Lexicon Pharmaceuticals Announces Publication of Positive Data for Zynquista™ (sotagliflozin) on Cardiorenal Clinical Biomarkers in Adults with Type 1 Diabetes

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Changes in Clinical Biomarkers Suggestive of Favorable Effects on Kidney Function in Patients with Type 1 Diabetes

Results Recently Published in Diabetes Care

The Woodlands, Texas, August 8, 2019 - Lexicon Pharmaceuticals, Inc. (Nasdaq: LXRX), today announced positive 52-week cardiorenal results from a pooled analysis from the inTandem1 and inTandem2 studies of Zynquista™ (sotagliflozin) in adults with type 1 diabetes. Zynquista demonstrated changes in clinical biomarkers such as estimated glomerular filtration rate (eGFR), hematocrit, serum albumin, uric acid, systolic blood pressure and urinary albumin-to-creatinine ratio (UACR) that suggest Zynquista may reduce cardiovascular risk and progression of chronic kidney disease. Zynquista was associated with short- and long-term renal hemodynamic changes. Importantly, after cessation of 52 weeks of therapy, eGFR was comparable to baseline and significantly higher than placebo in Zynquista-treated patients.

These results were recently published in Diabetes Care, the ADA's peer-reviewed research journal dedicated to diabetes treatment and prevention. The online publication, "The Impact of Sotagliflozin on Renal Function, Albuminuria, Blood Pressure, and Hematocrit in Adults with Type 1 Diabetes", may be accessed here https://doi.org/10.2337/dc19-0937.

New 52-week findings from a pooled analysis from inTandem1, a 793-patient, double-blind, placebo-controlled Phase 3 study, and inTandem2, a 782-patient double-blind, placebo-controlled Phase 3 study demonstrated that Zynquista 200 mg and 400 mg, in combination with insulin, were associated with short- and long-term renal hemodynamic changes. Generally consistent with what has been seen with selective SGLT2 inhibitors in type 2 diabetes, study participants randomized to Zynquista experienced a modest initial reduction in eGFR that quickly stabilized. In the pooled analysis, the placebo-corrected least squares mean change from baseline in eGFR was −2.0 mL/min/1.73 m2 ($p = 0.010$) and −0.5 mL/min/1.73 m2 ($p = 0.52$) for the 200 mg and 400 mg doses, respectively. Importantly, in the subset of patients (n = 370) with off drug follow-up laboratory records, defined as 7 days after last dose, eGFR returned to baseline for study participants randomized to Zynquista, but not to placebo, with a placebo-corrected LS mean change from baseline to off drug records of +3.0 mL/min/1.73 m2 ($p = 0.031$) and +2.7 mL/min/1.73 m2 ($p = 0.045$) for Zynquista 200 mg and 400 mg, respectively

Zynquista demonstrated meaningful effects on markers of hemoconcentration and plasma uric acid, where biochemical changes have been linked to cardiorenal protection associated with SGLT2 inhibitors. Mean serum hematocrit increased from 41.9% at baseline to 43.8% at Week 12 for Zynquista 200 mg and from 42.0% to 44.0% for Zynquista 400 mg. Relative to placebo, the LS mean difference was 1.8% and 1.9% for Zynquista 200 mg and 400 mg, respectively ($p < 0.0001$, for both). These changes persisted throughout the 52-week trial at both Zynquista doses ($p < 0.0001$). Mean baseline serum albumin concentrations were similar, at approximately 4.3 g/dL for all groups. LS mean serum albumin increased 0.06 g/dL and 0.07 g/dL with Zynquista 200 mg and 400 mg, respectively, at Week 4 ($p < 0.0001$, for both). At Week 52, placebo-corrected LS mean change was 0.03 g/dL ($p = 0.036$) for Zynquista 200 mg and 0.03 g/dL ($p = 0.053$) for Zynquista 400 mg. Zynquista also significantly reduced uric acid throughout 52 weeks ($p < 0.001$). The placebo-corrected LS mean change in serum uric acid was 20.29 mg/dL and 20.42 mg/dL ($p < 0.0001$ for both) at 4 weeks and 20.17 mg/dL ($p = 0.0003$) and 20.28 mg/dL ($p < 0.0001$) at 52 weeks for Zynquista 200 mg and 400 mg, respectively.

Zynquista demonstrated consistent lowering of blood pressure and urinary albumin-to-creatinine ratio (UACR). Systolic blood pressure difference was −2.9 and −3.6 mmHg ($p < 0.0001$ for both doses) for Zynquista 200 mg and Zynquista 400 mg, respectively, placebo-adjusted. Diastolic blood pressure changed by −1.4 ($p = 0.0033$) and −1.6 mmHg ($p = 0.0008$) placebo-adjusted. Of note, in patients whose current blood pressure targets were above and below 130/80 mmHg, the impact of Zynquista was comparable and resulted in clinically relevant blood pressure lowering. As for UACR, in patients with baseline UACR ≥30 mg/g, UACR decreased by 23.7% ($p = 0.054$) and 18.3% ($p = 0.18$) for Zynquista 200 mg and 400 mg, respectively, versus placebo.

About Zynquista (sotagliflozin)

Discovered using Lexicon's unique approach to gene science, Zynquista is an oral dual inhibitor of two proteins responsible for glucose regulation known as sodium-glucose co-transporter types 1 and 2 (SGLT1 and SGLT2). SGLT1 is responsible for glucose absorption in the gastrointestinal tract, and SGLT2 is responsible for glucose reabsorption by the kidney. Zynquista is approved in the European Union (EU) for use as an adjunct to insulin therapy to improve blood sugar (glycemic) control in adults with type 1

diabetes with a body mass index ≥ 27 kg/m2, who could not achieve adequate glycemic control despite optimal insulin therapy. Outside of such approval, Zynquista is investigational and has not been approved by any other regulatory authority for type 1 or type 2 diabetes.

Lexicon has granted Sanofi an exclusive worldwide (excluding Japan) license to develop, manufacture and commercialize Zynquista. Lexicon remains responsible for all clinical development activities relating to type 1 diabetes and Sanofi is responsible for all clinical development activities of Zynquista for the treatment of type 2 diabetes. Sanofi has delivered to Lexicon a notice purporting to terminate the alliance. Lexicon has notified Sanofi that it considers the notice invalid and Sanofi to be in breach of contract.

About Lexicon Pharmaceuticals

Lexicon is a fully integrated 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. In addition to its first commercial product, XERMELO, Lexicon has a pipeline of promising drug candidates in clinical and preclinical development in diabetes and metabolism, oncology and neuropathic pain. For additional information, please visit www.lexpharma.com.

Safe Harbor Statement

This press release contains "forward-looking statements," including statements relating to Lexicon's long-term outlook on its business, including the status of its alliance with Sanofi, the commercialization of XERMELO (telotristat ethyl) and Zynquista (sotagliflozin), and the clinical development of, the regulatory filings for, and the potential therapeutic and commercial potential of telotristat ethyl, sotagliflozin, LX2761 and LX9211. In addition, this press release also contains forward looking statements relating to Lexicon's growth and future operating results, discovery, development and commercialization 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 commercialize XERMELO, successfully conduct preclinical and clinical development and obtain necessary regulatory approvals of telotristat ethyl, sotagliflozin, LX2761, LX9211 and its other potential drug candidates on its anticipated timelines, 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, 2018, 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.

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