MINERALYS

Targeting Aldosterone in the Treatment of Cardiorenal Diseases

November 2024

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 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 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 or resistant 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.

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.

Mineralys: Targeting Aldosterone in the Treatment of Hypertension, CKD and Beyond

Lorundrostat is a selective aldosterone synthase inhibitor (ASI) targeting aldosterone

- Obesity epidemic is driving abnormally elevated aldosterone contributing to hypertension, chronic kidney disease (CKD) and heart failure
- Lorundrostat is a highly selective ASI that reduces aldosterone ~70% with once-daily dosing
- Proof-of-Concept trial demonstrated substantial overall BP reduction with once-daily dosing; enhanced response in obese subjects; well-tolerated with modest increase in potassium
- Pivotal HTN program initiated in 2023 with first pivotal trial readout in March of 2025 and the second trial readout in mid first half 2025
- Proof-of-Concept CKD trial initiated 2H 2023 with readout in 2Q 2025 creating a pipeline of disease opportunities

Unmet Need in Both Hypertension and CKD Addressable by Lorundrostat

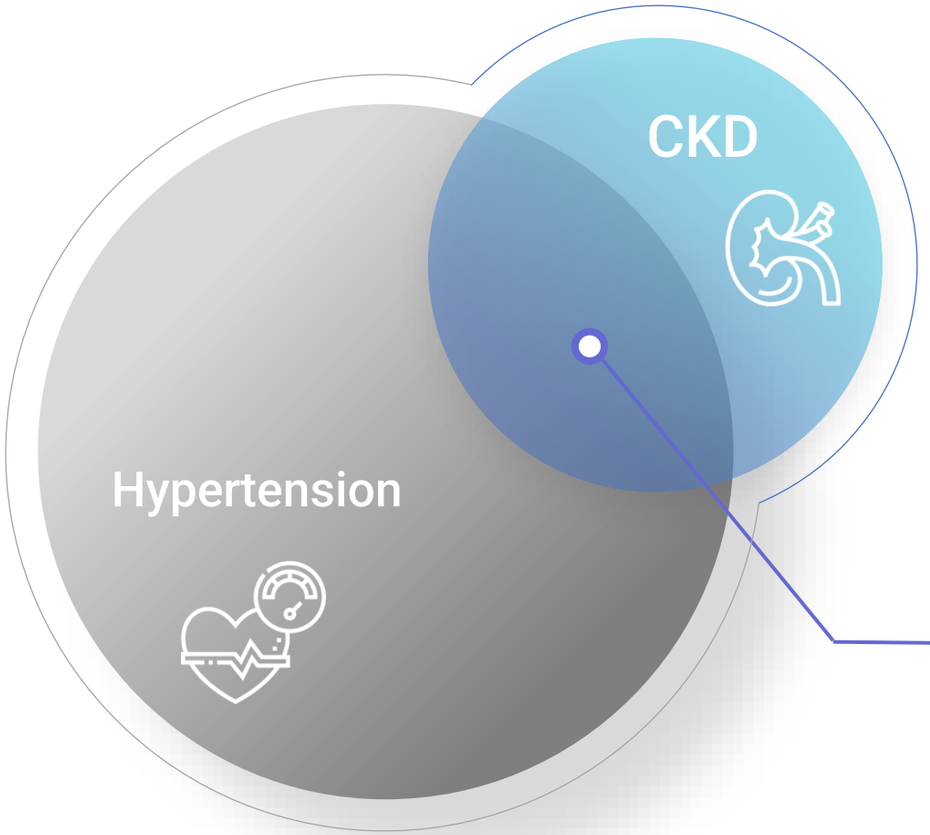
Significant overlap of hypertension, chronic kidney disease and obesity

Hypertension in the U.S.

115M Patients

60M Diagnosed

30M uncontrolled



CKD in the U.S.

