Data From Two Studies Demonstrating Positive Financial Impact of INPEFA® (sotagliflozin) to be Presented at the Academy of Managed Care Pharmacy (Amcp) Nexus 2023 National Meeting

October 18, 2023

Abstracts for cost-effectiveness data and budget-impact model published in the Journal of Managed Care & Specialty Pharmacy (JMCP)

INPEFA recently approved by FDA for treatment of heart failure

The Woodlands, Texas, October 17, 2023 – Lexicon Pharmaceuticals, Inc. (Nasdaq: LXRX) today highlighted upcoming presentations of two studies demonstrating positive financial impact of INPEFA® (sotagliflozin) at the Academy of Managed Care Pharmacy (AMCP) Nexus 2023 National Meeting, October 16-19, 2023, at the Orlando World Center Marriott, Expo Hall, Cypress 1 and 2, Orlando, Florida.

Highlights from the published abstracts:

"**Economic impact of sotagliflozin among patients with heart failure: Budget impact analysis from US payer perspective"**

The objective of this study was to quantify the payer budget impact of sotagliflozin following FDA approval in May 2023, and market entry one month later.

The budget impact was modeled as the change in medical and pharmacy costs from using sotagliflozin in addition to the standard of care (SoC) compared with the SoC alone among U.S. patients hospitalized with heart failure (HF). Costs included pharmacy, inpatient, emergency department visits, and other medical and adverse event costs. Budget impact was measured separately for commercial payer and all-payer scenarios.

Amongst treated patients on sotagliflozin, commercial payers incurred increased pharmacy costs of $7,276 per patient per year as compared to patients on SoC alone. However, reduced readmission rates and post-acute emergency department visits in treated patients on sotagliflozin contributed to a relative reduction in annual medical costs of $4,729 per patient per year (sotagliflozin $9,825 vs. SoC $14,554), resulting in an increase in total spending per patient of $2,547 per year (sotagliflozin $17,101 vs. SoC $14,554) for commercial payers. In the all-payer scenario, annual medical costs per patient per year were reduced on a relative basis by $2,367 (sotagliflozin $4,920 vs. SoC $7,287), resulting in an increase in total spending per patient of $4,909 per year (sotagliflozin $12,196 vs. SoC $7,287) for all payers. The resulting estimated financial impact across the entire health plan during the first year was an increase of $0.05 per member per month in the commercial scenario and an increase of $0.17 per member per month in the all-payer scenario.

The authors concluded that "Health plans adopting sotagliflozin can expect to see an increase in pharmacy costs, but about one-third of this cost was offset by lower medical cost."

"Cost-effectiveness of sotagliflozin for the treatment of patients with diabetes and recent worsening heart failure"

The objective of this study was to quantify the cost-effectiveness of sotagliflozin compared with SoC from a U.S. payer perspective for the treatment of patients hospitalized with HF and comorbid type 2 diabetes (T2D). Clinical outcomes of interest were hospital readmissions, emergency department (ED) visits, and all-cause deaths after an HF hospitalization. Patient health benefit was quantified using quality-adjusted life years (QALYs). Costs included pharmaceutical costs and costs from rehospitalizations, ED visits, and adverse events. Economic value was measured using the incremental cost-effectiveness ratio.

Study results showed reductions in annualized rehospitalization rates, annualized ED visits, and annualized mortality in patients treated with sotagliflozin as compared to SoC, resulting in a net relative increase in QALYs of 0.425 (sotagliflozin 2.305 vs. SoC 1.880). Driven by increased pharmaceutical costs, use of sotagliflozin increased total costs by $19,374 over the lifetime of patients treated with sotagliflozin as compared to SoC ($31,953 vs. $12,579), yielding an incremental cost-effectiveness ratio of $45,596 per increased QALY.

The authors concluded that "sotagliflozin is a cost-effective treatment for HF among patients with T2D and a recent HF hospitalization or urgent care visit."

"The studies presented at AMCP Nexus 2023 serve as evidence that INPEFA is an affordable treatment that offers important clinical value for heart failure patients, and significant financial value for payers," said Craig Granowitz, M.D., Ph.D., Lexicon's

senior vice president and chief medical officer. “We anticipate that these results will help facilitate meaningful dialogue and provide support for positive decisions from formulary decision-makers.”

Abstracts for each study are available in the Poster Abstracts Supplement to the *Journal of Managed Care & Specialty Pharmacy (JMCP)*, which can be found here.

On May 26, 2023, the U.S. Food and Drug Administration approved INPEFA, a once-daily oral tablet, to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with:

- heart failure or
- type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors.

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 treat diseases safely and effectively. Lexicon has advanced multiple medicines to market and has a pipeline of promising drug candidates in heart failure, neuropathic pain, diabetes and metabolism and other indications. For additional information, please visit www.lexpharma.com.

About INPEFA® (sotagliflozin)

Discovered using Lexicon’s unique approach to gene science, INPEFA ® (sotagliflozin) is an oral inhibitor of two proteins responsible for glucose regulation known as sodium-glucose cotransporter types 2 and 1 (SGLT2 and SGLT1). SGLT2 is responsible for glucose reabsorption by the kidney and SGLT1 is responsible for glucose absorption in the gastrointestinal tract. INPEFA has been studied in multiple patient populations encompassing heart failure, diabetes, and chronic kidney disease in clinical studies involving approximately 20,000 patients.

