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Mineralys Therapeutics Announces Late-Breaking Data from Advance-HTN Pivotal Trial of Lorundrostat in Uncontrolled and Resistant Hypertension Presented at the American College of Cardiology's Annual Scientific Session & Expo (ACC.25)

– Lorundrostat 50 mg dose achieved a 15.4 mmHg absolute reduction and 7.9 mmHg placebo-adjusted reduction (p=0.001), assessed by 24hr ABPM at week 12, with favorable safety and tolerability profile –

– Lorundrostat is a highly selective aldosterone synthase inhibitor that disrupts aldosterone biosynthesis rather than blocking the mineralocorticoid receptor –

– Data from Advance-HTN support the potential of lorundrostat as a best-in-class treatment for high-risk patients with uncontrolled or resistant hypertension who would normally be treated in a specialist setting –

RADNOR, Pa., March 29, 2025 (GLOBE NEWSWIRE) -- Mineralys Therapeutics, Inc. (Nasdaq: MLYS), a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, chronic kidney disease (CKD), obstructive sleep apnea (OSA) and other diseases driven by dysregulated aldosterone, today announced detailed results from the Phase 2 Advance-HTN trial, one of two pivotal trials evaluating lorundrostat in patients with confirmed uncontrolled hypertension (uHTN) or resistant hypertension (rHTN). In the trial, lorundrostat 50 mg demonstrated a 15.4 mmHg absolute reduction and a 7.9 mmHg placebo-adjusted reduction at week 12. Additionally, lorundrostat demonstrated a favorable safety and tolerability profile, with modest changes in potassium, sodium and eGFR, and a low discontinuation rate.

"With the recent announcement of data from our two pivotal trials, we now have a comprehensive dataset demonstrating the robust and consistent blood pressure reductions of lorundrostat in two distinct but complementary patient populations—real-world setting in Launch-HTN, and those with optimally treated yet uncontrolled hypertension in the specialist setting in Advance-HTN," stated Jon Congleton, Chief Executive Officer of Mineralys Therapeutics. "These findings underscore lorundrostat's clinical utility across diverse care settings and also provide critical insights for both primary care providers, who manage the vast majority of hypertension patients, and specialists, who treat the most complex cases. We are excited about the potential impact lorundrostat could have as a novel treatment to address a significant unmet need in hypertension care."

"Twenty-four-hour ambulatory blood pressure monitoring is the gold standard for assessing

the true impact of an antihypertensive therapy, as it provides a more comprehensive picture of blood pressure control beyond the office setting, including overnight readings," stated Luke Laffin, M.D., co-director of the Center for Blood Pressure Disorders in the Heart, Vascular & Thoracic Institute at Cleveland Clinic and the study's lead author. "Along with rigorous evaluations in the Advance-HTN trial, the double-digit drop in blood pressure readings observed with lorundrostat in this trial are particularly notable given the complex characteristics of the patient population, which included a high proportion of individuals who have been historically underrepresented in hypertension clinical trials and who face a disproportionate burden of treatment-resistant hypertension."

Following the recently announced positive topline data from both Advance-HTN and Launch-HTN pivotal trials, detailed results from Advance-HTN were presented in a late-breaking session at the American College of Cardiology's Annual Scientific Session & Expo (ACC.25) on Saturday, March 29, 2025, at 1:30 p.m. CT.

Efficacy Results

The Advance-HTN trial was a randomized, double-blind, placebo-controlled Phase 2 pivotal trial that evaluated the efficacy and safety of lorundrostat for the treatment of confirmed uncontrolled or resistant hypertension, when used as add-on therapy to an optimized background treatment of two or three antihypertensive medications in adult subjects. The trial was designed to evaluate lorundrostat in an uncontrolled or resistant hypertensive population at the highest risk and which would normally be treated by a specialist given severity of their condition.