~35M Patients

4M Diagnosed

~23M

Hypertension patients have comorbid CKD*

~50% prevalence of obesity in hypertension and CKD patients; respectively

* USRDS.org; High blood pressure redefined for first time in 14 years. American Heart Associate/American College of Cardiology Guidelines, retrieved from Heart.org; Chronic kidney disease in the general population (2010), retrieved from USRDS.org, accessed June 2022; Chronic kidney disease in the general population (2020), retrieved from USRDS.org, accessed June 2022

Abnormally Elevated Aldosterone Is a Key Driver in Multiple Cardiorenal Diseases

Genomic Effects

(mineralocorticoid receptor)

Na+ and water retention drives blood volume and blood pressure

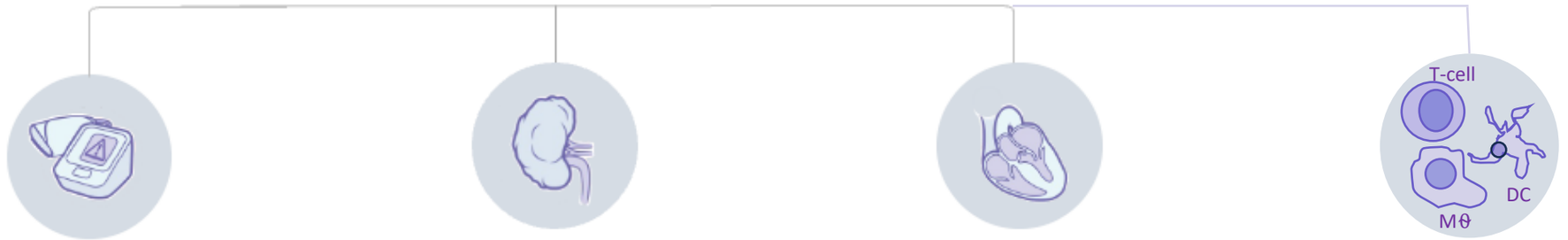
ALDOSTERONE

Non-Genomic Effects

(GPR30 receptor)

Drives endothelial and renal tubular oxidative stress, microvascular fibrosis, inflammation and HF

Aldosterone-driven Cardiorenal Disorders



Uncontrolled and Resistant Hypertension (uHTN; rHTN) [1]

Chronic Kidney Disease [2]

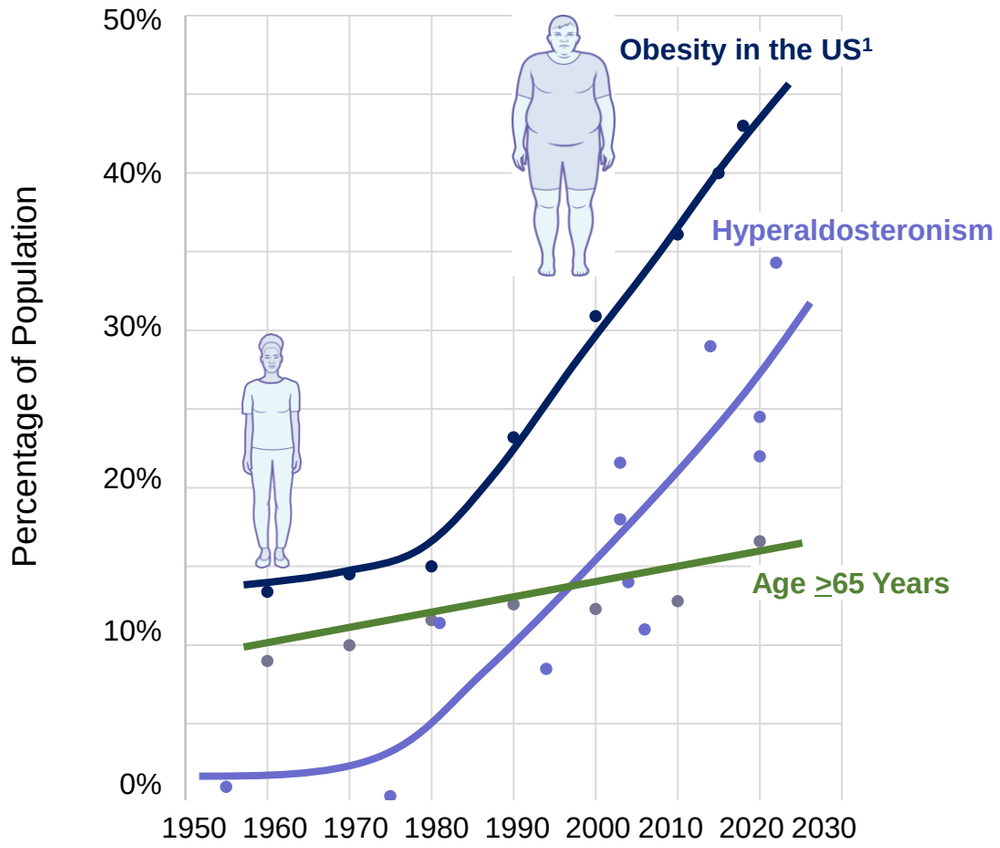
Heart Failure HFpEF & HFrEF [3]