INDICATION

INPEFA is indicated to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with:

- heart failure or
- type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors

IMPORTANT SAFETY INFORMATION

Dosing: Assess renal function and volume status and, if necessary, correct volume depletion prior to initiation of INPEFA. INPEFA dosing for patients with decompensated heart failure may begin when patients are hemodynamically stable, including when hospitalized or immediately upon discharge.

Contraindications: INPEFA is contraindicated in patients with hypersensitivity to any component.

Warnings and Precautions:

Ketoacidosis: INPEFA increases the risk of ketoacidosis in patients with type 1 diabetes mellitus (T1DM). Type 2 diabetes mellitus (T2DM) and pancreatic disorders are also risk factors. The risk of ketoacidosis may be greater with higher doses. There have been postmarketing reports of fatal events of ketoacidosis in patients with type 2 diabetes using sodium glucose transporter 2 (SGLT2) inhibitors. Before initiating INPEFA, assess risk factors for ketoacidosis. Consider ketone monitoring in patients with T1DM and consider ketone monitoring in others at risk for ketoacidosis, and educate patients on the signs/symptoms of ketoacidosis. Patients receiving INPEFA may require monitoring and temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis.

Assess patients who present with signs and symptoms of metabolic acidosis or ketoacidosis, regardless of blood glucose level. If suspected, discontinue INPEFA, evaluate, and treat promptly. Monitor patients for resolution of ketoacidosis before restarting INPEFA.

Volume Depletion: INPEFA can cause intravascular volume depletion which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. There have been post-marketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors. Patients with impaired renal function (eGFR < 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating INPEFA in patients with one or more of these characteristics, assess volume status and renal function, and monitor for signs and symptoms of hypotension during therapy.

Urosepsis and Pyelonephritis: Treatment with SGLT2 inhibitors, including INPEFA, increases the risk for urinary tract infections. Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been reported. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues: Insulin and insulin secretagogues are known to cause hypoglycemia. INPEFA may increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used with INPEFA.

Necrotizing Fasciitis of the Perineum (Fournier's Gangrene): Reports of Fournier's Gangrene, a rare but serious and life-threatening necrotizing infection requiring urgent surgical intervention, have been identified in post-marketing surveillance in patients with diabetes mellitus receiving SGLT2 inhibitors. Assess patients who present with pain, tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue INPEFA, closely monitor patient signs and symptoms, and provide appropriate alternative therapy for heart failure.

Genital Mycotic Infections: INPEFA increases the risk of genital mycotic infections. Monitor and treat as appropriate.

Urinary Glucose Test and 1,5-anhydroglucitol (1,5-AG) Assay: these are not reliable for patients taking SGLT2 inhibitors. Use alternative testing methods to monitor glucose levels.

Common Adverse Reactions: the most commonly reported adverse reactions (incidence ≥ 5%) were urinary tract infection, volume depletion, diarrhea, and hypoglycemia.

Drug Interactions:

- **Digoxin:** Monitor patients appropriately as there is an increase in the exposure of digoxin when coadministered with INPEFA 400 mg.
- **Uridine 5'-diphospho-glucuronosyltransferase (UGT) Inducer:** The coadministration of rifampicin, an inducer of UGTs, with sotagliflozin resulted in a decrease in the exposure of sotagliflozin.
- **Lithium:** Concomitant use of an SGLT2 inhibitor with lithium may decrease serum lithium concentrations. Monitor serum lithium concentration more frequently during INPEFA initiation and with dosage changes.

Use in Specific Populations:

- **Pregnancy and Lactation:** INPEFA is not recommended during the second and third trimesters of pregnancy, nor while breastfeeding.
- **Geriatric Use:** No INPEFA dosage change is recommended based on age. No overall differences in efficacy were detected between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Elderly patients may be at increased risk for volume depletion adverse reactions, including hypotension.
- **Renal Impairment:** INPEFA was evaluated in patients with chronic kidney disease (eGFR 25 to 60 mL/min/1.73 m^2) and in patients with heart failure with eGFR <60 mL/min/1.73 m^2. The safety profile of INPEFA across eGFR subgroups in these studies was consistent with the known safety profile. There was an increase in volume-related adverse events (e.g., hypotension, dizziness) in patients with eGFR <30 mL/min/1.73m^2 relative to the overall safety population. Efficacy and safety studies with INPEFA did not enroll patients with an eGFR less than 25 mL/min/1.73 m2 or on dialysis. After starting therapy in the studies, patients were discontinued if eGFR fell below 15 mL/min/1.73 m2 or were initiated on chronic dialysis.
- **Hepatic Impairment:** INPEFA is not recommended in patients with moderate or severe hepatic impairment.

Click here for full Prescribing Information.

Safe Harbor Statement

This press release contains "forward-looking statements," including statements relating to the therapeutic and commercial potential, research and clinical development and regulatory status of INPEFA® (sotagliflozin). In addition, this press release also contains forward looking statements relating to 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 commercialize INPEFA in heart failure on the timeline and/or at the prices currently contemplated or at all, conduct preclinical and clinical development and obtain necessary regulatory approvals of INPEFA (in other indications), LX9211 and its other 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, 2022 and other subsequent disclosure documents 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.