Primary Endpoint	**50 mg** *(n=94)*	**50 to 100mg** *(n=94)*
Change in 24-Hour Average SBP at Week 12	-7.9 mmHg placebo-adjusted change (p=0.001)	-6.5 mmHg placebo-adjusted change (p=0.006)
Key Secondary Endpoints	**50 mg (n=188, at Week 4)**	
Change in 24-Hour Average SBP at Week 4	-11.5 mmHg absolute change, -5.3 mmHg placebo-adjusted change (p<0.001)	
Proportion with 24-Hour Average SBP < 125 mmHg at Week 4	41% compared to 18% on placebo (p<0.001)	
Change in 24-Hour Average SBP at Week 4 in Patients on 2 Background Medications	-11.2 mmHg absolute change, -6.1 mmHg placebo-adjusted change (p=0.001)	
Change in 24-Hour Average SBP at Week 4 in Patients on 3 Background Medications	-11.8 mmHg absolute change, -4.6 mmHg placebo-adjusted change (p=0.060)	

Safety and Tolerability Results

Lorundrostat demonstrated a favorable safety and tolerability profile in the Advance-HTN trial, with modest changes in potassium, sodium and eGFR, and a low discontinuation rate. The anticipated on-target effects on serum electrolytes, increased serum potassium and reduced serum sodium were modest and rapidly reversible upon discontinuation of lorundrostat. Suppression of cortisol production was not observed and there was a very low incidence of drug-related serious adverse events (SAEs) resulting in discontinuation or dose-adjustment of study medication.

- SAEs occurred in 6%, 8% and 2% of patients in the lorundrostat 50 mg, lorundrostat 50 to 100 mg and placebo arms, respectively.

- Treatment-related SAEs occurred in 2%, 1% and 0% of patients in the lorundrostat 50 mg, lorundrostat 50 to 100 mg and placebo arms, respectively.
- The incidence of hyperkalemia (serum potassium >6.0 mmol/L) at the scheduled study visit was 5.3% and 7.4% in the 50 mg and 50 to 100 mg arms, respectively. The per-protocol procedure for validation of suspected factitious hyperkalemia specified a repeat potassium measurement within 72 hours while still taking study medication to ascertain the true incidence of hyperkalemia. After exclusion of the spurious results, the values for confirmed hyperkalemia were 2.1% and 3.2%, respectively.

"The safety findings from the Advance-HTN trial further reinforce lorundrostat's favorable benefit-risk profile, even in a high-risk population that would normally be treated by specialists rather than general practitioners. The study enrolled patients with confirmed uncontrolled or resistant hypertension—40% were women and over half (53%) were Black, a group that bears a disproportionate burden of the disease," stated David Rodman, MD, Chief Medical Officer of Mineralys Therapeutics. "The anticipated on-target effects on serum electrolytes, including modest increases in potassium, were manageable and reversible, with low rates of treatment discontinuation due to adverse events. Importantly, the incidence of serious drug-related adverse events was very low, highlighting the potential for lorundrostat to be a well-tolerated, once-daily therapy for patients in need."

Mineralys plans to provide additional data from the pivotal Phase 3 Launch-HTN at an upcoming medical conference and in a peer-reviewed publication. Additionally, the ongoing Transform-HTN open-label extension trial allows subjects to continue to receive lorundrostat and obtain additional safety and efficacy data.

Conference Call

The Company's management team will host a conference call on Tuesday, April 1, 2025, at 8:00 a.m. ET. To access the call, please dial 1-877-704-4453 in the U.S. or 1-201-389-0920 outside the U.S. A live webcast of the conference call may be found here. A replay of the call will be available on the "News & Events" page in the Investor Relations section of the Mineralys Therapeutics website (click here).

About Hypertension

Having sustained, elevated blood pressure (or hypertension) increases the risk of heart disease, heart attack and stroke, which are leading causes of death in the U.S. In 2020, more than 670,000 deaths in the U.S. included hypertension as a primary or contributing cause. Hypertension and related health issues resulted in an average annual economic burden of about $219 billion in the U.S. in 2019.

Less than 50% of hypertension patients achieve their blood pressure goal with currently available medications. Dysregulated aldosterone levels are a key factor in driving hypertension in approximately 30% of all hypertensive patients.

