NEWS RELEASE

RECORDATI: RESULTS FROM THE PHASE III LINC-3 STUDY OF ISTURISA® (OSILODROSTAT) FOR THE TREATMENT OF CUSHING'S DISEASE PUBLISHED IN *LANCET DIABETES & ENDOCRINOLOGY*.

Data from the Phase III LINC-3 study, published in *Lancet Diabetes & Endocrinology*, demonstrate that Isturisa® (osilodrostat) rapidly decreases mean urinary-free cortisol (mUFC) in patients with Cushing's disease.

Lebanon, NJ, July 28, 2020 – Recordati Rare Diseases Inc. announces today that *Lancet Diabetes & Endocrinology* has published results from the Phase III LINC-3 pivotal study of ISTURISA, recently approved for the treatment of Cushing's disease in adults. Patients with Cushing's disease have an increased risk of significant comorbidities, including cardiovascular and cerebrovascular diseases as a result of excessive cortisol levels.[1] Data from the large LINC-3 study, which enrolled 137 patients with Cushing's disease, demonstrate that ISTURISA rapidly reduces mUFC and sustains this reduction alongside improvements in comorbidities, clinical signs and patients' quality of life over 48 weeks.

"The exciting data, published today, underscore the efficacy and safety of ISTURISA in a prospective setting, and represent a significant advance for the management of patients with Cushing's disease, a serious and potentially life-threatening rare condition," said Rosario Pivonello, MD, Professor of Endocrinology at the Federico II University of Naples, Italy. "I would like to thank all the patients who participated in the LINC-3 study, and their families, who have helped to bring this new and welcome treatment option to this underserved patient population."

The LINC-3 study met its primary endpoint, with significantly more patients maintaining normal mUFC with ISTURISA without a dose increase than placebo (86% vs 29%; P<0.0001) following 8 weeks of randomized withdrawal (week 34). Further analysis of patients' mUFC response found:

- Over half (53%) of patients achieved the key secondary endpoint of a normal mUFC after an initial 24 weeks of open-label treatment with ISTURISA, without any dose increase after week 12
- Most (72%) patients had normal mUFC at week 12
- Two-thirds (66%) of patients had normal mUFC at the end of the 48-week study
- Almost all (96%) patients achieved normal mUFC at some point during the study, with a median time to first complete response of 41 days

Decreases in mUFC levels during treatment with ISTURISA were accompanied by improvements in clinical signs and cardiovascular-related risk factors (weight, BMI, blood glucose, blood pressure, and total cholesterol). ISTURISA is well tolerated, with the most common adverse effects in LINC-3 being nausea (42%), headache (34%), fatigue (28%) and adrenal insufficiency (28%).

"The publication of these data in Lancet Diabetes & Endocrinology confirms ISTURISA as an effective new treatment option for patients with Cushing's syndrome," said Andrea Recordati, CEO. "Following the

recent approval of ISTURISA in the US and EU, we are excited to bring ISTURISA to all of those patients who need it."

The full manuscript can be accessed online at:
http://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30240-0/fulltext

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 hypoglycaemia.

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

  Decrease or temporarily discontinue ISTURISA if urinary 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 hypokalaemia and/or hypomagnesaemia 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 hypokalaemia, oedema and hypertension. Hypokalaemia should be corrected prior to initiating ISTURISA. Monitor patients treated with ISTURISA for hypokalaemia, worsening of hypertension and oedema. 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 oedema.

- **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.**

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 1 week after treatment.

Please refer to Full Prescribing Information at www.isturisa.com/pdf/isturisa-prescribing-information.pdf

About Cushing's disease

Cushing's disease is a form of Cushing's syndrome, in which chronically elevated cortisol levels is triggered by a pituitary adenoma secreting excess adrenocorticotropic hormone (ACTH).[2] It is a rare, serious and difficult-to-treat disease that affects approximately one to two patients per million per year. Prolonged exposure to elevated cortisol levels is associated with considerable morbidity, mortality and impaired quality of life as a result of complications and comorbidities.[3] Normalization of cortisol levels is therefore a primary objective in the treatment of Cushing's disease.[4]

About LINC-3

LINC-3 is a prospective, multicentre, 48-week trial with an 8-week, double-blind, randomized withdrawal phase to evaluate the safety and efficacy of ISTURISA in patients with Cushing's disease. The primary endpoint in the LINC-3 trial is the proportion of patients randomized to ISTURISA and placebo, separately, at Week 26 with a mUFC ≤ULN at the end of the 8-week randomized withdrawal period (Week 34), without a dose increase during this period. The key secondary endpoint is the proportion of enrolled patients with a mUFC ≤ULN after an initial 24 weeks of open-label treatment with ISTURISA without any dose increase after Week 12. LINC-3 involved 137 patients with persistent or recurrent Cushing's disease despite pituitary surgery or de novo patients for whom surgery was not indicated or who had refused surgery.

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 is 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.[5] In March 2020, the FDA granted marketing authorization for ISTURISA in the United States. For more information visit www.isturisa.com.

1. Pivonello R *et al. Lancet Diabetes Endocrinol* 2020; doi: 10.1016/S2213-8587(20)30240-0 [Epub ahead of print]
2. Lacroix A *et al. Lancet* 2015;386:913–27
3. Pivonello R *et al. Lancet Diabetes Endocrinol* 2016;4:611–29
4. Nieman LK *et al. J Clin Endocrinol Metab* 2015;100:2807–31
5. ISTURISA® Prescribing Information. March 2020

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 is a part of 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.

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

For a full list of products, please click here: www.recordatirarediseases.com/us/products

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