

Targeting Aldosterone in the Treatment of Cardiorenal Diseases

Explore-CKD Phase 2 Trial Topline Data
June 17, 2025

Forward-Looking Statements and Market Data

Mineralys Therapeutics cautions you that statements contained in this presentation 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 and market opportunity for lorundrostat; the Company's expectation that aldosterone synthase inhibitors with a sodium-glucose cotransporter 2 inhibitor may provide additive clinical benefits to patients; the Company's expectation that Advance-HTN and Launch-HTN 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 chronic kidney disease, uncontrolled hypertension, resistant hypertension or obstructive sleep apnea in patients with hypertension; 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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.



Agenda

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Introduction

Jon Congleton, CEO of Mineralys Therapeutics

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Explore-CKD Data

Dr. David Rodman, M.D., CMO of Mineralys Therapeutics

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Hypertension in CKD and Emerging Treatments

**Dr. Matthew Weir, Div. Head of Nephrology
Univ. of Maryland School of Medicine**

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Conclusion

Jon Congleton

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Positive Topline Results from Explore-CKD

- Explore-CKD is the **FOURTH positive clinical trial** of lorundrostat completed in uHTN or rHTN
- 25mg lorundrostat **demonstrated a meaningful BP benefit** assessed by automated office BP at end of treatment, week 4
- **Reduction in UACR comparable** to recent trials of ASIs and MRAs when added to an SGLT2 inhibitor
- **No new safety signals observed** and the rate of hyperkalemia similar to other ASIs when added to an SGLT2 inhibitor and ACE inhibitor or ARB background treatment
- **Demonstrated the potential for aldosterone synthase inhibition** in cardiorenal disorders and the benefit of targeting it therapeutically

Lorundrostat Development Program with Positive Pivotal Data and Market Expansion Proof-of-Concept Trials

TRIAL		SAFETY	PROOF OF CONCEPT	PIVOTAL	KEY MILESTONES
Hypertension COMPLETED		uHTN & rHTN Standardized background AHT			-15.4 mmHg absolute change in SBP at Week 12
Hypertension COMPLETED		uHTN & rHTN Existing background AHT			-19.0 mmHg absolute change in SBP at Week 12
Hypertension and Chronic Kidney Disease (CKD)		CKD + HTN PoC & Profiling			-9.3 mmHg absolute change in SBP at Week 4 -31% spot UACR at Week 4
Hypertension and Obstructive Sleep Apnea (OSA)		OSA + HTN PoC & Profiling			Initiated 1Q 2025
Open-Label Extension		uHTN & rHTN			

CKD Proof-of-Concept and Profiling Trial

Proof-of-Concept in hypertensive nephropathy aimed to demonstrate benefit on blood pressure and kidney function

2 WEEK RUN-IN		4 WEEKS		4 WEEKS		4 WEEKS	
Background regimen including SGLT2 inhibitor and ACE inhibitor or ARB							
Initiate SGLT2 inhibitor in naïve participants	LORUNDROSTAT 25MG		WASHOUT		PLACEBO QD		Open-Label Extension on Lorundrostat
	PLACEBO QD		WASHOUT		LORUNDROSTAT 25MG		
INCLUSION CRITERIA - Existing or naïve to SGLT2 inhibitor treatment - AOBP SBP ≥135 on an ACE inhibitor or an ARB - eGFR ≥ 30 mL/min/1.73m² - Serum K+ ≤5.0		PRIMARY EFFICACY ENDPOINT Placebo-adjusted change in AOBP SBP at Week 4		EXPLORATORY ENDPOINTS - Placebo-adjusted change in UACR at Week 4 - Placebo-adjusted change in eGFR at Week 4		SAFETY AND PK	

Baseline Demographics



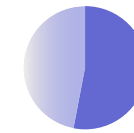
65

Years (mean age)



69%

Male



66%

White

17%

Black or African
American



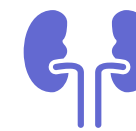
76%

Diabetes



33 kg/m²

Mean BMI



54.6 ml/min/1.73m²

Mean eGFR (Creatinine)



