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Mineralys Therapeutics Presents Target-HTN Phase 2 Trial Results in Late-Breaking Science Session at 2023 AHA Hypertension Scientific Sessions

– Lorundrostat, a highly selective aldosterone synthase inhibitor, demonstrated robust, double-digit reduction in systolic blood pressure (BP), including an enhanced response in individuals with elevated body mass index (BMI) –

– Results simultaneously published in the Journal of the American Medical Association (JAMA) –

– Pivotal clinical program for lorundrostat as a treatment of patients with uncontrolled and resistant hypertension ongoing, with topline data from Advance-HTN and Launch-HTN trials expected in first half of 2024 and mid-2025, respectively –

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 presented final results from the Target-HTN Phase 2 trial of lorundrostat, a highly selective aldosterone synthase inhibitor, in individuals with uncontrolled hypertension (uHTN) and resistant hypertension (rHTN). The data were presented during a late-breaking science session at the 2023 American Heart Association (AHA) Hypertension Scientific Sessions, which is being held in Boston from September 7–10, and simultaneously published in the *Journal of the American Medical Association (JAMA)*.

Target-HTN trial results demonstrate treatment with lorundrostat at doses of 50mg and 100mg once daily (QD) led to a statistically and clinically significant reduction of systolic blood pressure (BP) in inadequately controlled hypertensive individuals on at least two background antihypertensive medications. The reduction in BP was particularly evident among participants with hypertension and concomitant obesity.

“The final results from our Target-HTN trial demonstrate lorundrostat had a robust, double-digit reduction in systolic blood pressure with a well-tolerated profile in the intention-to-treat population of individuals with uncontrolled hypertension and resistant hypertension. In support of our targeted development strategy for lorundrostat, a pre-specified sub-analysis of subjects with elevated BMI demonstrated enhanced reduction in systolic blood pressure that is likely due, in part, to visceral fat driving abnormal aldosterone levels,” stated Jon Congleton, Chief Executive Officer of Mineralys Therapeutics. “Results from the Target-HTN trial were instrumental in our decision to advance the ongoing pivotal program and we look forward to announcing the results from our initial pivotal study expected in the first half of 2024.”

Key clinical data from Target-HTN suggest robust BP reductions in the treatment of patients with uHTN and rHTN:

- Target-HTN successfully met its primary endpoint, demonstrating a statistically significant change from baseline in systolic automated office BP (AOBP) with lorundrostat 50mg (n=28) and 100mg (n=25) QD doses versus placebo (n=29):
  - -13.7 mmHg systolic AOBP change at 50mg QD, or -9.6 mmHg placebo-adjusted change (p=0.01)
  - -11.9 mmHg systolic AOBP change at 100mg QD, or -7.8 mmHg placebo-adjusted change (p=0.04)
- Key secondary endpoint results demonstrated a change in diastolic AOBP of -7.1 mmHg with 50mg QD (or -5.5 mmHg placebo-adjusted change; p=0.02) and -5.8 mmHg with 100mg QD (or -4.1 mmHg placebo-adjusted change; p=0.09)
- Other secondary endpoints, including assessment of 24-hour average BP, supported the efficacy of the QD dosing regimen.
- A pre-specified analysis examined the impact of body mass index (BMI) on the degree of BP lowering with lorundrostat, testing the hypothesis that aldosterone-dependent hypertension may be more significant in obese individuals:
  - With 50mg QD, changes in systolic AOBP were 2.2 mmHg in subjects with a BMI 25-30 kg/m^2, versus -16.7 in subjects with a BMI ≥30 kg/m^2 (placebo-adjusted; p<0.01)
  - With 100mg QD, changes in systolic AOBP were -4.5 mmHg in subjects with a BMI 25-30 kg/m^2, versus -12.3 in subjects with a BMI ≥30 kg/m^2 (placebo-adjusted; p=0.03)

Key safety and tolerability findings from Target-HTN suggest lorundrostat was well-tolerated with a favorable safety profile, particularly with 50mg lorundrostat QD:

- Lorundrostat was well tolerated at all dose levels
- There was a modest, dose-dependent increase in mean serum potassium (0.25-0.29 mmol/L) and low incidence of elevated serum potassium (3.6% subjects with serum potassium levels above 6.0 mmol/L)
- Three serious adverse events occurred, only one (worsening of pre-existing hyponatremia with 100mg lorundrostat QD) was deemed treatment-related

Target-HTN trial results support the transition to late-stage development of lorundrostat as a treatment for inadequately controlled hypertension. The Company's ongoing pivotal development program for lorundrostat to treat uHTN and rHTN is currently enrolling subjects in the Advance-HTN trial, and the Phase 3 Launch-HTN trial is expected to be initiated in the second half of the year, with topline data expected in the first half of 2024 and mid-2025, respectively.

The presentation at the 2023 AHA Hypertension Scientific Sessions, titled, "Aldosterone Synthase Inhibition with Lorundrostat for Uncontrolled Hypertension: The Target-HTN Phase 2 Randomized Clinical Trial," can be accessed on the publications page of the Mineralys corporate website.

About Target-HTN
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 on BP for the treatment of uncontrolled and resistant hypertension 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 QD, 50mg QD, 100mg QD, 12.5mg twice daily [BID], and 25mg BID) were compared to placebo in hypertensive subjects. 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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