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Positive Topline Results for Lorundrostat in Hypertension

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Lorundrostat, a hypertension drug from Mineralys Therapeutics, has shown positive results in two pivotal trials for the treatment of uncontrolled or resistant hypertension the company announced on Monday.

Both trials met their primary endpoints and had good safety and tolerability results. "This is a significant outcome" for about 20 million people with uncontrolled hypertension in the United States alone who could benefit from a targeted aldosterone-directed treatment, said Jon Congleton, CEO of Mineralys, in a conference call.

Launch-HTN was a placebo-controlled phase 3 clinical trial of 1083 adults who failed to achieve their blood pressure goal despite being on 2-5 antihypertensive medications. It found that those who were given 50 mg of lorundrostat daily in addition to their existing medications had an absolute reduction in blood pressure of 16.9 mmHg and a placebo-adjusted reduction of 9.1 mmHg after 6 weeks.

Launch-HTN Trial

Further reductions of 19.0 mmHg (absolute) and 11.7 mmHg (placebo-adjusted) were seen after 12 weeks. Patients whose doses were increased to 100 mg per day after 6 weeks had an absolute reduction of 15.7 mmHg and a placebo-adjusted reduction of 8.4 mmHg after 12 weeks.

The change in blood pressure in response to lorundrostat in patients using two background antihypertensives or 3-5 were similar.

"Reductions in blood pressure of this magnitude have been linked to significant decreases in overall cardiovascular risk," said Congleton. "We believe these results position lorundrostat as a transformative option for patients with uncontrolled or resistant hypertension."

Lorundrostat is an aldosterone synthase inhibitor that reduces aldosterone levels by inhibiting CYP11B2, the enzyme responsible for its production. In previous studies, it demonstrated approximately a 70% reduction in plasma aldosterone concentration in patients with hypertension.

A second phase 2 trial, Advance-HTN, evaluated the efficacy and safety of lorundrostat for the treatment of uncontrolled or resistant hypertension when used as an add-on therapy to a standardized background treatment of two or three antihypertensive medications.

Advance-HTN Trial

Patients enrolled in the trial had their existing hypertension medications discontinued and were given a standard regimen of an angiotensin II receptor

blocker and a diuretic (if previously on two medications) or angiotensin receptor blocker, diuretic, and calcium channel blocker (if previously on 3-5 medications). They were then randomly assigned to receive either 50 mg of lorundrostat daily, 50 mg with the option to increase to 100 mg daily after 4 weeks, or placebo.

The trial found a placebo-adjusted reduction from baseline in systolic blood pressure assessed with 24-hour average blood pressure measurement at week 12 of 7.9 mmHg in subjects treated with 50 mg of lorundrostat.

"We believe the efficacy and safety findings in this especially rigorous trial support a favorable benefit-risk profile for lorundrostat in patients with confirmed uncontrolled or resistant hypertension," said David Rodman, MD, chief medical officer of Mineralys, in the conference call.

The full results from the Advance-HTN trial will be presented at the American College of Cardiology Scientific Session in Chicago on March 29.

Congleton and Rodman are both employees of Mineralys Therapeutics.