November 16, 2022

Mineralys Therapeutics Announces Positive Topline Phase 2 Data for MLS-101 in the Target-HTN Trial Evaluating the Treatment of Uncontrolled and Resistant Hypertension

Successfully Met Primary and Secondary Endpoints, with Mean Placebo-Adjusted Reduction in Systolic Blood Pressure of 9.7 mmHg in Uncontrolled and Resistant Hypertensive Subjects at 50 mg Once Daily (p=0.01 vs. placebo)

Subjects Using a Thiazide Diuretic (Approximately Half of the Study Population) Showed a Mean Placebo-Adjusted Reduction in Systolic Blood Pressure of 13.2 mmHg at 50 mg Once Daily (p=0.01 vs. placebo)

Well Tolerated with No Notable Effect on Serum Cortisol, and Modest Increase and Rapid Reversibility of Serum Potassium

PHILADELPHIA, Nov. 16, 2022 /PRNewswire/ -- Mineralys Therapeutics, Inc., a private, clinical-stage biopharmaceutical company committed to developing a novel therapy for the treatment of hypertension and associated cardiovascular diseases, today announced topline results from the Phase 2 Target-HTN trial in individuals with uncontrolled and resistant hypertension. MLS-101, a highly selective investigational aldosterone synthase inhibitor, at doses of 50 mg and 100 mg once daily (QD), met its primary endpoint with statistically significant and clinically meaningful reduction in systolic blood pressure (SBP) in inadequately controlled hypertensive patients on at least two background antihypertensive medications. Robust placebo-adjusted reductions in SBP and diastolic blood pressure (DBP) were observed in the office as well as with 24-hour ambulatory blood pressure monitoring (ABPM) of 24-hour average, night-time, and central blood pressure.

"We are very pleased to report that the Target-HTN trial met its primary and secondary endpoints, with MLS-101 demonstrating substantial placebo-adjusted reduction in blood pressure for 24 hours with once-daily, morning dosing," said Jon Congleton, Chief Executive Officer of Mineralys. "These data reinforce our belief that MLS-101 has the potential to transform the treatment of uncontrolled hypertension, impacting over 30 million individuals in the U.S. alone, by targeting a principal underlying cause, aldosterone. We would like to

thank the 200 patients whose participation and commitment to this study was invaluable."

Key clinical data from Target-HTN demonstrated clinically meaningful efficacy in the treatment of patients with uncontrolled and resistant hypertension.

Target-HTN successfully met its primary endpoints, demonstrating statistically significant mean change from baseline in seated automated office SBP versus placebo in the full intent-to-treat analysis. A prespecified sub-analysis demonstrated that blood pressure reduction by MLS-101 was further enhanced in subjects whose background antihypertensive regimen included a thiazide diuretic:

- Placebo-adjusted reduction in SBP of 1.4 mmHg (12.5 mg QD, p=NS), 9.7 mmHg (50 mg QD, p=0.010) and 7.9 mmHg (Part 1, 100 mg QD, p=0.037)
- Thiazide diuretic as part of background medications placebo-adjusted reduction in SBP of 5.3 mmHg (12.5 mg QD, p=NS), 13.2 mmHg (50 mg QD, p=0.010) and 11.4 mmHg (Part 1, 100 mg QD, p=0.028)

Secondary endpoint results, such as DBP and 24-hour ABPM of 24-hour average, night-time, and central blood pressure, were supportive of the primary findings, and will be featured in a future medical publication and medical conference presentation.

"In Target-HTN there was a progressive increase in clinical response as dose and exposure increased with MLS-101 in inadequately controlled or treatment resistant hypertension patients. The blood pressure reduction was substantial and further augmented in individuals using a thiazide diuretic," said David Rodman, M.D., Chief Medical Officer of Mineralys. "In addition to securing proof-of-concept for MLS-101, clinically meaningful benefit was seen with all doses greater than 12.5 mg per day with maximum reduction in automated office-measured blood pressure seen with 50 mg once daily dose of MLS-101. We look forward to sharing additional data on 24-hour ambulatory assessment of nighttime and central blood pressure in the future."

Key clinical safety and tolerability findings from Target-HTN of MLS-101 support a safe and well-tolerated profile.

