Xeris Biopharma Announces FDA Grants Orphan-drug Exclusivity for Recorlev®

January 30, 2023

CHICAGO--(BUSINESS WIRE)--Jan. 30, 2023-- Xeris Biopharma Holdings, Inc. (Nasdaq: XERS), a growth-oriented biopharmaceutical company committed to improving patient lives by developing and commercializing innovative products across a range of therapies, today announced that the Food and Drug Administration (FDA) granted its subsidiary Xeris Pharmaceuticals, Inc., orphan-drug exclusivity (ODE) for Recorlev® (levoketoconazole) for the treatment of adult patients with endogenous Cushing's syndrome for whom surgery is not an option or has not been curative.

As the first approval of levoketoconazole (Recorlev) for Cushing's syndrome, Xeris is entitled to seven years of orphan-drug market exclusivity from its FDA approval date of December 30, 2021. The FDA's Orphan Drug Designation program is designed to advance the development of drugs that treat a condition affecting 200,000 or fewer U.S. patients annually. This regulatory exclusivity is in addition to the patent exclusivity under Xeris' U.S. patents covering Recorlev and its therapeutic use, which extends to at least March 2040.

"Cushing's syndrome is a rare disease that can be physically and emotionally devastating to the patient. Most patients endure years of symptoms prior to obtaining a diagnosis and are then faced with limited effective treatment options," said Paul R. Edick, Xeris' Chairman and CEO. "We are excited to receive this important orphan-drug exclusivity approval for Recorlev on a new therapeutic option that can address symptoms while treating the root cause of the disease for this underserved Cushing's patient community."

Mr. Edick continued, "Recorlev is an important and welcome therapeutic option for clinicians to help manage patients with endogenous Cushing's syndrome, a severe, potentially life-threatening rare disease. The approval of Recorlev was based upon data from two positive Phase 3 studies that evaluated a combined study population of 166 patients and was shown to be effective for reducing and normalizing cortisol."

In order to serve and support this community, Xeris is committed to ensuring everyone who needs access to their therapies will receive it. Xeris has created Xeris CareConnection™ to provide a comprehensive program for patients and their caregivers throughout the treatment journey, including financial assistance, one-on-one support, and educational resources. Xeris CareConnection also supports healthcare professionals and their teams through education on access and reimbursement. For more information visit our website (www.recorlev.com) or contact Xeris CareConnection (available Monday–Friday from 8 a.m–7 p.m ET) at 1-844-444-RCLV (7258).

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 fatal 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 urinary free cortisol.[1]

The Phase 3 program for Recorlev included LOGICS and SONICS, two multinational studies designed to evaluate the safety and efficacy of Recorlev when used to treat endogenous Cushing's syndrome. LOGICS, a double-blind, placebo-controlled, randomized-withdrawal study met its key endpoint of normalizing and maintaining therapeutic response compared with placebo.[1] The supportive SONICS study met its primary and secondary endpoints, significantly reducing and normalizing mean urinary free cortisol concentrations without a dose increase.[1,2] 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 growth-oriented biopharmaceutical company committed to improving patients' lives by developing and commercializing innovative products across a range of therapies. Xeris has three commercially available products; Gvoke®, a ready-to-use liquid glucagon for the treatment of severe hypoglycemia, Keveyis®, the first FDA-approved therapy for primary periodic paralysis, and Recorlev® for the treatment of endogenous Cushing's syndrome. Xeris also has an increasingly diverse pipeline of development and partnered programs using its proprietary formulation technology platforms, XeriSol™ and XeriJect™, bringing new products forward for the company as well as its partners

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 Recorlev, the market and therapeutic potential of its products and product candidates, expectations regarding clinical data or results from planned clinical trials, the timing of clinical trials, the timing or likelihood of regulatory approval and commercialization of its product candidates, the potential utility of its formulation technology platforms and its ability to bring new products forward for the company and its partners, and other statements containing the words "will," "would," "continue," "expect," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. 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, geopolitical factors 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. Various factors could cause Xeris' actual results, performance or achievements, industry results and developments to differ materially from those expressed in or implied by such forward-looking statements, including the impact of COVID-19 on our business operations and clinical activities, our financial position and need for financing, including to fund our product development programs or commercialization efforts, whether our products will achieve and maintain market acceptance, our reliance on third-party suppliers, including single-source suppliers, our reliance on third parties to conduct clinical trials, the ability of our product candidates to compete successfully with existing and new drugs, and our and collaborators' ability to protect our intellectual property and proprietary technology. No assurance can be given that our expectations will be realized and persons reading this communication are, therefore, cautioned not to place undue reliance on these forward-looking statements. Additional information about potential impacts of COVID-19, financial, operational, economic, competitive, regulatory, governmental, technological, and other factors that may affect Xeris is set forth in the "Risk Factors" section of our most recently filed Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, the contents of which are not incorporated by reference into, nor do they form part of, this communication. 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 reasonable, actual results may differ materially. 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.

312-736-1237

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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