

## **RECORDATI: ISTURISA® (OSILODROSTAT) APPROVED IN THE U.S.**

**Recordati Announces US NDA Approval of Isturisa® (osilodrostat), the First and Only FDA Approved Cortisol Synthesis Inhibitor for Patients with Cushing's Disease. Company Builds Endocrinology Business Unit in the U.S.**

*Milan, 9 March 2020* – Recordati today announces the FDA approval of Isturisa® (osilodrostat) for the treatment of patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative. Isturisa® is the first and only FDA-approved inhibitor of 11-beta-hydroxylase that has demonstrated normalization of cortisol levels in a significant portion of adult patients with a manageable safety profile, making this a novel treatment option for patients with Cushing's disease.

"We are pleased with FDA's recognition of Isturisa® as an effective and safe treatment for patients with Cushing's disease," stated Andrea Recordati, CEO. "We extend our deepest gratitude to the patients who participated in the clinical trials and their families and caregivers who supported them. We also appreciate the hard work of the investigators, clinicians and study staff to bring this therapy to patients in need. Recordati Rare Diseases is committed to working to ensure everyone who needs access to this therapy will receive it."

"Isturisa® (osilodrostat) is an important and welcomed therapy in treating patients with this severe, potentially life-threatening rare disease," said Maria Fleseriu, M.D., FACE, professor of Medicine and Neurological Surgery and director of the Pituitary Center at Oregon Health Sciences University. "Cushing's disease results in an increased risk of cardiovascular and cerebrovascular diseases, as well as hypercoagulability, diabetes, infections, depression, and decreased quality of life. If not appropriately treated, Cushing's disease has increased mortality. Until now, patients in need of medications to reduce cortisol levels have had few approved options, either with limited efficacy or with too many adverse effects. With this demonstrated effective oral treatment, we have a therapeutic option that will help address patients' needs in this underserved patient population."

The approval is based on data generated by the clinical program, showing that Isturisa® leads to normalization of cortisol levels in the majority of patients, as well as improvement in multiple clinical features of the disease. In the Phase 3 LINC-3 study, a significantly higher proportion of patients treated with Isturisa® maintained normal mean urinary free cortisol (mUFC) at the end of the 8-week randomized withdrawal period (week 34) versus placebo (86% vs 29%). Cortisol level control is the primary objective in the treatment of patients with Cushing's disease. Adverse drug reactions associated with Isturisa® and occurring in greater than 20% of patients are adrenal insufficiency, fatigue, nausea, headache, and edema.

The FDA decision also confirmed the orphan status of Isturisa® providing 7 years of market exclusivity. Recordati expects Isturisa® to become commercially available in the U.S. in the second or third quarter of 2020.

Recordati Rare Diseases Inc., part of the rare diseases business within the Recordati Group, recently launched an endocrinology business unit in the U.S. and is actively building its commercial, medical,

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and market access teams. The Company is developing a comprehensive distribution model with specialty pharmacies that will provide services to support patients and healthcare providers.

### **Important Safety Information for Isturisa®**

#### **Indications and Usage**

ISTURISA (osilodrostat) is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

#### **Warnings and Precautions**

- **Hypocortisolism:** ISTURISA lowers cortisol levels and can lead to hypocortisolism and sometimes life-threatening adrenal insufficiency. Lowering of cortisol can cause nausea, vomiting, fatigue, abdominal pain, loss of appetite, and dizziness. Significant lowering of serum cortisol may result in hypotension, abnormal electrolyte levels, and hypoglycemia.

Hypocortisolism can occur at any time during ISTURISA treatment. Evaluate patients for precipitating causes of hypocortisolism (infection, physical stress, etc). Monitor 24-hr urine free cortisol, serum or plasma cortisol, and patient's signs and symptoms periodically during ISTURISA treatment.

Decrease or temporarily discontinue ISTURISA if urine free cortisol levels fall below the target range, there is a rapid decrease in cortisol levels, and/or patients report symptoms of hypocortisolism. Stop ISTURISA and administer exogenous glucocorticoid replacement therapy if serum or plasma cortisol levels are below target range and patients have symptoms of adrenal insufficiency. After ISTURISA discontinuation, cortisol suppression may persist beyond the 4-hour half-life of ISTURISA. Please see section 5.1 of full Prescribing Information.

Educate patients on the symptoms associated with hypocortisolism and advise them to contact a healthcare provider if they occur.