516 mg/g

Geometric Mean Spot
Urine UACR



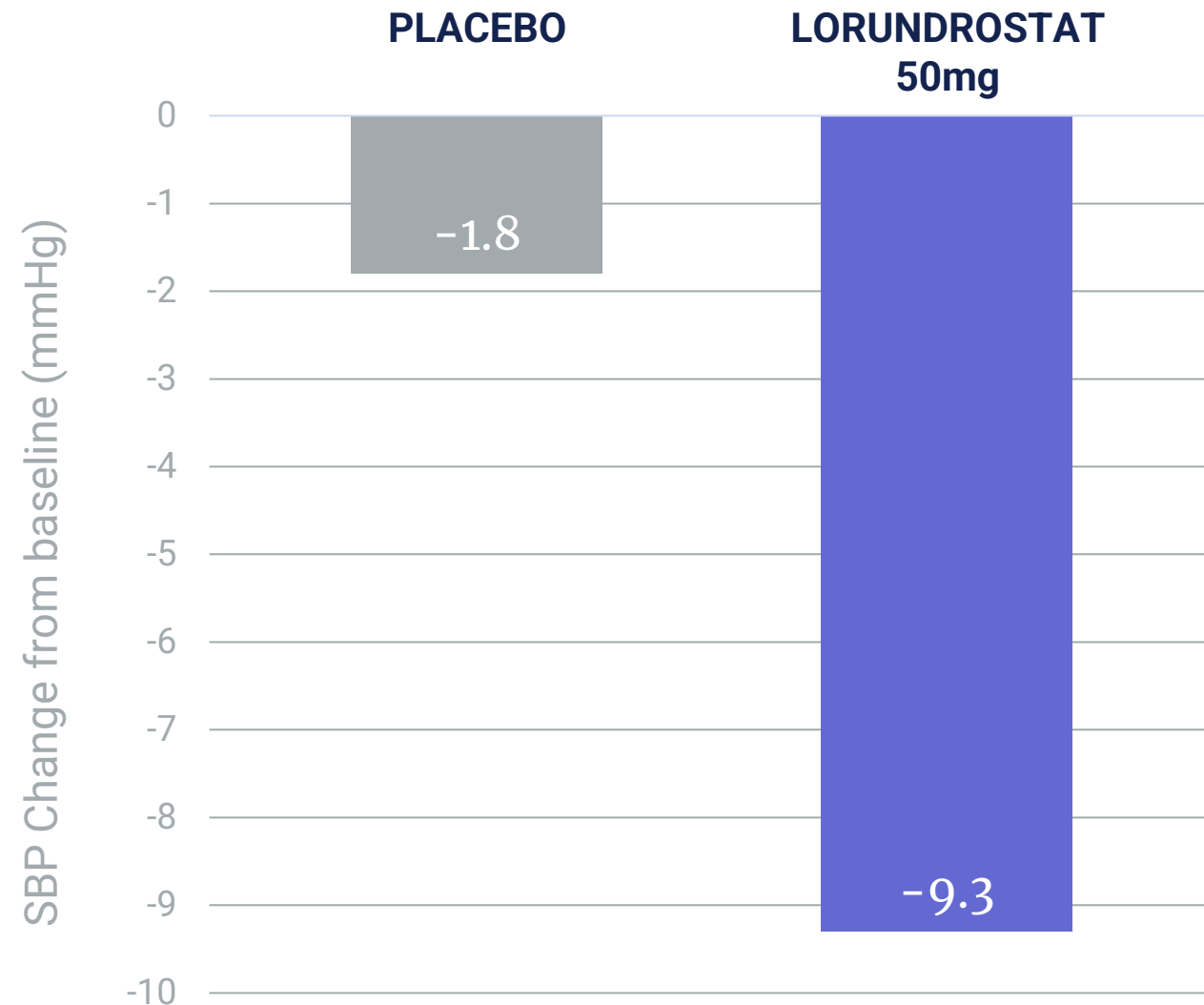
149 mmHg

Mean Systolic AOBP

Explore-CKD Efficacy

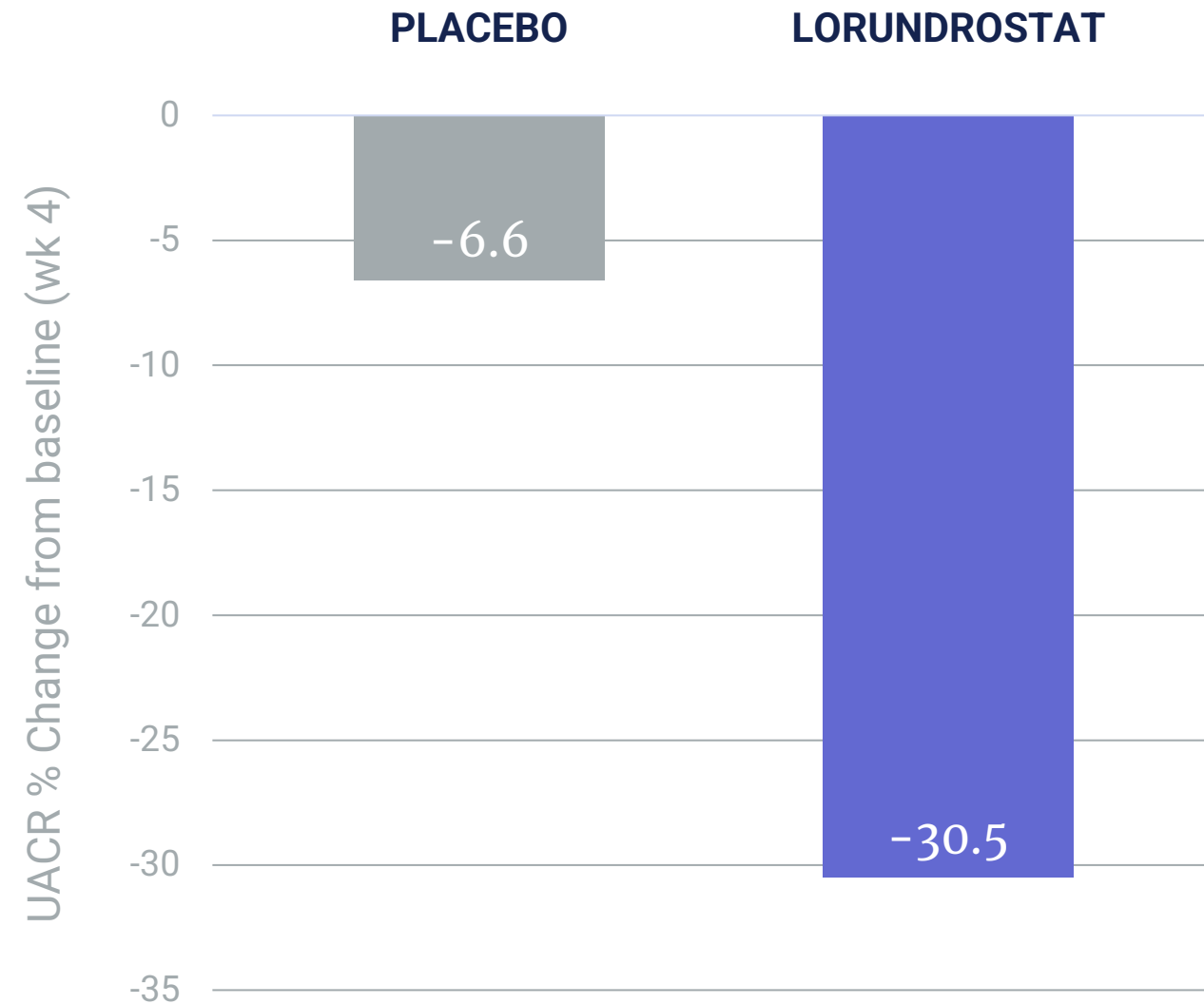
Clinically Meaningful Systolic BP Reduction at 4 Weeks with 25mg QD

- SysBP measured in office (AOBP)
- Absolute reduction in systolic BP of 9.3 mmHg
- Placebo-adjusted change in systolic BP -7.5 mmHg (90%, C.I. -11.6, -3.4, $p=0.002$)