Vascular and systemic Inflammation [4]

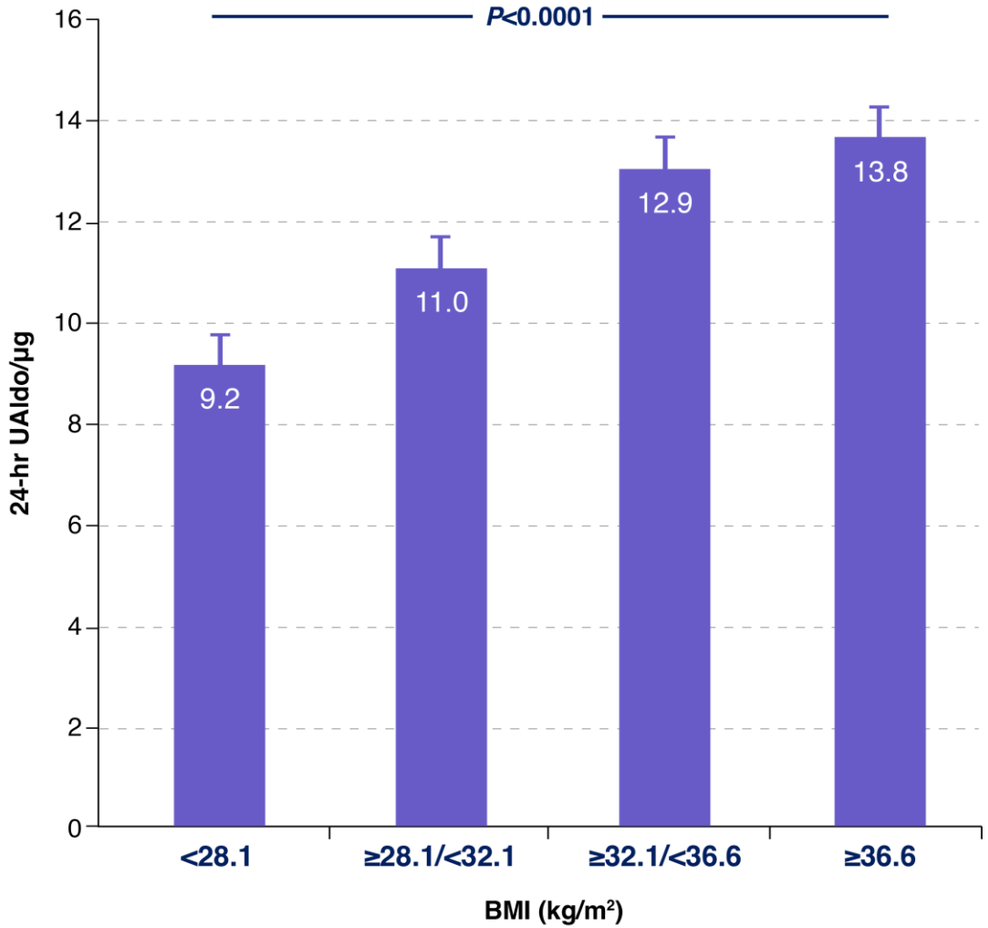
1. Sim JJ, Bhandari SK, Shi J, et al. *Am J Hypertens*. 2012;25(3):379-388. 2**.** Hundemer GL, Curhan GC, Yozamp N, Wang M, Vaidya A. *Hypertension*. 2018;72(3):658-666.3**.** Monticone S, D'Ascenzo F, Moretti C, et al. *Lancet Diabetes Endocrinol*. 2018;6(1):41-50. 4) Ferreira N, Tostes RC, Paradis P, Shiffrin E. Am J Hypertens. 2021, 34(1):15-27. 5.

