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Mineralys Therapeutics Announces Publication of Pivotal Phase 2 Advance-HTN Results in the New England Journal of Medicine (NEJM)

– Significant blood pressure reductions among patients with uncontrolled or resistant hypertension treated with lorundrostat reinforce key role of dysregulated aldosterone in disease onset and progression –

– Detailed results from the second pivotal Phase 3 Launch-HTN trial to be presented at an upcoming medical conference and published in a peer-reviewed publication –

RADNOR, Pa., April 23, 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 that the *New England Journal of Medicine (NEJM)* published the detailed results from the Company's pivotal Phase 2 Advance-HTN trial, the first of two pivotal trials evaluating lorundrostat in patients with uncontrolled hypertension (uHTN) or resistant hypertension (rHTN). The full manuscript is titled, "Lorundrostat Efficacy and Safety in Patients with Uncontrolled Hypertension," and is featured in the April 23, 2025 issue of *NEJM*.

The key data from the publication showed that lorundrostat 50 mg demonstrated a 15.4 mmHg absolute reduction and a 7.9 mmHg placebo-adjusted reduction *(p=0.001),* in 24-hour ambulatory blood pressure at week 12. Lorundrostat worked equally well in those taking two baseline medications and those taking three or more, and in both men and women as well as in white and black patients. Lorundrostat demonstrated a favorable safety and tolerability profile, with modest changes in potassium, sodium and eGFR.

"The publication of our Advance-HTN trial results in the *New England Journal of Medicine* is a significant milestone that underscores both the strength of our clinical data and the potentially transformative nature of this new class of medicines that could help address dysregulated aldosterone, an unaddressed, key driver of hypertension," stated Jon Congleton, Chief Executive Officer of Mineralys Therapeutics. "Prior studies have shown that even modest reductions in systolic blood pressure can lead to a substantial decrease in the incidence of major cardiovascular events. The blood pressure reductions with lorundrostat observed in the Advance-HTN trial are particularly meaningful given the well-established correlation between elevated blood pressure, dysregulated aldosterone production and cardiovascular risk."

"The significant blood pressure lowering with lorundrostat 50 mg in the Advance-HTN trial was seen in patients treated by specialists who were taking an optimized standardized antihypertensive regimen – those patients with true uncontrolled or resistant hypertension

that desperately need new options to lower their blood pressure," 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. "Currently available therapies to treat hypertension do not decrease aldosterone production in the body, and we know aldosterone dysregulation is a driving factor in the blood pressure elevation of many of our patients. The findings reinforce the critical role of aldosterone in the pathogenesis of hypertension and the potential of lorundrostat to address unmet medical needs facing patients with uncontrolled or treatment-resistant disease."

The *NEJM* publication of the detailed Advance-HTN results follows a late-breaking presentation of the data at the American College of Cardiology's Annual Scientific Session & Expo (ACC.25) in Chicago on March 29, 2025, and the announcement of positive topline results from both Advance-HTN and Launch-HTN earlier in March.

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.

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 uHTN or rHTN, 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 uHTN or rHTN, when used as an add-on therapy to a standardized background treatment of two or three antihypertensive medications in adult subjects. Subjects who met screening criteria had their existing hypertension medications discontinued and started 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.

Contact:
Investor Relations
investorrelations@mineralystx.com

Media Relations
Tom Weible
Elixir Health Public Relations
Phone: (1) 515-707-9678
Email: tweible@elixirhealthpr.com

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