NEWS RELEASE

RECORDATI RARE DISEASES ANNOUNCES POSITIVE DATA FROM PHASE III LINC 4, PHASE III LINC 3, AND ILLUSTRATE ISTURISA® STUDIES PRESENTED AT ENDO 2022

- **ISTURISA® (osilodrostat) maintained normal mean urinary free cortisol (mUFC) long-term in patients with Cushing's disease.**
- **Adrenal hormone levels changed during early treatment with ISTURISA and stabilized during long-term treatment.**
- **Patients treated with a prolonged titration interval tended to have greater persistence with therapy.**

Lebanon, NJ, June 15, 2022 – Recordati Rare Diseases Inc. announced today that multiple positive data sets highlighting ISTURISA were presented at the annual ENDO 2022 meeting in Atlanta, Georgia. The Phase III LINC 4 study demonstrates ISTURISA maintained normal mean urinary free cortisol (mUFC) long-term in patients with Cushing's disease, the Phase III LINC 3 study found adrenal hormone levels changed during early treatment with ISTURISA while stabilizing during long-term treatment, and the ILLUSTRATE study showed patients treated with a prolonged titration interval tended to have greater persistence with therapy. ISTURISA is a cortisol synthesis inhibitor indicated in the United States for the treatment of adult patients with Cushing's disease.

Cushing's disease is a rare, serious illness caused by a pituitary tumor that leads to overproduction of cortisol by the adrenal glands. Excess cortisol can contribute to an increased risk of morbidity and mortality. Treatment for the condition seeks to lower cortisol levels to a normal range.

According to the abstract titled, "Long-term results from the Phase III LINC 4 study: osilodrostat maintained normal mUFC in patients with Cushing's disease, with a favorable safety profile," ISTURISA provided long-term control of cortisol production during the LINC 4 study.

Key Phase III LINC 4 Study Findings:

- The proportion of patients with normal mean mUFC was 68.5% (n=50/73) at week 48, 61.5% (n=40/65) at week 72 and 72.4% (n=42/58) at the end-of-treatment extension (EOT) visit.
- Median mUFC decreased from 2.5x the upper limit of normal (ULN) (core baseline) to 0.5xULN at weeks 48 and 72, to 0.4xULN (EOT).
- The most common adverse events during the entire study were decreased appetite (46.6%), arthralgia (45.2%), fatigue (39.7%), nausea (37.0%), headache (34.2%) and

dizziness (30.1%).

Androgens and Adrenal Hormones
The abstract presented titled, "Effect of osilodrostat on androgens and adrenal hormones in patients with Cushing's disease: Long-term findings from the Phase III, prospective LINC 3 study," summarized the influence ISTURISA has on hormone levels and examines related side effects by analyzing data from the LINC 3 Phase III study (n=137). Patients received treatment for up to 4.7 years, with the median ISTURISA exposure being 130 weeks.

According to the abstract, changes in androgen and adrenal hormone levels happened during initiation of ISTURISA treatment, and remain stable or decrease during long-term therapy. The study found no clear link to ISTURISA dose.

Key Phase III LINC 3 Study Findings:

- Following an initial increase during the core phase, mean (SD) testosterone levels decreased towards baseline levels in females and stabilized in males during long-term treatment.
- Of female patients with assessments at baseline and follow up, hirsutism score improved or did not change from baseline in 63/76 patients at week 48 and 55/64 patients at week 72.
- Overall, few patients discontinued because of adrenal hormone precursor accumulation-related AEs (1.5%; n=2/137).

Real-World Study of Dosing and Titration
Finally, the abstract, "Dosing and Titration of Osilodrostat in a Real-World Cohort of US Patients with Endogenous Cushing's Disease: Analysis of the ILLUSTRATE Study," reports findings from a retrospective chart review study that examined the medical records of 42 patients with endogenous Cushing's syndrome (34 with Cushing's disease) who were prescribed ISTURISA, in order to describe how their dosage was started and managed.

According to the abstract, approximately 2/3 of the 34 Cushing's disease patients included in the analysis were started at a dose similar to clinical trial dosing.

Key ILLUSTRATE Study Findings:

- Overall, consistent with prior research data, patients with a gradual dose up-titration (i.e., prolonged titration interval) tended to have greater persistence with therapy.
- Treatment persistence for those enrolled ≥ 6 months prior to study end was 95.8%, mean (SD) duration of therapy was 339.2 (106.8) days.
- There were no new safety findings.

"The data from these studies reinforces the efficacy and safety of ISTURISA as a treatment for patients with Cushing's disease," said Mohamed Ladha, President and General Manager North America. "We are pleased to share these data with the endocrine community and are excited to provide patients with a much-needed step forward in the management of this rare, debilitating, and potentially life-threatening condition."

All educational content of the ENDO annual meeting is planned by its program committee, and ENDO does not endorse, promote, approve, or recommend the use of any products, devices or services.

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-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 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.**

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.

About Cushing's disease

Cushing's disease is a form of Cushing's syndrome, in which chronically elevated cortisol levels are triggered by a pituitary adenoma secreting excess adrenocorticotropic hormone (ACTH). 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 QoL due to complications and comorbidities. Normalization of cortisol levels is therefore a primary objective in the treatment of Cushing's disease.

About LINC 3
LINC 3 is a prospective, multicenter, 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 LINC-4
LINC-4 is a large randomized, double-blinded, multicenter, 48-week trial with an initial 12-week placebo-controlled period to evaluate the safety and efficacy of osilodrostat in patients with Cushing's disease. The primary endpoint in the LINC-4 trial is the proportion of patients randomized to ISTURISA or placebo with a mUFC ≤ULN at the end of the 12-week placebo-controlled period. The key secondary endpoint is the proportion of patients in both arms combined with a mUFC ≤ULN after 36 weeks. LINC-4 involved 73 patients with persistent or recurrent Cushing's disease or those with de *novo* disease who were not candidates for surgery.

About ISTURISA
ISTURISA is a cortisol synthesis inhibitor that works by inhibiting 11-beta-hydroxylase, an enzyme responsible for the final step of cortisol biosynthesis in the adrenal gland. 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. In March 2020, the FDA granted marketing authorization for ISTURISA in the United States. For more information visit www.isturisa.com .

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. https://www.recordatirarediseases.com/us

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

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