Xeris Announces Full Results From the Logics Study of Recorlev® and Presentation of New Burden of Illness in Cushing's Syndrome Data at AACE Annual Meeting May 12-14

May 12, 2022

CHICAGO--(BUSINESS WIRE)--May 12, 2022-- Xeris Biopharma Holdings, Inc. (Nasdaq: XERS), a biopharmaceutical company developing and commercializing unique therapies for patient populations in endocrinology, neurology, and gastroenterology, today announced it is presenting new data on the burden of illness in Cushing's syndrome (CS) and the double-blind, placebo-controlled LOGICS study of Recorlev ® (levoketoconazole) in CS during the Pituitary Disorders/Neuroendocrinology ePoster sessions at the American Association of Clinical Endocrinology (AACE) Annual Meeting, May 12-14, 2022.

Levoketoconazole in the Treatment of Endogenous Cushing's Syndrome: A Double-Blind, Placebo-Controlled, Randomized Withdrawal Study (abstract link here)

LOGICS, a phase 3 double-blind, placebo-controlled randomized-withdrawal (RW) study evaluated the drug-specificity of cortisol normalization in adults with CS by comparing the effect of withdrawing levoketoconazole to placebo versus continuing levoketoconazole treatment. The study, which included titration-maintenance, randomized withdrawal and restoration phases, met its previously reported primary endpoint of significantly more patients on placebo having loss of mean urinary-free cortisol (mUFC) response than those who continued on levoketoconazole at end of RW phase. Restoration of levoketoconazole therapy reversed loss of cortisol control in most patients who had received placebo; of 20 placebo group patients with mUFC >ULN at restoration phase baseline, 12 (60%) were normalized at the end of the restoration phase. In the RW phase, mean total and LDL cholesterol levels were significantly increased with placebo versus levoketoconazole; these increases were reversed during the restoration phase. Throughout the study, no new safety signals of levoketoconazole treatment were identified, and known risks were manageable with appropriate monitoring.

The full data will be shared during a poster presentation scheduled for May 12, 1:00–1:15 PM (PST).

Patient-Reported Burden of Illness in Endogenous Cushing's Syndrome (abstract link here)

The burden of illness (BOI) study captured the burden and health-related quality of life (HRQoL) associated with CS using validated patient reported outcome (PRO) measures of CushingQoL, Pain Visual Analog Scale (VAS), Brief Fatigue Inventory (BFI), PROMIS Sleep Disturbance (T-score) and PROMIS Anxiety SF 8a (T-score). Results showed that patients with CS experience a substantial and multi-faceted HRQoL burden. On the CushingQoL measure, respondents experienced moderate HRQoL impairment due to CS. The mean VAS score was 3.6 out of 10, indicating relatively low levels of pain; however, 89% of all respondents reported taking over-the-counter analgesics to manage their symptoms. Patients reported moderate/severe fatigue (BFI), and moderate sleep and anxiety burden (PROMIS). Patients experienced symptoms of CS on approximately half the days in a typical month, and those who were employed missed 2 workdays every month, amounting to approximately 25 days per year due to CS.

The full data will be shared during a poster presentation scheduled for May 12, 4:10–4:25 PM (PST).

About Cushing's Syndrome

Endogenous Cushing's syndrome is a rare, serious, and potentially fatal endocrine disease caused by chronic elevated cortisol exposure–often the result of a benign tumor of the pituitary gland. This benign tumor tells the body to overproduce high levels of cortisol for a sustained period of time, which often results in characteristic physical signs and symptoms that are distressing to patients. The disease is most common among adults between the ages of 30–50, and it affects women three times more often than men. Women with Cushing's syndrome may experience a variety of health issues including menstrual problems, difficulty becoming pregnant, excess male hormones (androgens), primarily testosterone, which can cause hirsutism (growth of coarse body hair in a male pattern), oily skin, and acne.[3]

Additionally, the multisystem complications of the disease are potentially life threatening. These include metabolic changes such as high blood sugar or diabetes, high blood pressure, high cholesterol, fragility of various tissues including blood vessels, skin, muscle, and bone, and psychological disturbances such as depression, anxiety, and insomnia.[3] Untreated, the five-year survival rate is only approximately 50%.[4]

About Recorlev

Recorlev® (levoketoconazole) is a cortisol synthesis inhibitor for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.[1] Endogenous Cushing's syndrome is a rare but serious and potentially lethal endocrine disease caused by chronic elevated cortisol exposure.[2] Recorlev is the pure 2S,4R enantiomer of ketoconazole, a steroidogenesis inhibitor.[1] Recorlev has demonstrated in two successful Phase 3 studies to significantly reduce mean urine free cortisol.[1]

The Phase 3 program for Recorlev included SONICS and LOGICS, two multinational studies designed to evaluate the safety and efficacy of Recorlev when used to treat endogenous Cushing's syndrome. The SONICS study met its primary and secondary endpoints, significantly reducing and normalizing mean urinary free cortisol concentrations without a dose increase.[1,2] The LOGICS study, which met its primary endpoint and key secondary endpoint, was a double-blind, placebo-controlled randomized-withdrawal study of Recorlev that was designed to supplement the efficacy and safety information provided by SONICS.[1] The ongoing open-label OPTICS study will gather further useful information related to the long- term use of Recorlev.