Reduction in Proteinuria Demonstrated with Lorundrostat is a Surrogate for Renal Protection

- 31% reduction in spot UACR (p < 0.0001)



Explore-CKD Safety

Modest change in potassium in renally impaired population

- Mean change in potassium of 0.5 mmol/L in lorundrostat treatment periods
- One subject with potassium >6.5 mmol/L and low eGFR discontinued (1.7%)

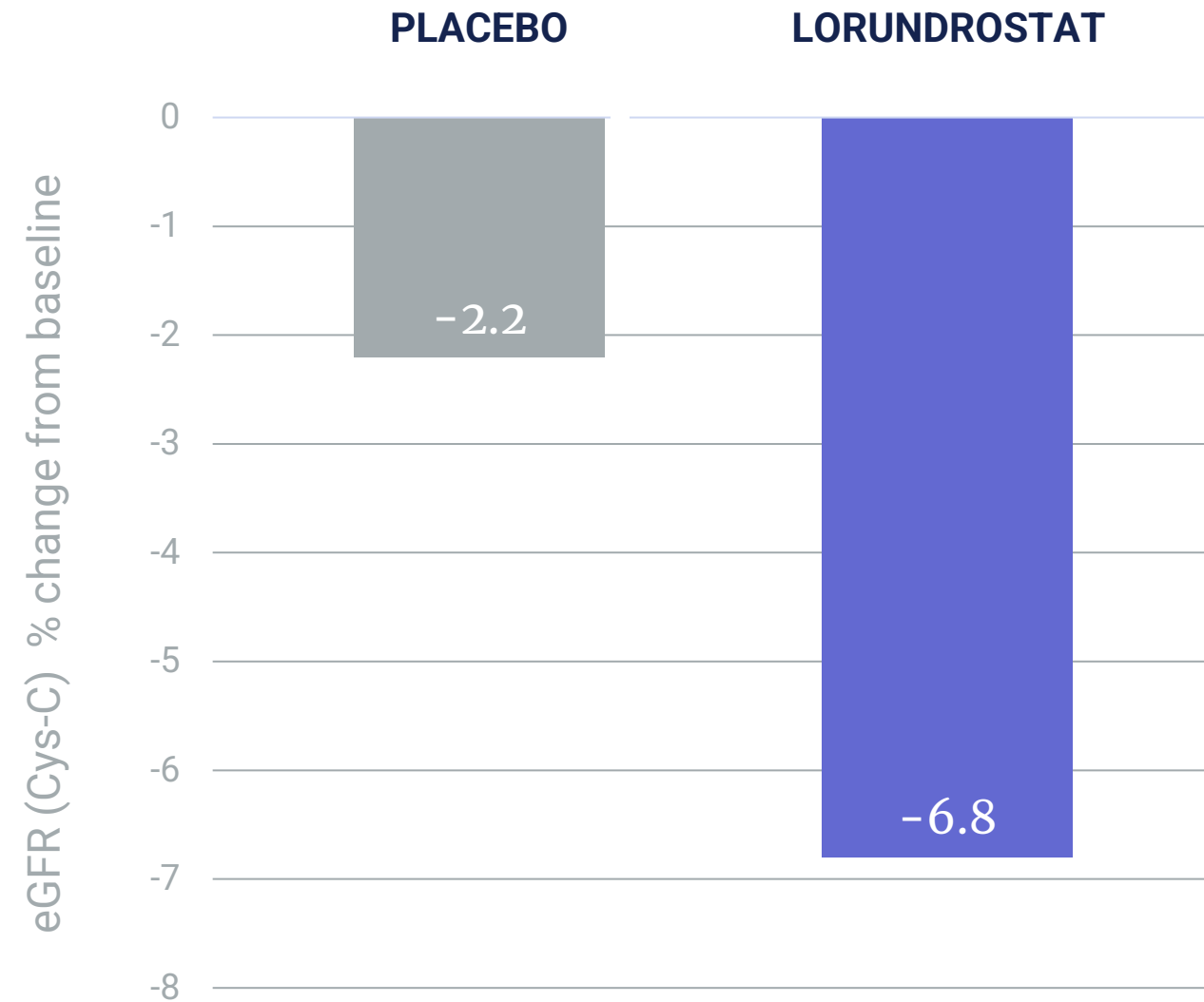
Confirmed Hyperkalemia

SERUM POTASSIUM (mmol/L)	PLACEBO (N=59)	25 mg QD* (N=58)
≤5.5	58 (98.3)	51 (87.9)
>5.5	1 (1.7)	7 (12.1)
>6.0	0 (0.0)	3 (5.2)
>6.5	0 (0.0)	1 (1.7)

