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

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 29, 2022

Lexicon Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**000-30111**	**76-0474169**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification Number)**

2445 Technology Forest Blvd., 11th Floor
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	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001	LXRX	The Nasdaq Global Select Market

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events

On June 29, 2022, we announced top-line results of RELIEF-DPN-1, our Phase 2 proof-of-concept study of LX9211 in painful diabetic neuropathy. LX9211 achieved the primary endpoint of the study, demonstrating a statistically significant reduction in average daily pain score (ADPS) at week 6 compared to placebo in the low dose arm with results that plateaued in the high dose arm. Separation from placebo was seen by week 1 in both dose arms, and the effect was consistent across age, sex, concurrent use of medications for painful diabetic neuropathy, and baseline pain score.

Patient reported outcomes (global impression of change) were improved in patients treated with LX9211 compared to placebo. Adverse events were more frequent in the LX9211 treatment arms and at the higher dose, with the most common being dizziness, headache and nausea. Nearly all adverse events were reported as mild or moderate. There were no drug-related serious adverse events reported in the study.

RELIEF-DPN-1 is a Phase 2 randomized, double-blind, placebo-controlled, parallel-group, multicenter study evaluating the efficacy, safety and pharmacokinetics of LX9211 in the treatment of painful diabetic neuropathy, also referred to as diabetic peripheral neuropathic pain. The study enrolled 319 patients at approximately 40 U.S. clinical sites, evaluating three treatment groups receiving placebo or one of two dosing regimens of LX9211 (an initial dose of 100 mg followed by once-daily doses of 10 mg or an initial dose of 200 mg followed by once-daily doses of 20 mg). The primary efficacy endpoint under evaluation was the change from baseline to week 6 in ADPS, based on the 11-point numerical rating scale. The results of the study on the primary endpoint showed a reduction from baseline in ADPS of 1.39 points ($p=0.007$ versus placebo) in the low dose arm and 1.27 points ($p=0.030$ versus placebo) in the high dose arm, compared to 0.72 in the placebo arm. Under the statistical analysis plan for the study, a p-value of less than 0.028 was considered statistically significant.

On June 29, 2022, we issued a press release announcing the top-line results of RELIEF-DPN-1. A copy of the press release is attached to this current report on Form 8-K as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.		Description
99.1	—	Press Release of Lexicon Pharmaceuticals, Inc. dated June 29, 2022
EX-104	—	Cover Page Interactive Data File (embedded within the Inline XBRL document)

Signatures

Pursuant to the requirements 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: June 30, 2022

By: /s/ Brian T. Crum

Brian T. Crum

Senior Vice President and General Counsel

Exhibit 99.1

LEXICON ANNOUNCES POSITIVE TOP-LINE RESULTS FROM PHASE 2 PROOF-OF-CONCEPT STUDY OF LX9211 IN PAINFUL DIABETIC NEUROPATHY

Study Supports Translation of Potential New Mechanism of Action for Neuropathic Pain and Advancement of LX9211 Development in Painful Diabetic Neuropathy

Conference Call and Webcast at 8:00 a.m. Eastern Time June 30, 2022

The Woodlands, Texas, June 29, 2022 - Lexicon Pharmaceuticals, Inc. (Nasdaq: LXRX) today announced top-line results of RELIEF-DPN-1, its Phase 2 proof-of-concept study of LX9211 in painful diabetic neuropathy. LX9211 achieved the primary endpoint of the study, demonstrating a statistically significant reduction in average daily pain score (ADPS) at week 6 compared to placebo in the low dose arm with results that plateaued in the high dose arm. Separation from placebo was seen by week 1 in both dose arms, and the effect was consistent across age, sex, concurrent use of medications for painful diabetic neuropathy, and baseline pain score.

Patient reported outcomes (global impression of change) were improved in patients treated with LX9211 compared to placebo. Adverse events were more frequent in the LX9211 treatment arms and at the higher dose, with the most common being dizziness, headache and nausea. Nearly all adverse events were reported as mild or moderate. There were no drug-related serious adverse events reported in the study.

A full analysis of the results from RELIEF-DPN-1 will be submitted for publication at an upcoming medical conference and in a peer-reviewed journal.

“The results of this study support the translation of a potential new mechanism of action for neuropathic pain and serve as a testament to the strength of Lexicon’s science,” said Craig Granowitz, M.D., Ph.D., Lexicon’s senior vice president and chief medical officer. “Our scientists were the first to identify AAK1 as a novel target with potential for the treatment of neuropathic pain, making an initial discovery in knockout mice, validating that discovery in collaboration with Bristol-Myers Squibb with small molecule inhibition of the target in animal models, and now translating that discovery in this human clinical proof-of-concept study. This is an important step towards bringing the benefits of our science to patients, in an area where novel targets are rare and there is a tremendous need for new therapies.”