Recorlev received orphan drug designation from the FDA and the European Medicines Agency for the treatment of endogenous Cushing's syndrome.

Indication & Important Safety Information for Recorlev®

BOXED WARNING: HEPATOTOXICITY AND QT PROLONGATION

HEPATOTOXICITY

Cases of hepatotoxicity with fatal outcome or requiring liver transplantation have been reported with oral ketoconazole. Some patients had no obvious risk factors for liver disease. Recorlev is associated with serious hepatotoxicity. Evaluate liver enzymes prior to and during treatment.

QT PROLONGATION

Recorlev is associated with dose-related QT interval prolongation. QT interval prolongation may result in life-threatening ventricular dysrhythmias such as torsades de pointes. Perform ECG and correct hypokalemia and hypomagnesemia prior to and during treatment.

INDICATION

Recorlev is a cortisol synthesis inhibitor indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative.

Limitations of Use

Recorlev is not approved for the treatment of fungal infections.

CONTRAINDICATIONS

- Cirrhosis, acute liver disease or poorly controlled chronic liver disease, baseline AST or ALT > 3 times the upper limit of normal, recurrent symptomatic cholelithiasis, a prior history of drug induced liver injury due to ketoconazole or any azole antifungal therapy that required discontinuation of treatment, or extensive metastatic liver disease.
- Taking drugs that cause QT prolongation associated with ventricular arrhythmias, including torsades de pointes.
- Prolonged QTcF interval > 470 msec at baseline, history of torsades de pointes, ventricular tachycardia, ventricular fibrillation, or prolonged QT syndrome.
- Known hypersensitivity to levoketoconazole, ketoconazole or any excipient in Recorlev.
- Taking certain drugs that are sensitive substrates of CYP3A4 or CYP3A4 and P-gp.

WARNINGS AND PRECAUTIONS

Hepatotoxicity

Serious hepatotoxicity has been reported in patients receiving Recorlev, irrespective of the dosages used or the treatment duration. Drug-induced liver injury (peak ALT or AST greater than 3 times upper limit of normal) occurred in patients using Recorlev. Avoid concomitant use of Recorlev with hepatotoxic drugs. Advise patient to avoid excessive alcohol consumption while on treatment with Recorlev. Routinely monitor liver enzymes and bilirubin during treatment.

QT Prolongation

Use Recorlev with caution in patients with other risk factors for QT prolongation, such as congestive heart failure, bradyarrhythmias, and uncorrected electrolyte abnormalities, with more frequent ECG monitoring considered. Routinely monitor ECG and blood potassium and magnesium levels during treatment.

Hypocortisolism

Recorlev lowers cortisol levels and may lead to hypocortisolism with a potential for life-threatening adrenal insufficiency. Lowering of cortisol levels can cause nausea, vomiting, fatigue, abdominal pain, loss of appetite, and dizziness. Significant lowering of serum cortisol levels may result in adrenal insufficiency that can be manifested by hypotension, abnormal electrolyte levels, and hypoglycemia. Routinely monitor 24-hour urine free cortisol, morning serum or plasma cortisol, and patient's signs and symptoms for hypocortisolism during treatment.

Hypersensitivity Reactions

Hypersensitivity to Recorlev has been reported. Anaphylaxis and other hypersensitivity reactions including urticaria have been reported with oral ketoconazole.

Risks Related to Decreased Testosterone

Recorlev may lower serum testosterone in men and women. Potential clinical manifestations of decreased testosterone concentrations in men may include gynecomastia, impotence, and oligospermia. Potential clinical manifestations of decreased testosterone concentrations in women include decreased libido and mood changes.

ADVERSE REACTIONS

Most common adverse reactions (incidence > 20%) are nausea/vomiting, hypokalemia, hemorrhage/contusion, systemic hypertension, headache, hepatic injury, abnormal uterine bleeding, erythema, fatigue, abdominal pain/dyspepsia, arthritis, upper respiratory infection, myalgia, arrhythmia, back pain, insomnia/sleep disturbances, and peripheral edema.