Prevalence of Elevated Aldosterone Linked to Rise in Obesity

As percent of population with obesity has risen in the US, so has hyperaldosteronism



BMI is significantly correlated with aldosterone levels[2]



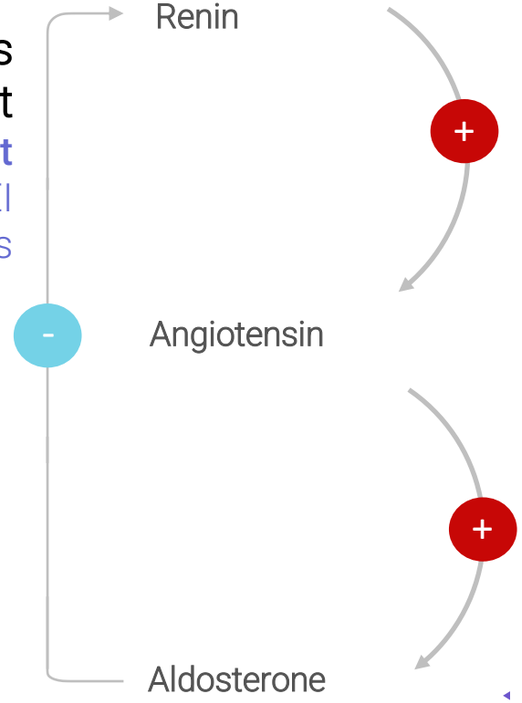
1. https://usafacts.org/articles/obesity-rate-nearly-triples-united-states-over-last-50-years. **2.** Dudenbostel T, Ghazi L, Liu M, Li P, Oparil S, Calhoun DA. *Hypertension*. 2016;68(4):995-1003.

In Obesity, via Visceral Adipocytes, Leads to Elevated Aldosterone Levels

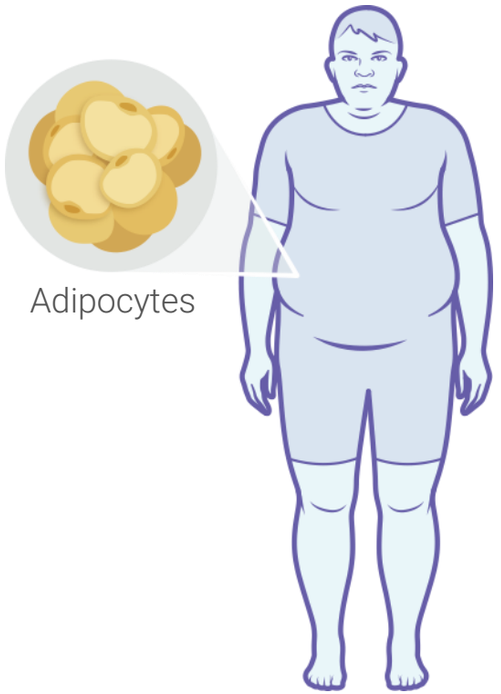
Lorundrostat targets both the RAAS-dependent and -independent axes, providing a more complete solution to abnormally elevated aldosterone

RAAS-dependent Axis

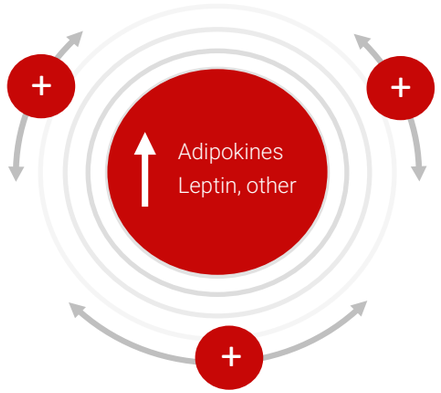
Blocks RAAS-dependent
Lorundrostat
ACEI
ARBs



RAAS-independent Axis



Blocks RAAS-independent
Lorundrostat



Lorundrostat Is a Highly Selective, Best-in-Class ASI

Aldosterone Synthase Inhibitor Comparison Table

	Lorundrostat (Mineralys)	**LCI699** (Novartis)[1]	**Baxdrostat** (Astra Zeneca)[2, 3]	**BI690517** (Boehringer Ingelheim)[4]
Selectivity	**374X**	3.6X	100X	250X
Half-life	**10-12 hours**	~4 hours	25-31 hours	noted to be “short”
Reduction in PAC	**65-70%**	65-70%	65-70%	66%
Adrenal insufficiency or decrease in cortisol	**no**	yes	no	yes
Metabolism	**Hepatic**	Hepatic	Renal	n/a

