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Mineralys Therapeutics Presents New Post-Hoc Analysis from Target-HTN Phase 2 Trial of Lorundrostat in Late-Breaking Poster Session at ASN Kidney Week 2023 Meeting

– Analysis further supports obesity-associated dysregulated aldosterone as an endotype predictive of enhanced response to lorundrostat treatment in patients with uncontrolled or treatment-resistant hypertension –

–Endotype identification from Target-HTN may represent a shift towards targeted, precision-directed therapy for hypertension management in future treatment paradigm –

– Ongoing Advance-HTN trial, first of two pivotal studies, will further characterize hypertensive endotype for enhanced response to lorundrostat treatment –

RADNOR, Pa., Nov. 02, 2023 (GLOBE NEWSWIRE) -- Mineralys Therapeutics, Inc. (Nasdaq: MLYS), a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, chronic kidney disease (CKD) and other diseases driven by abnormally elevated aldosterone, today presented a new post-hoc analysis 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 the Late-Breaking Posters session at the American Society of Nephrology (ASN) Kidney Week 2023, which is being held in Philadelphia from November 2–5.

In this new analysis, investigators identified a population of responders to lorundrostat who experienced a median reduction in systolic blood pressure (BP) of 32 millimeters of mercury (mmHg). The enhanced response was proportional to the elevation in body mass index (BMI) and may indicate an obesity-related, aldosterone-dependent hypertensive endotype.

“We were able to show in this post-hoc analysis additional evidence corroborating the association between BMI and blood pressure reduction with lorundrostat. Individuals trying to manage obesity and hypertension in tandem are at an increased risk for poor outcomes, and a treatment that can provide an enhanced response to this population holds great promise,” stated David Rodman, M.D., Chief Medical Officer for Mineralys. “We continue to believe that we’re entering a precision-medicine era when it comes to hypertension treatments – an era in which physicians can identify and confidently prescribe an anti-hypertensive treatment for each patient according to their underlying biological factors, such as obese individuals with aldosterone-dependent hypertension.”

Consistent with the pre-specified categorical analysis from Target-HTN that demonstrated an

enhanced treatment response in individuals with an elevated BMI, a post-hoc linear regression analysis demonstrated a statistically significant association between BMI and reduction in systolic BP in subjects with a BMI ranging from 22.5 to 40kg/m^2. The modeled reduction in observed systolic BP was approximately 12mmHg at a BMI of 30kg/m^2, and 19mmHg at a BMI of 40kg/m^2. The distribution of responses was substantially left-skewed, with the upper quartile of subjects having a median reduction in systolic BP of approximately 32mmHg.

The Target-HTN trial demonstrated that treatment with lorundrostat at doses of 50mg and 100mg once daily (QD) led to a statistically and clinically significant reduction of systolic BP in uncontrolled hypertensive individuals on at least two background antihypertensive medications. Full results from the trial were published in the *Journal of the American Medical Association (JAMA)* and simultaneously presented during a late-breaking science session at the 2023 American Heart Association (AHA) Hypertension Scientific Sessions in September.

Target-HTN trial results support the transition to late-stage development of lorundrostat as a treatment for uncontrolled and resistant 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 before the end of the year.

The late-breaking poster at ASN Kidney Week 2023, titled, "Identification of a Hypertensive Endotype with a Median Treatment Effect of -32 mmHg in Response to the Novel Aldosterone Synthase Inhibitor Lorundrostat," 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 approximately 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 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% 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, CKD 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 or uncontrolled hypertension; 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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