DRUG INTERACTIONS

- Consult approved product labeling for drugs that are substrates of CYP3A4, P-gp, OCT2, and MATE prior to initiating Recorlev.
- Sensitive CYP3A4 or CYP3A4 and P-gp Substrates: Concomitant use of Recorlev with these substrates is contraindicated or not recommended.
- Atorvastatin: Use lowest atorvastatin dose possible and monitor for adverse reactions for dosages exceeding 20 mg daily.
- Metformin: Monitor glycemia, kidney function, and vitamin B12 and adjust metformin dosage as needed.
- Strong CYP3A4 Inhibitors or Inducers: Avoid use of these drugs 2 weeks before and during Recorlev treatment.
- Gastric Acid Modulators: See Full Prescribing Information for recommendations regarding concomitant use with Recorlev.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed during treatment and for one day after final dose.

To report SUSPECTED ADVERSE REACTIONS, contact Xeris Pharmaceuticals, Inc. at 1-877-937-4737 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Full Prescribing Information, including Boxed Warning.

About Xeris

Xeris (Nasdaq: XERS) is a biopharmaceutical company developing and commercializing unique therapies for patient populations in endocrinology, neurology, and gastroenterology. Xeris has three commercially available products; Gvoke®, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis®, the first and only FDA-approved therapy for primary periodic paralysis, and Recorlev® for the treatment of endogenous Cushing's syndrome. Xeris also has a robust pipeline of development programs to extend the current marketed products into important new indications and uses and bring new products forward using its proprietary formulation technology platforms, XeriSol™ and XeriJect™, supporting long-term product development and commercial success.

Xeris Biopharma Holdings is headquartered in Chicago, IL. For more information, visit www.xerispharma.com, or follow us on Twitter, LinkedIn, or Instagram.

Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for Xeris Biopharma Holdings, Inc. including statements regarding the market and therapeutic potential of its products and product candidates, expectations regarding the long-term use of Recorlev, and other statements containing the words "will," "would," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, reliance on third-party suppliers for Gvoke®, Ogluo®, Keveyis®, and Recorlev® the regulatory approval of its product candidates, its ability to market and sell its products, failure to realize the expected benefits of the acquisition, failure to promptly and effectively integrate Strongbridge's businesses, general economic and business conditions that affect the combined company following the consummation of the acquisition, the impact of the COVID-19 pandemic on the combined company following the consummation of the transaction, changes in global, political, economic, business, competitive, market and regulatory forces, future exchange and interest rates, changes in tax laws, regulations, rates and policies, future business acquisitions or disposals and competitive developments and the other risks described in our Quarterly Report on Form 10-Q and other reports we file from time to time with the SEC. These forward-looking statements are based on numerous assumptions and assessments made in light of Xeris' experience and perception of historical trends, current conditions, business strategies, operating environment, future developments, and other factors it believes appropriate. By their nature, forward-looking statements involve known and unknown risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. The factors described in the context of such forward-looking statements in this communication could cause Xeris' plans with respect to Strongbridge, Xeris' plans with respect to its products and product candidates, Xeris' actual results, performance or achievements, industry results and developments to differ materially from those expressed in or implied by such forward-looking statements. Although it is believed that the expectations reflected in such forward-looking statements are reasonable, no assurance can be given that such expectations will prove to have been correct and persons reading this communication are therefore cautioned not to place undue reliance on these forward-looking statements which speak only as at the date of this communication. Additional information about economic, competitive, governmental, technological, and other factors that may affect Xeris is set forth in Item 1A, "Risk Factors," in Xeris' 2020 Annual Report on Form 10-K, which has been filed with the SEC and other important factors in Xeris' subsequent filings with the SEC, the contents of which are not incorporated by reference into, nor do they form part of, this communication. Additional information about economic, competitive, governmental, technological, and other factors that may affect Strongbridge is set forth in Item 1A, "Risk Factors," in Strongbridge's 2020 Annual Report on Form 10-K, which has been filed with the SEC, the contents of which are not incorporated by reference into, nor do they form part of, this communication. Any forward-looking statements in this communication are based upon information available to Xeris, as of the date of this communication and, while believed to be true when made, may ultimately prove to be incorrect. Subject to any obligations under applicable law, Xeris does not undertake any obligation to update any forward- looking statement whether as a result of new information, future developments or otherwise, or to conform any forward-looking statement to actual results, future events, or to changes in expectations. All subsequent written and oral forward-looking statements attributable to Xeris or any person acting on behalf of any of them are expressly qualified in their entirety by this paragraph.

1. Recorlev [prescribing information]. Chicago, IL: Xeris Pharmaceuticals, Inc.; 2021. 2. Fleseriu M, et al. *Lancet Diabetes Endocrinol*. 2019;7(11):855-865. 3. Pivonello R et al. *Lancet Diabetes Endocrinol.* 2016; 4: 611-29. 4. Plotz CM, et al. *Am J Med.* 1952 November;13(5):597-614.

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Allison Wey
Senior Vice President, Investor Relations and Corporate Communications awey@xerispharma.com
(312) 736-1237

Source: Xeris Biopharma Holdings, Inc.