LEXICON PHARMACEUTICALS, INC./DE
Form 10-K
March 08, 2010

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the Fiscal Year Ended December 31, 2009
or

q 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 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 þ

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 þ

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 þ 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. þ

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 þ 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 þ

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 $99.1 million, based on the closing price of the common stock on the Nasdaq Global Market on June 30, 2009 of $1.24 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 1, 2010, 175,633,988 shares of common stock were outstanding.

Documents Incorporated by Reference

Certain sections of the registrant's definitive proxy statement relating to the registrant's 2010 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, 2009, are incorporated by reference into Part III of this annual report on
Form 10-K.

Lexicon Pharmaceuticals, Inc.

Table of Contents

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

Factors Affecting Forward Looking Statements

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.

Table of Contents

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 our proprietary gene knockout technologies and an integrated platform of advanced medical technologies to systematically study the physiological and behavioral functions of almost 5,000 genes in mice and assessed the utility of the proteins encoded by the corresponding human genes as potential drug targets. We have identified and validated in living animals, or in vivo, more than 100 targets with promising profiles for drug discovery. For targets that we believe have high pharmaceutical value, we engage in programs for the discovery and development of potential new drugs, focusing in the core therapeutic areas of immunology, metabolism, cardiology and ophthalmology.

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

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

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

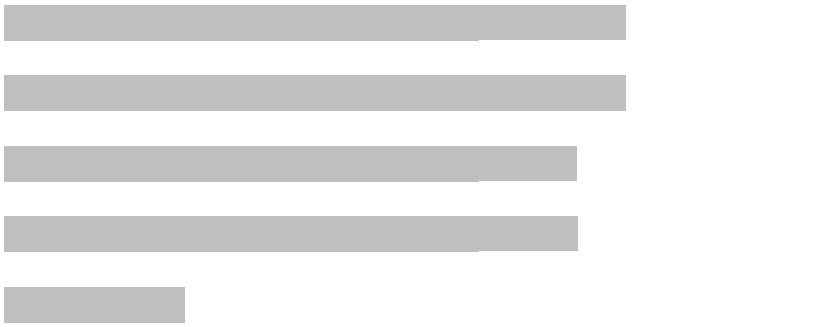
should not be considered part of this annual report on Form 10-K.

Our Drug Development Pipeline

Human clinical trials are currently underway for four of our drug candidates, with one additional drug candidate in preclinical development and compounds from a number of additional programs in various stages of preclinical research:

Table of Contents

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



LX1031

LX1031 is an orally-delivered small molecule compound 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, which began in December 2008, 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 LX1031in preparation for use in future clinical trials.

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 designed LX1031 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 was internally generated by our medicinal chemists as an inhibitor of 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 demonstrated a dose-dependent reduction of serotonin levels in the gastrointestinal tract of multiple species without affecting brain serotonin levels.

Clinical development of LX1031 is being funded through our product development collaboration with Symphony Icon Holdings LLC, or Holdings, pursuant to which we have licensed to a wholly-owned subsidiary of Holdings, Symphony Icon, Inc. or Symphony Icon, the intellectual property rights related to LX1031 and hold an exclusive option to acquire all the equity of Symphony Icon, thereby allowing us to reacquire LX1031. See "—Our Commercialization Strategy—Drug Development Financing Collaborations—Symphony Icon."

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 LX4211and its effects on biomarkers associated with type 2 diabetes. The Phase 2 trial, which began in September 2009, 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 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 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 throughout the study period relative to placebo. Patients in both dose groups 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 are presently completing a 13-week preclinical toxicology study of LX4211 to permit longer-term clinical trials following which we intend to conduct a bioavailability study of a solid oral dose formulation of LX4211 in 2010 before initiating a Phase 2 dose-ranging study.

Table of Contents

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 to target sodium-glucose cotransporter type 2, or SGLT2, a transporter responsible for most of the glucose reabsorption performed by the kidney. Our scientists discovered that mice lacking SGLT2 have improved glucose tolerance and increased urinary glucose excretion. LX4211 also inhibits 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. 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.

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 initiated a Phase 2 clinical trial in August 2009 to evaluate the safety and tolerability of LX2931 and its effects on symptoms and signs associated with rheumatoid arthritis. The Phase 2 trial is expected to enroll up to 200 patients with rheumatoid arthritis who are also taking methotrexate, a standard therapy, in a double-blind, randomized, placebo-controlled study of three dose levels of LX2931 against placebo over a 12-week treatment period. The efficacy endpoints under evaluation in the trial include ACR20 at 12 weeks and ACR20/50/70 and DAS28 at four, eight and 12 weeks. Top-line data from this trial are expected to be available in late 2010 or shortly thereafter.

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 and produced a dose-dependent decrease in absolute lymphocyte counts, with systemic exposure plateauing at doses of 100 to 125 mg. 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, potentially representing dose-limiting tolerability. 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.

Table of Contents

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 tolerability of LX1032 and its effects on symptoms associated with carcinoid syndrome. The Phase 2 trial is expected to enroll up to 28 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, followed by cohort expansion at optimal 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. Top-line data from this trial are expected to be available in the second half of 2010. We also intend to initiate a complementary open-label clinical trial of LX1032 in the first half of 2010, which is expected to enroll up to 16 additional patients.

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, but LX1032 is chemically distinct and, unlike LX1031, 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 status from the United States Food and Drug Administration, or FDA, which provides for an expedited review process that may shorten FDA approval times.

Clinical development of LX1032 is being funded through our product development collaboration with Holdings, pursuant to which we have licensed to Symphony Icon the intellectual property rights related to LX1032 and hold an exclusive option to acquire all the equity of Symphony Icon, thereby allowing us to reacquire LX1032. See “—Our Commercialization Strategy—Drug Development Financing Collaborations—Symphony Icon.”

LX7101

LX7101 is a topically-delivered small molecule compound that we are developing for the potential treatment of glaucoma. We have commenced preclinical studies of LX7101 and certain associated back-up molecules.

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 an animal model of ocular hypertension.

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. Through the end of 2009, we had 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 our patented 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.

Table of Contents

We engage in programs for the discovery of potential small molecule drugs for those in vivo-validated drug targets that we consider to have high pharmaceutical value. We have established extensive internal small molecule drug discovery capabilities, in which we use our own sophisticated libraries of drug-like chemical compounds in high-throughput screening assays to identify "hits," or chemical compounds demonstrating activity, against these targets. We then employ medicinal chemistry efforts to optimize the potency and selectivity of these hits and to identify lead compounds for potential development. We have established extensive internal ca