributable to Lexicon Pharmaceuticals, Inc.	$(26,070)	$(25,193)	$(27,513)	(22,999)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	$(0.13)	$(0.07)	$(0.08)	(0.07)
Shares used in computing net loss per common share	197,239	337,404	337,404	337,407
2009				
Revenues	$4,168	$2,989	$2,131	$1,412
Loss from operations	$(23,570)	$(22,782)	$(21,757)	$(21,847)
Net loss attributable to Lexicon Pharmaceuticals, Inc.	$(21,560)	$(20,073)	$(19,142)	$(22,005)
Net loss attributable to Lexicon Pharmaceuticals, Inc. per common share, basic and diluted	$(0.16)	$(0.15)	$(0.14)	$(0.13)
Shares used in computing net loss per common share	137,075	137,331	137,313	169,872