Best-in-class selectivity

Aldosterone inhibition with reduced risk of cortisol inhibition or off-target AEs

Optimal half-life

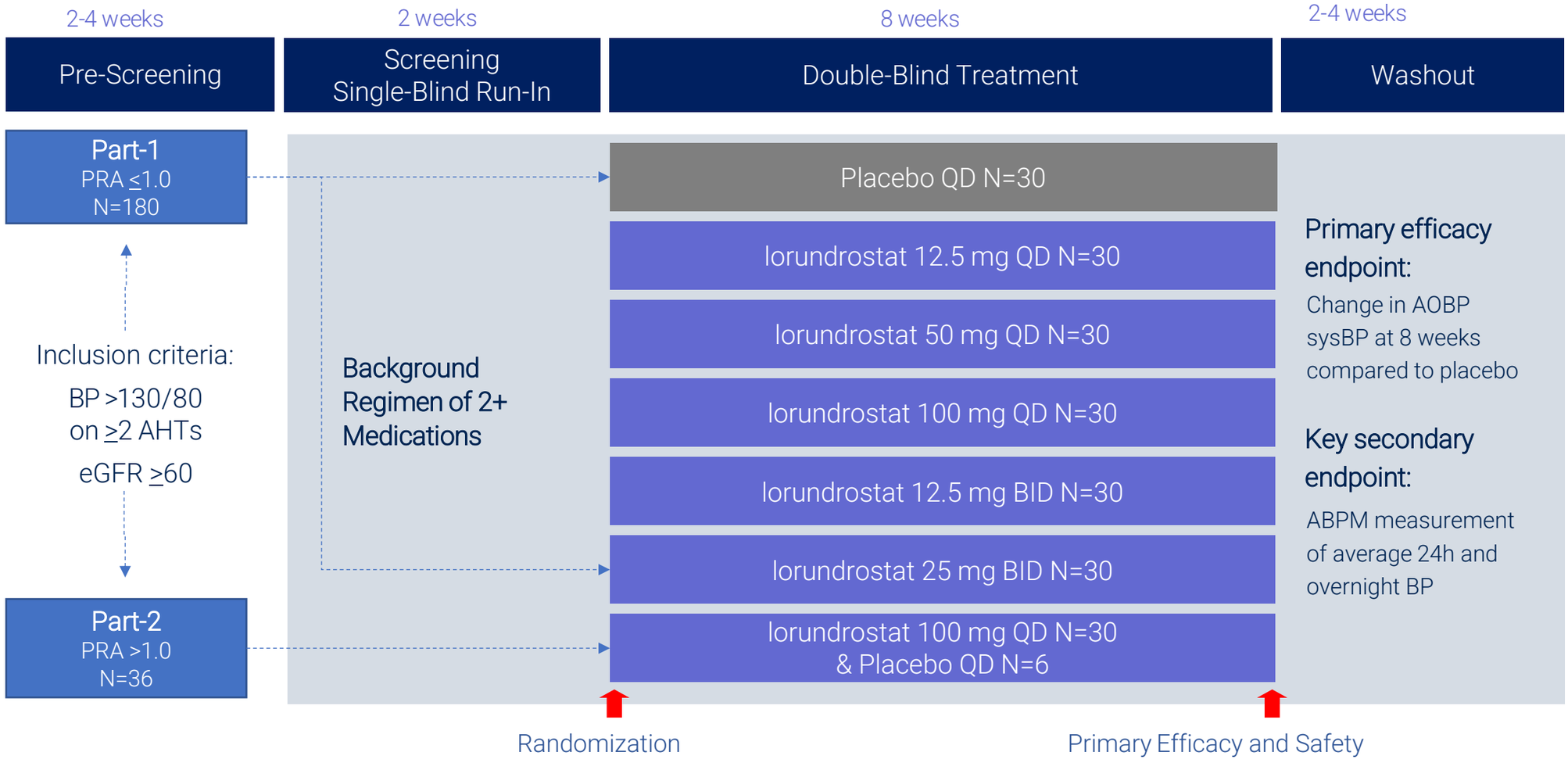
Aldosterone inhibition with rapid reversibility— essential for patients who may not tolerate a significant BP drop or are at risk for hyperkalemia, including patients with CKD

1. Schumacher CD, Steele RE, Brunner HR. *J Hypertens*. 2013;31(10):2085-2093. **2.** Bogman K, Schwab D, Delporte ML, et al. *Hypertension*. 2017;69(1):189-196. **3.** CinCor S1 filing 2020, 4. BI presentation at ASN meeting.