About Lorundrostat

Lorundrostat is a proprietary, orally administered, highly selective aldosterone synthase inhibitor being developed for the treatment of uncontrolled or resistant hypertension, as well

as CKD and OSA. Lorundrostat was designed to reduce aldosterone levels by inhibiting CYP11B2, the enzyme responsible for its production. Lorundrostat has 374-fold selectivity for aldosterone-synthase inhibition versus cortisol-synthase inhibition *in vitro*, an observed half-life of 10-12 hours and demonstrated approximately a 70% reduction in plasma aldosterone concentration in hypertensive subjects.

In a Phase 2, proof-of-concept trial (Target-HTN) in uncontrolled or resistant hypertensive subjects, once-daily lorundrostat demonstrated statistically significant and clinically meaningful blood pressure reduction in both automated office blood pressure measurement and 24-hour ambulatory blood pressure monitoring. Adverse events observed were a modest increase in serum potassium, decrease in estimated glomerular filtration rate, urinary tract infection and hypertension with one serious adverse event possibly related to study drug being hyponatremia.

About Advance-HTN

The Advance-HTN trial (NCT05769608) was a randomized, double-blind, placebo-controlled Phase 2 clinical trial that 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 in adult subjects. Subjects who meet screening criteria had their existing hypertension medications discontinued and start on a standard regimen of an angiotensin II receptor blocker (ARB) and a diuretic, if previously on two medications, or a standard regimen of ARB, diuretic and calcium channel blocker if previously on three to five medications. Subjects who remained hypertensive despite the standardized regimen were then randomized into three cohorts and treated for twelve weeks: lorundrostat 50 mg once-daily (QD), lorundrostat 50 mg QD and an option to titrate to 100 mg QD at week four based on defined criteria, or placebo. The trial's primary endpoint was the change in 24-hour ambulatory systolic blood pressure at week twelve from baseline for active cohorts versus placebo.

About Mineralys

Mineralys Therapeutics is a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, CKD, OSA and other diseases driven by dysregulated aldosterone. Its initial product candidate, lorundrostat, is a proprietary, orally administered, highly selective aldosterone synthase inhibitor that Mineralys Therapeutics is developing for the treatment of cardiorenal conditions affected by dysregulated aldosterone, including hypertension, CKD and OSA. Mineralys is based in Radnor, Pennsylvania, and was founded by Catalys Pacific. For more information, please visit https://mineralystx.com. Follow Mineralys on LinkedIn and Twitter.

Forward Looking Statements

Mineralys Therapeutics cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to, statements regarding: the potential therapeutic benefits of lorundrostat; the Company's expectation that Advance-HTN and Launch-HTN may serve as pivotal trials in any submission of a new drug application (NDA) to the United States Food and Drug Administration (FDA); the Company's ability to evaluate lorundrostat as a potential treatment

for CKD, OSA, uHTN or rHTN; and the planned future clinical development of lorundrostat and the timing thereof. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in our business, including, without limitation: topline results that we report are based on a preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such topline data may not accurately reflect the complete results of a clinical trial; our future performance is dependent entirely on the success of lorundrostat; potential delays in the commencement, enrollment and completion of clinical trials and nonclinical studies; later developments with the FDA may be inconsistent with the feedback from the completed end of Phase 2 meeting, including whether the proposed pivotal program will support registration of lorundrostat which is a review issue with the FDA upon submission of an NDA; the results of our clinical trials, including the Advance-HTN and Launch-HTN trials, may not be deemed sufficient by the FDA to serve as the basis for an NDA submission or regulatory approval of lorundrostat; our dependence on third parties in connection with manufacturing, research and clinical and nonclinical testing; unexpected adverse side effects or inadequate efficacy of lorundrostat that may limit its development, regulatory approval and/or commercialization; unfavorable results from clinical trials and nonclinical studies; results of prior clinical trials and studies of lorundrostat are not necessarily predictive of future results; regulatory developments in the United States and foreign countries; our reliance on our exclusive license with Mitsubishi Tanabe Pharma to provide us with intellectual property rights to develop and commercialize lorundrostat; and other risks described in our filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in our annual report on Form 10-K, and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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