LX9211 is a potent, orally delivered, selective small molecule inhibitor of AAK1, which preclinical studies have shown to reduce pain behavior in models of neuropathic pain without affecting opiate pathways. LX9211 has received Fast Track designation from the U.S. Food and Drug Administration for the development in diabetic peripheral neuropathic pain.

About the RELIEF-DPN-1 Study

RELIEF-DPN-1 is a Phase 2 randomized, double-blind, placebo-controlled, parallel-group, multicenter study evaluating the efficacy, safety and pharmacokinetics of LX9211 in the treatment of painful diabetic neuropathy, also referred to as diabetic peripheral neuropathic pain. The study enrolled 319 patients at approximately 40 U.S. clinical sites, evaluating three treatment groups receiving placebo or one of two dosing regimens of LX9211 (an initial dose of 100 mg followed by once-daily doses of 10 mg or an initial dose of 200 mg followed by once-daily doses of 20 mg). The primary efficacy endpoint under evaluation was the change from baseline to week 6 in ADPS, based on the 11-point numerical rating scale. The

results of the study on the primary endpoint showed a reduction from baseline in ADPS of 1.39 points in the low dose arm and 1.27 points in the high dose arm, compared to 0.72 in the placebo arm.

The RELIEF-DPN-1 study is the first of two Phase 2 proof-of-concept studies evaluating LX9211 in neuropathic pain. LX9211 is also under evaluation in RELIEF-PHN-1, a study in patients with post-herpetic neuralgia, from which Lexicon is targeting top-line results around the end of the third quarter of 2022.

About LX9211

Discovered using Lexicon's unique approach to gene science, LX9211 is a potent, orally delivered, selective small molecule inhibitor of adaptor-associated kinase 1 (AAK1). Lexicon identified AAK1 in its target discovery efforts as a promising approach for the treatment of neuropathic pain and identified LX9211 and another development candidate in a neuroscience drug discovery alliance with Bristol-Myers Squibb from which Lexicon holds exclusive development and commercialization rights. Preclinical studies of LX9211 demonstrated central nervous system penetration and reduction in pain behavior in models of neuropathic pain without affecting opiate pathways. LX9211 has received Fast Track designation from the U.S. Food and Drug Administration for the development in diabetic peripheral neuropathic pain.

Conference Call and Webcast Information

Lexicon management will hold a live conference call and webcast on June 30, 2022 at 8:00 am ET / 7:00 am CT to discuss the RELIEF-DPN-1 top-line results. The dial-in number for the conference call is 888-886-7786 (U.S./Canada) or 416-764-8658 (international). The conference ID for all callers is 20954316. The live webcast and replay may be accessed by visiting Lexicon's website at www.lexpharma.com/events. An archived version of the webcast will be available on the website for 14 days.

About Lexicon Pharmaceuticals

Lexicon is a biopharmaceutical company with a mission of pioneering medicines that transform patients' lives. Through its Genome5000™ program, Lexicon scientists studied the role and function of nearly 5,000 genes and identified more than 100 protein targets with significant therapeutic potential in a range of diseases. Through the precise targeting of these proteins, Lexicon is pioneering the discovery and development of innovative medicines to safely and effectively treat disease. Lexicon advanced one of these medicines to market and has a pipeline of promising drug candidates in discovery and clinical and preclinical development in heart failure, neuropathic pain, diabetes and metabolism and other indications. For additional information, please visit www.lexpharma.com.

Safe Harbor Statement

This press release contains "forward-looking statements," including statements relating to the clinical development of and potential therapeutic and commercial potential of LX9211. In addition, this press release also contains forward looking statements relating to the clinical development of, regulatory filings for and potential therapeutic and commercial potential of sotagliflozin and Lexicon's other potential drug candidates, as well as Lexicon's financial position and long-term outlook on its business, growth and future operating results, discovery and development of products, strategic alliances and intellectual property, as well as other matters that are not historical facts or information. All forward-looking statements are based on management's current assumptions and expectations and involve risks, uncertainties and other important factors, specifically including Lexicon's ability to meet its capital

requirements, successfully conduct preclinical and clinical development and obtain necessary regulatory approvals of sotagliflozin, LX9211 and its other potential drug candidates on its anticipated timelines, successfully commercialize any products for which it obtains regulatory approval, achieve its operational objectives, obtain patent protection for its discoveries and establish strategic alliances, as well as additional factors relating to manufacturing, intellectual property rights, and the therapeutic or commercial value of its drug candidates. Any of these risks, uncertainties and other factors may cause Lexicon's actual results to be materially different from any future results expressed or implied by such forward-looking statements. Information identifying such important factors is contained under "Risk Factors" in Lexicon's annual report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission. Lexicon undertakes no obligation to update or revise any such forward-looking statements, whether as a result of new information, future events or otherwise.

For Inquiries:

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