Phase 2 Proof-of-Concept Study Design

TARGET-HTN

Evaluating the safety, efficacy and dose-response of lorundrostat in uncontrolled and resistant hypertension

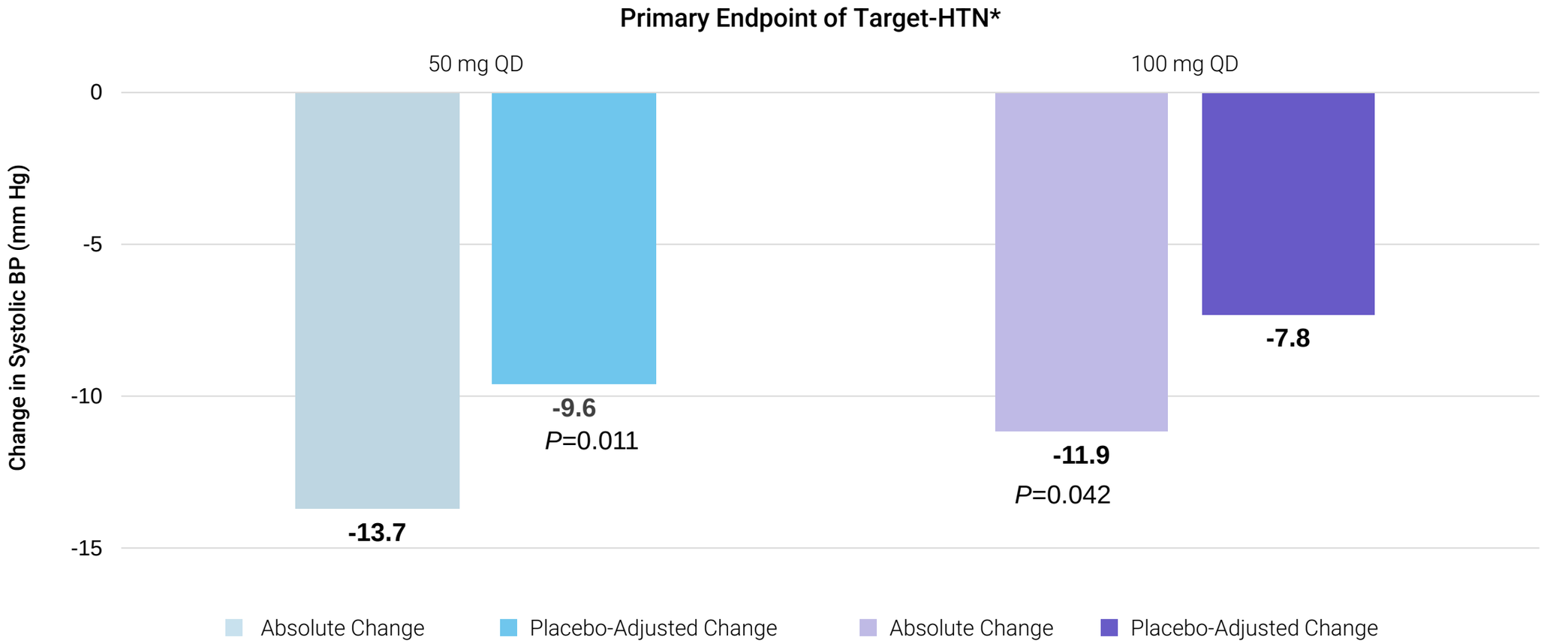


Baseline Demographics and Disposition

90% of the randomized patients completed Part 1 of the Target-HTN trial

Category	Mean ± SEM of Baseline
Systolic BP (mm Hg)	142.2 ± 0.98
Diastolic BP (mm Hg)	81.5 ± 0.76
Body Mass Index (kg/m^2)	31.2 ± 0.41
Mean Baseline eGFR	78.9 ± 1.3
Race % Black or African American	39.3%
Sex % Male	41.7%
Ethnicity % Hispanic or Latino	46.6%
Diabetes	37.4%
Heart Failure	3.1%
Previous Myocardial Infarction	5.5%
Number of Background Antihypertensive Medications	2 medications = 52.8% / 3 or more medications = 47.2%
Use of Thiazide or Thiazide-like Diuretic	56.4%
Use of ACE or ARB	77.9%

