Isturisa® (osilodrostat) – New orphan drug approval

- On March 6, 2020, the FDA announced the approval of Recordati's Isturisa (osilodrostat), for the treatment of adult patients with Cushing's disease for whom pituitary surgery is not an option or has not been curative.

- Cushing's disease is caused by a pituitary tumor that releases too much adrenocorticotropin, which stimulates the adrenal gland to produce an excessive amount of cortisol. Cushing's disease can cause significant health issues, such as high blood pressure, obesity, type 2 diabetes, blood clots, bone loss and fractures, a weakened immune system, and depression.

    — The disease is most common among adults between the ages of 30 to 50, and it affects women three times more often than men.

- Isturisa is the first FDA-approved drug to directly address this cortisol overproduction by blocking the enzyme known as 11-beta-hydroxylase and preventing cortisol synthesis.

- The efficacy of Isturisa was established in a 48-week study in patients with Cushing's disease. In the 24-week, single-arm, open-label period of the study, all patients (N = 137) received Isturisa. At the end of this 24-week period, about half of patients had cortisol levels within normal limits. After this point, 71 patients who did not need further dose increases and tolerated the drug for the last 12 weeks entered an 8-week, double-blind, randomized withdrawal study where they received Isturisa or placebo. The primary endpoint was the percentage of complete responders at the end of the 8week randomized withdrawal period.

    — At the end of the randomized withdrawal period, the percentage of complete responders was 86% and 29% in the Isturisa and placebo groups, respectively (treatment difference: 57; 95% CI: 38, 76; $p < 0.001$).

- Warnings and precautions for Isturisa include hypocortisolism, QTc prolongation, and elevations in adrenal hormone precursors and androgens.

- The most common adverse reactions (> 20%) with Isturisa use were adrenal insufficiency, fatigue, nausea, headache, and edema.

- The recommended initial dose of Isturisa is 2 mg orally twice daily, with or without food. The dose should be initially titrated by 1 to 2 mg twice daily, no more frequently than every 2 weeks based on the rate of cortisol changes, individual tolerability and improvement in signs and symptoms of Cushing's disease. The maximum recommended maintenance dosage of Isturisa is 30 mg twice daily.

    — Refer to the Isturisa drug label for complete dosing and administration recommendations.

- Recordati plans to launch Isturisa in the second or third quarter of 2020. Isturisa will be available as a 1 mg, 5 mg, and 10 mg tablet.