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Mineralys Therapeutics Announces JAMA Publication of Full Target-HTN Phase 2 Trial Results for Lorundrostat in Uncontrolled and Treatment-Resistant Hypertension

– Lorundrostat, a highly selective aldosterone synthase inhibitor, demonstrated robust, double-digit reduction in systolic blood pressure (BP) with a well-tolerated profile –

– Enhanced reduction in systolic BP seen in individuals with elevated body mass index (BMI) –

– Robust trial design and results led to lorundrostat being first of new class, aldosterone synthase inhibitors, to start pivotal clinical program in hypertension –

RADNOR, Pa., Sept. 10, 2023 (GLOBE NEWSWIRE) -- Mineralys Therapeutics, Inc. (Nasdaq: MLYS), a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, chronic kidney disease and other diseases driven by abnormally elevated aldosterone, today announced that full results from the Target-HTN Phase 2 trial of lorundrostat, a highly selective aldosterone synthase inhibitor, in individuals with uncontrolled hypertension (uHTN) and treatment-resistant hypertension (rHTN) were published in the *Journal of the American Medical Association (JAMA)*.

“Despite the multitude of currently available treatments, half of all patients treated for hypertension are not able to reach their blood pressure goal. Up to 25 percent of all people with hypertension exhibit abnormal aldosterone levels,” said Luke Laffin, M.D., lead investigator and co-director of the Center for Blood Pressure Disorders in the Heart, Vascular & Thoracic Institute at Cleveland Clinic. “Importantly, the Target-HTN study of lorundrostat demonstrated data compelling enough to warrant its advancement into late-stage clinical trials, representing a first-in-class milestone that will further the goal of understanding a new way of treating uncontrolled and treatment-resistant hypertension that takes the underlying causes into account.”

In the Target-HTN Phase 2 trial, lorundrostat demonstrated a significant, double-digit reduction in SBP with a well-tolerated profile in the intent-to-treat population of uHTN and rHTN. Subjects with an elevated BMI, and participants taking a thiazide-type diuretic, demonstrated an enhanced reduction in SBP.

The publication notes that blood pressure guidelines recommend similar medication combinations for most patients, regardless of underlying comorbidities or the dominant underlying contributor to hypertension, and that new treatments are needed as management of blood pressure in the U.S. is relatively poor, and hypertension remains a major cause of

excess morbidity and mortality.

“We are gratified that *JAMA* chose to highlight our Target-HTN Phase 2 trial results. These results demonstrated potentially transformative blood pressure reduction in difficult-to-treat hypertension, particularly so in obese individuals, who are known to have elevated aldosterone and suffer from excess cardiovascular morbidity and mortality,” stated David Rodman, M.D., Chief Medical Officer for Mineralys. "We believe this trial confirms the link between obesity, excess aldosterone production and hypertension. Based on the beneficial response observed in Target-HTN, our recently initiated pivotal program lays the groundwork to facilitate identification of patients who may benefit from an aldosterone-targeted therapy like lorundrostat.”

The trial results support further study of lorundrostat as a treatment for uHTN, including the Company’s ongoing pivotal development program for lorundrostat to treat uHTN and rHTN. Under this program, the Company is currently enrolling subjects in the pivotal Advance-HTN trial and expects to initiate the pivotal Launch-HTN trial in the second half of the year, with topline data expected in the first half of 2024 and mid-2025, respectively.

The Target-HTN (NCT05001945) Phase 2 proof-of-concept trial was a randomized, double-blind, placebo-controlled, dose-ranging, multicenter trial conducted in the U.S. The trial was designed to evaluate the safety, efficacy, tolerability and dose response of orally administered lorundrostat for the treatment of uHTN and rHTN when used as add-on therapy to stable background treatment of two or more antihypertensive agents in 200 male and female subjects 18 years of age or older. Five active doses of lorundrostat (12.5mg once daily QD, 50mg QD, 100mg QD, 12.5mg twice daily [BID], and 25mg BID) were compared to placebo in hypertensive subjects. Pharmacokinetic, pharmacodynamic and response data established that a once-daily dosing regimen was optimal. 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 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 $130 billion each year in the U.S., averaged over 12 years from 2003 to 2014.

Less than 50 percent of hypertension patients achieve their blood pressure goal with currently available medications. Abnormally elevated aldosterone levels are a key factor in driving hypertension in up to 25 percent of all hypertensive patients.

About Lorundrostat
Lorundrostat is a proprietary, orally administered, highly selective aldosterone synthase inhibitor being developed for the treatment of uncontrolled hypertension and chronic kidney disease (CKD). 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 percent reduction in plasma

aldosterone concentration in hypertensive subjects.

About Mineralys Therapeutics
Mineralys Therapeutics is a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, chronic kidney disease and other diseases driven by abnormally elevated aldosterone. Its initial product candidate, lorundrostat, is a proprietary, orally administered, highly selective aldosterone synthase inhibitor that Mineralys Therapeutics is developing for cardiorenal conditions affected by abnormally elevated aldosterone, including hypertension and CKD. 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 aldosterone synthase inhibitors with an SGLT2 inhibitor may provide additive clinical benefits to patients; the Company's expectation that the Advance-HTN and the planned Phase 3 clinical trial of lorundrostat 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; the planned future clinical development of lorundrostat and the timing thereof; and the expected timing of commencement and enrollment of patients in clinical trials and topline results from clinical trials. 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: 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; 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; our ability to maintain undisrupted business operations due to any pandemic or future public health concerns; 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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