- **QTc Prolongation:** ISTURISA is associated with a dose-dependent QT interval prolongation which may cause cardiac arrhythmias. Perform an ECG to obtain a baseline QTc interval measurement prior to initiating therapy with ISTURISA and monitor for an effect on the QTc interval thereafter. Correct hypokalemia and/or hypomagnesemia prior to ISTURISA initiation and monitor periodically during treatment with ISTURISA. Use with caution in patients with risk factors for QT prolongation and consider more frequent ECG monitoring. Please see section 5.2 of full Prescribing Information.
- **Elevations in Adrenal Hormone Precursors and Androgens:** ISTURISA blocks cortisol synthesis and may increase circulating levels of cortisol and aldosterone precursors and androgens. This may activate mineralocorticoid receptors and cause hypokalemia, edema and hypertension. Hypokalemia should be corrected prior to initiating ISTURISA. Monitor patients treated with ISTURISA for hypokalemia, worsening of hypertension and edema. Inform patients of the symptoms associated with hyperandrogenism and advise them to contact a healthcare provider if they occur. Please see section 5.3 of full Prescribing Information.

#### **Adverse Reactions**

- Most common adverse reactions (incidence >20%) are adrenal insufficiency, fatigue, nausea, headache, and edema.



- To report SUSPECTED ADVERSE REACTIONS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### **Drug Interactions**

- **CYP3A4 Inhibitor:** Reduce the dose of ISTURISA by half with concomitant use of a strong CYP3A4 inhibitor.
- **CYP3A4 and CYP2B6 Inducers:** An increase of ISTURISA dosage may be needed if ISTURISA is used concomitantly with strong CYP3A4 and CYP2B6 inducers. A reduction in ISTURISA dosage may be needed if strong CYP3A4 and CYP2B6 inducers are discontinued while using ISTURISA.

#### **Use in Specific Populations**

- **Lactation:** Breastfeeding is not recommended during treatment with ISTURISA and for at least one week after treatment.

Please refer to Full Prescribing Information.

#### **About Cushing's Disease**

Cushing's disease is a form of Cushing's syndrome, in which excess cortisol production is triggered by a pituitary adenoma secreting excess adrenocorticotrophic hormone (ACTH). It is a rare but serious disease that affects approximately one to two patients per million per year. Cushing's disease most commonly affects adults as young as 20 to 50 years and affects women three times more often than men. It may present with weight gain, central obesity, a round, red full face, severe fatigue and weakness, striae (purple stretch marks), high blood pressure, depression and anxiety. Cushing's disease can cause severe illness and death with mortality up to four times higher than in the healthy population.

#### **About Isturisa®**

Isturisa® is a cortisol synthesis inhibitor that works by preventing 11-betahydroxylase, an enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland, from being created. Isturisa® will be available as 1-mg, 5-mg and 10-mg film-coated tablets. Please see prescribing information for detailed recommendations for the use of this product. In January 2020, the European Commission granted marketing authorization for Isturisa® in the European Union (EU).

#### **About Recordati Rare Diseases Inc.**

Recordati Rare Diseases Inc. is a biopharmaceutical company committed to providing often-overlooked orphan therapies to the underserved rare disease communities of the United States. Recordati Rare Diseases Inc. is a part of the rare disease business within the Recordati Group, a public international specialty pharmaceutical company committed to the research and development of new specialties with a focus on treatments for rare diseases.

Recordati Rare Diseases' mission is to reduce the impact of extremely rare and devastating diseases by providing urgently needed therapies. We work side-by-side with rare disease communities to increase awareness, improve diagnosis and expand availability of treatments for people with rare diseases.

For a full list of our U.S. products please click here: [www.recordatirarediseases.com/us/products](http://www.recordatirarediseases.com/us/products).



The company's U.S. corporate headquarters is located in Lebanon, NJ, with global headquarter offices located in Milan, Italy.

#### **About the Recordati group**

Recordati, established in 1926, is an international pharmaceutical group, listed on the Italian Stock Exchange (Reuters RECI.MI, Bloomberg REC IM, ISIN IT 0003828271), with a total staff of more than 4,100, dedicated to the research, development, manufacturing and marketing of pharmaceuticals. Headquartered in Milan, Italy, Recordati has operations throughout the whole of Europe, including Russia, Turkey, North Africa, the United States of America, Canada, Mexico, some South American countries, Japan and Australia. An efficient field force of medical representatives promotes a wide range of innovative pharmaceuticals, both proprietary and under license, in a number of therapeutic areas including a specialized business dedicated to treatments for rare diseases. Recordati is a partner of choice for new product licenses for its territories. Recordati is committed to the research and development of new specialties with a focus on treatments for rare diseases. Consolidated revenue for 2019 was € 1,481.8 million, operating income was € 465.3 million and net income was € 368.9 million.

For further information:

Recordati website: [www.recordati.com](http://www.recordati.com)

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