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# Mineralys Therapeutics Announces Positive Topline Results from Phase 2 Explore-CKD Trial of Lorundrostat for the Treatment of Hypertension in Subjects with CKD and Albuminuria

*– Explore-CKD met its primary endpoint; lorundrostat 25 mg once daily achieved a 9.3 mmHg reduction in systolic blood pressure, and a 7.5 mmHg placebo-adjusted reduction (p=0.0024) at four weeks –*

*– Lorundrostat showed a clinically meaningful reduction in the pre-defined endpoint spot urine albumin-to-creatinine ratio of 31% (p<0.0001) –*

*– Lorundrostat demonstrated a favorable safety and tolerability profile –*

*– Conference call today at 8:00 a.m. ET –*

RADNOR, Pa., June 17, 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 cardiovascular diseases driven by dysregulated aldosterone, today announced positive topline data from its Phase 2 Explore-CKD trial evaluating the safety and efficacy of 25 mg of lorundrostat in subjects with hypertension and comorbid CKD. The crossover trial met the primary endpoint and demonstrated clinically meaningful reductions in both systolic automated office blood pressure (AOBP) and urine albumin-to-creatinine ratio (UACR), and demonstrated a favorable safety and tolerability profile.

“The Explore-CKD trial is the fourth trial showing clinically meaningful effects of lorundrostat for the treatment of hypertension. In a renally compromised hypertensive population, this trial demonstrated the benefit of lorundrostat in safely reducing both systolic blood pressure and proteinuria – a surrogate of kidney protection,” said Jon Congleton, Chief Executive Officer of Mineralys. “Explore-CKD established that lorundrostat 25 mg once daily has a favorable clinical profile for this patient population. Along with the successful pivotal trials, Launch-HTN and Advance-HTN, and the ongoing open-label extension trial, these results comprise the core package for our planned NDA submission.”

**Efficacy, Safety and Tolerability Results**

The Explore-CKD trial was a randomized, double-blind, placebo controlled, crossover trial. This phase 2 trial was designed to evaluate efficacy in terms of systolic blood pressure (BP) and UACR reduction, and safety of four-week 25 mg once daily (QD) lorundrostat added to a background treatment that included a sodium-glucose cotransporter 2 (SGLT2) inhibitor and

an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB) in CKD subjects with an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73m$^2$ and albuminuria (UACR of 200-5,000 mg/g). The trial was highly statistically significant and was clinically meaningful in both of these endpoints and demonstrated a favorable safety and tolerability profile.

**Explore-CKD Phase 2 Trial (N=59)**

| | Placebo | Lorundrostat 25 mg | Placebo-adjusted |
|---|---|---|---|
| Change in systolic BP (mmHg)* | -1.76 | -9.25 | -7.5 (p=0.0024) |
| Change in spot UACR (mg/g) | -6.60% | -30.51% | -25.60% (p=0.0015) |
| Change in eGFR** (mL/min/1.73m2) | -2.20% | -6.78% | -4.58% (p=0.0362) |
| Treatment Emergent Adverse Events (TEAEs) leading to discontinuation of study drug | 1/57 (2%) | 2/58 (3%) | |
| Confirmed hyperkalemia*** (K+ >6.0 mmol/L) | 0/59 (0%) | 3/58 (5%) | |

BP, blood pressure; UACR, Urine albumin-to-creatinine ratio; TEAE, Treatment-emergent adverse event

** Primary endpoint.*

*** Cystatin-C formula, a surrogate biomarker of renal function not subject to MATE1 transport and elimination in the glomeruli of the kidney.*

**** Per protocol Systolic BP, UACR, and eGFR estimates and p values from Mixed Effects Model for a crossover trial with multiple baselines.*

Serious Adverse Events were reported in two subjects (3%) during the lorundrostat treatment period and none during the placebo treatment period. TEAEs leading to discontinuation occurred in one subject (2%) during the placebo treatment period and in two subjects (3%) during the lorundrostat treatment period.

During lorundrostat treatment, one subject discontinued treatment due to elevation of potassium associated with reduced eGFR and one subject discontinued treatment due to reduction in eGFR alone. During the lorundrostat treatment period, an anticipated, modest decrease in mean eGFR was observed (-6.8% lorundrostat, -4.6% mL/min/1.73m$^2$ placebo-adjusted). Reduction in eGFR is also seen with other renin-angiotensin-aldosterone pathway inhibitors, including ACE inhibitors, ARBs and mineralocorticoid receptor antagonists (MRAs). This is the result of a reduction in the deleterious over-perfusion of glomeruli due, in part, to reduced blood pressure.

These findings add to a growing body of evidence supporting the efficacy and safety of aldosterone synthase inhibitors (ASIs) in addressing the underlying mechanisms of hypertension, including in individuals with comorbid CKD. The reduction in UACR observed in this trial is consistent with the potential of lorundrostat to have renal protective effects.