*10 cases of observed elevated K+, upon retest 3 /10 deemed factitious

Modest change in mean eGFR (Cys-C) consistent with that observed in the Launch-HTN trial

- One subject with low eGFR discontinued (1.7%)



Low incidence of Adverse Event of Special Interest and SAEs

SAEs:

- 2 (3%) subjects during lorundrostat treatment period
- 0 subjects during placebo treatment

* 2 (3.4%) potassium 5.1 to 5.5mmol/L, 3 (5.2%) potassium > 6.0mmol/L

** Attribution by investigator based on eGFR (Creatinine) which overestimated the reduction in kidney function based on MATE1 effect on increasing serum creatinine

Adverse Events of Special Interest

	PLACEBO (N=57)			LORUNDROSTAT 25 mg QD (N=58)		
	%	N	Events	%	N	Events
Hyperkalemia	0	0	0	8.6	5*	5
Hyponatremia	1.8	1	1	1.7	1	1
Severely elevated BP	0	0	0	1.7	1	1
Reduction in kidney function	0	0	0	10.3	6**	6
Hypercortisolism	0	0	0	0	0	0
Hypocortisolism	0	0	0	0	0	0



- Meaningful absolute reduction in systolic BP of 9.3 mmHg and placebo adjusted of 7.5 mmHg at week 4 with 25mg dosed once daily
- Meaningful reduction in UACR of 31% a key surrogate of kidney protection
- Manageable safety with only two subjects discontinuing lorundrostat treatment
- Well-tolerated profile

Matthew R. Weir, M.D.

Professor of Nephrology

University of Maryland School of Medicine



- Matthew R. Weir, M.D. is attending physician and Director of the Division of Nephrology in the Department of Medicine at the University of Maryland Hospital and Professor of Medicine at the University of Maryland School of Medicine.
- Dr. Weir's primary research interests include the use of antihypertensive therapy for the treatment of diabetic nephropathy, hypertensive renal injury in African Americans, cardiovascular disease in patients with chronic kidney disease, and mineralocorticoid receptor antagonism to treat atherosclerosis.
- He has written more than 600 manuscripts and book chapters about these topics. He has edited 8 books on topics in nephrology, transplantation, and hypertension. He has presented at numerous international scientific association meetings, hospitals, and medical schools.
- Professional Memberships:
 - American Society of Nephrology
 - National Kidney Foundation
 - American Heart Association
 - American Society of Transplantation.
- Scientific Advisor for: AstraZeneca, Bayer, CSL Vifor, Corcept, Novo Nordisk, Mineralys, Vera
- Dr. Weir serves as an expert, outside consultant and was not an investigator in the Explore-CKD trial

Lorundrostat Data Demonstrate a Consistent, Clinically Meaningful Profile with the Potential to Benefit a Spectrum of Hypertension Patients

Lorundrostat Clinical Program			
	 LAUNCH-HTN	 ADVANCE-HTN	 EXPLORE-CKD
Intent of Trial	Real world	Specialist	Compromised Kidney Function
Size of the trial	1,083	285	60
Duration of Trial	12 wks PBO controlled	12 wks PBO controlled	4 wk treatment, 3 period crossover
SysBP Absolute Reduction (SysBP PBO-Adjusted)	19mmHg (12 wk) (11.7 mmHg)	15.4mmHg (12 wk) (7.9 mmHg)	9.3mmHg (4 wk) (7.5 mmHg)
Reduction in Spot UACR	n/a	n/a	31%
Hyperkalemia > 6.0	0.6%	2.1%	5.2%



Q&A



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