- The data from the Target-HTN trial demonstrated no notable effects on serum cortisol, supporting the selectivity of MLS-101 for aldosterone synthesis.
- Treatment-emergent, serious adverse events were reported in three subjects. Two subjects were deemed unrelated to study drug treatment, and one was deemed to be related to MLS-101 in a subject with worsening of pre-existing hyponatremia that reversed after discontinuation of MLS-101.
- There was an anticipated, modest increase in serum potassium in the two active QD dose cohorts: 0.25 mmol/L in the 50 mg cohort, and 0.35 mmol/L in the 100 mg cohort. Six individuals across the five active dose cohorts experienced an instance of elevated potassium above 6 mmol/L. Per-protocol, study drug administration was reduced, temporarily held or discontinued and consistent with the short half-life of MLS-101; all episodes were rapidly reversible.
- An Independent Data Safety Monitoring Board expressed no concerns about the effect of MLS-101 on serum potassium in the Target-HTN trial.

"Millions of Americans suffer from the complications and shortened lifespan resulting from

inadequately treated hypertension. The MLS-101 Phase 2 data support the potential of aldosterone synthase inhibition, an important strategy for blood pressure control," 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. "MLS-101 has the potential to deliver a differentiated efficacy, safety and tolerability profile compared to mineralocorticoid receptor antagonists, the only other class of antihypertensive to directly target aldosterone biology."

Target-HTN (NCT05001945) was a Phase 2 randomized, double-blind, placebo-controlled, dose-ranging, multicenter trial conducted in the U.S. The trial was designed to evaluate the safety, efficacy, and tolerability of orally administered MLS-101 on blood pressure 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 MLS-101 (12.5 mg QD, 50 mg QD, 100 mg QD, 12.5 mg twice daily [BID], and 25 mg BID) were compared to placebo in hypertensive subjects.

About Hypertension

Having high 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. High blood pressure and related health issues resulted in an average annual economic burden of about $131 billion each year in the U.S., averaged over 12 years from 2003 to 2014.

Less than 50 percent of hypertension patients achieve control of their blood pressure with currently available medications. Hypertension can be attributed to obesity in 78 percent of men and 65 percent of women, and autonomous aldosterone overproduction (hyperaldosteronism) is an underlying driver of hypertension in approximately 25 percent of all hypertension patients. Over the last 50 years, increased prevalence of obesity (rather than aging of the population) tracks with increased prevalence of hyperaldosteronism.

About MLS-101

MLS-101 is a proprietary, orally administered, highly selective aldosterone synthase inhibitor, licensed from Mitsubishi Tanabe Pharma Corporation, that is being developed for the treatment of hypertension. MLS-101 is designed to reduce aldosterone levels by inhibiting CYP11B2, the enzyme responsible for producing the hormone, without the untoward effects of blocking the mineralocorticoid receptor. MLS-101 has demonstrated high selectivity (374:1 for CYP11B2:CYP11B1) for the synthesis of aldosterone without affecting cortisol with an observed half-life of 10-12 hours. MLS-101's observed selectivity supports the potential for treatment of blood pressure in hypertensive patients with abnormally elevated aldosterone production, an underlying cause of hypertension prevalent in approximately 25 percent of all hypertensive patients.

About Mineralys Therapeutics, Inc.

Headquartered in Radnor, PA, Mineralys Therapeutics, Inc. is a clinical-stage biopharmaceutical company, founded by Catalys Pacific, and focused on developing

medicines to target disease, driven by abnormally elevated aldosterone. The Company is driven to bring a targeted approach to the management of hypertension via the development of MLS-101. MLS-101, licensed from Mitsubishi Tanabe Pharma Corporation, is a highly selective aldosterone synthase inhibitor that is being investigated for the treatment of hypertension. Mineralys is funded by a global group of investors which include Catalys Pacific, Samsara BioCapital, HBM Healthcare Investments, RA Capital Management, Andera Partners, Adams Street Partners, RTW Investments, Rock Springs Capital, SR One Capital Management, Sectoral Asset Management, Ysios Capital, HealthCor Management and Boulder Ventures. For more information, please visit https://mineralystx.com/.

###

Contact:
Melyssa Weible
Elixir Health Public Relations
Phone: (1) 201-723-5805
Email: mweible@elixirhealthpr.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/mineralys-therapeutics-announces-positive-topline-phase-2-data-for-mls-101-in-the-target-htn-trial-evaluating-the-treatment-of-uncontrolled-and-resistant-hypertension-301679522.html

SOURCE Mineralys Therapeutics