“Prolonged elevations in blood pressure in patients with compromised renal function can damage the small blood vessels in the kidneys, further reducing their ability to function properly,” said Dr. Matthew Weir, Director of the Division of Nephrology at the University of Maryland Medical Center and Professor of Medicine at the University of Maryland School of Medicine. “The evidence generated from this trial demonstrates the unique mechanism of action and benefit of lorundrostat in lowering systolic blood pressure and UACR. Lorundrostat shows significant potential in the management of hypertension and related

kidney disease."

The Explore-CKD trial was designed to provide data that augments the antihypertensive profile of lorundrostat by evaluating the efficacy and safety of lorundrostat in subjects with compromised renal function. The Company had already completed three trials of lorundrostat for the treatment of subjects with uncontrolled hypertension (uHTN), including resistant hypertension (rHTN); the pivotal Phase 3 Launch-HTN and Phase 2 Advance-HTN trials, and the Phase 2, dose-ranging, Target-HTN trial, which demonstrated clinically meaningful reductions in systolic BP and a favorable safety and tolerability profile. The Company continues to study lorundrostat in the ongoing, open-label Transform-HTN extension trial, which is evaluating long-term efficacy, safety, and tolerability. Additionally, the Explore-OSA trial, initiated in the first quarter of 2025, continues to enroll subjects with OSA and uncontrolled hypertension.

**Conference Call**

The Company's management team will host a conference call today, June 17, 2025, at 8:00 a.m. ET. To access the call, please dial 1-877-704-4453 in the United States or 1-201-389-0920 outside the United States. 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 Explore-CKD**

The Explore-CKD trial (NCT06150924) was a randomized, double-blind, placebo-controlled, two-period, two-sequence (2x2) crossover trial. This Phase 2 trial was designed to evaluate BP reduction and safety of 25 mg QD lorundrostat when added to background treatment with an ACEi or ARB and an SGLT2 inhibitor for the treatment of hypertension in subjects with CKD subjects with an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73m2 and albuminuria (UACR of 200-5,000 mg/g). The primary efficacy endpoint of the trial was change from baseline in systolic BP at week four in the active versus placebo treatment period. Exploratory endpoints included change from baseline in UACR and eGFR at week four in the active versus placebo treatment period.

**About CKD**

CKD, which is characterized by the gradual loss of kidney function, is estimated to affect more than 10% of the global population and is one of the leading causes of mortality worldwide. According to the U.S. Centers for Disease Control and Prevention (CDC), an estimated 1-in-7 (approximately 37 million) U.S. adults have CKD, and approximately 22 million people in the United States are living with both hypertension and CKD.[1] The relationship between these conditions is tightly linked: sustained hypertension may contribute to impaired kidney function, and progressive decrease in kidney function may lead to worsening BP control. [2] When CKD is present in patients with hypertension, the risk of cardiovascular disease and mortality rises significantly.[3]

Emerging evidence points to dysregulated aldosterone as a key driver of both diseases. Excess aldosterone promotes sodium retention, vascular inflammation, and fibrosis, contributing to both uncontrolled BP and kidney injury. [4,5] Despite the availability of existing

therapies, a significant proportion of patients remain uncontrolled or undertreated.[6] Early detection and targeted interventions that address underlying mechanisms, such as aldosterone dysregulation, may offer the potential to slow CKD progression, reduce cardiovascular risk, and improve long-term outcomes.[4] Without effective management, CKD can advance to kidney failure, requiring dialysis or transplantation.[7]

**About Hypertension**

Having sustained, elevated BP (or hypertension) increases the risk of heart disease, heart attack and stroke, which are leading causes of death in the United States.[8] In 2022, more than 685,000 deaths in the United States included hypertension as a primary or contributing cause. [9] Hypertension and related health issues resulted in an estimated annual economic burden of about $219 billion in the United States in 2019.[10]

Less than 50% of hypertension patients achieve their BP goal with currently available medications.[6] Dysregulated aldosterone levels are a key factor in driving hypertension in approximately 30% of all hypertensive patients.[11]

**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 a 40-70% reduction in plasma aldosterone concentration in hypertensive subjects.

The Company has now completed four successful clinical trials of lorundrostat supporting the efficacy and safety profile while also validating aldosterone as an integral therapeutic target in uHTN and rHTN. The Company has completed two pivotal, registrational trials, including the Phase 3 Launch-HTN trial and Phase 2 Advance-HTN trial, which support the robust, durable and clinically meaningful reductions in systolic BP by lorundrostat. Lorundrostat was well tolerated in both trials with a favorable safety profile.

**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, Twitter and Bluesky.

**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 ASIs with an SGLT2 inhibitor may provide additive clinical benefits to patients; the Company's expectation that Advance-HTN, Launch-HTN and Explore-CKD may serve as pivotal trials in submission of a new drug application (NDA) to the U.S. Food and Drug Administration (FDA); the Company's ability to evaluate lorundrostat as a potential treatment for CKD, OSA, uHTN or rHTN; the planned future clinical development of lorundrostat and the timing thereof; and the expected timing of commencement and enrollment of participants 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: 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; macroeconomic trends and uncertainty with regard to high interest rates, elevated inflation, tariffs, and the potential for a local and/or global economic recession; 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.

**References**

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