Clinically Meaningful Changes in Systolic BP

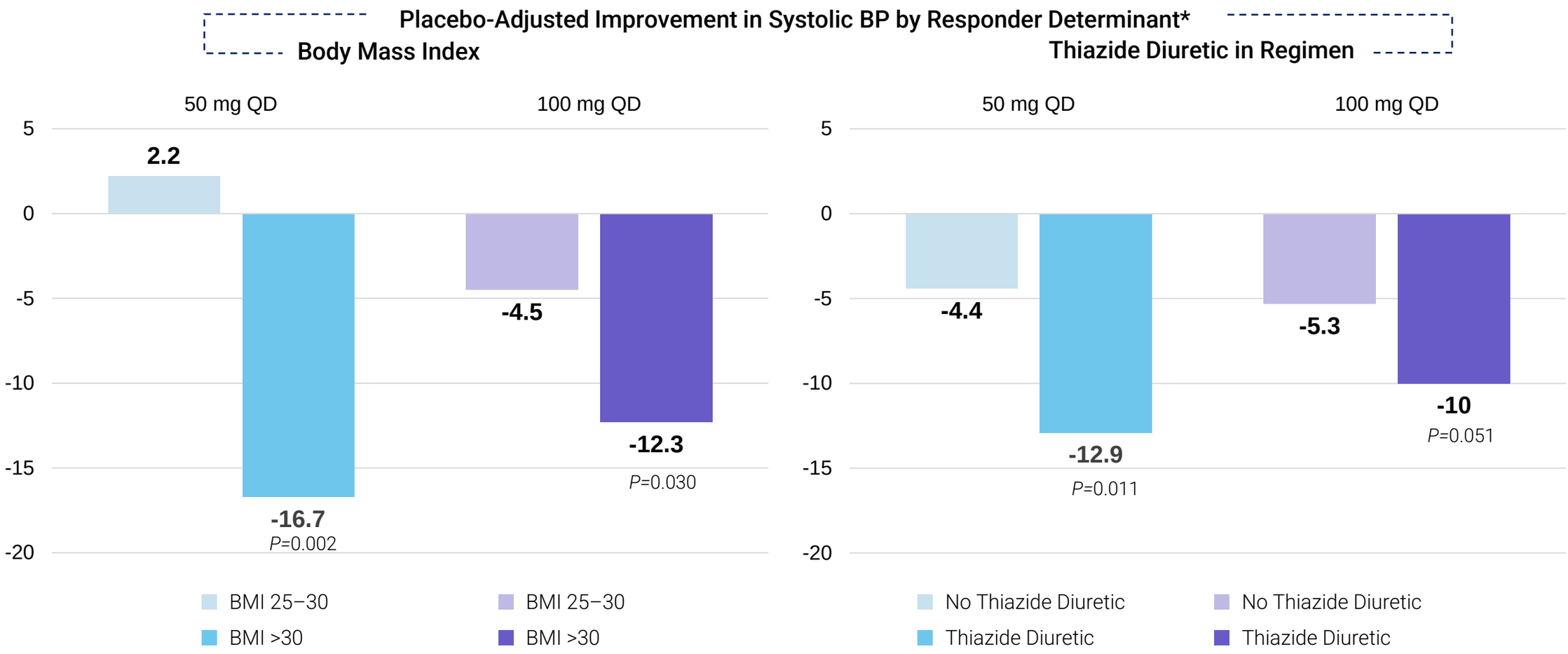


Analysis using a mixed model repeated measures (MMRM) approach with fixed effects of categorical terms for treatment, week, and treatment by week interaction, and analyte as a fixed continuous covariate.

*Part 1 of Phase 2 Target-HTN Proof-of-Concept Trial.

Enhanced Systolic BP Reduction in Targeted Segments

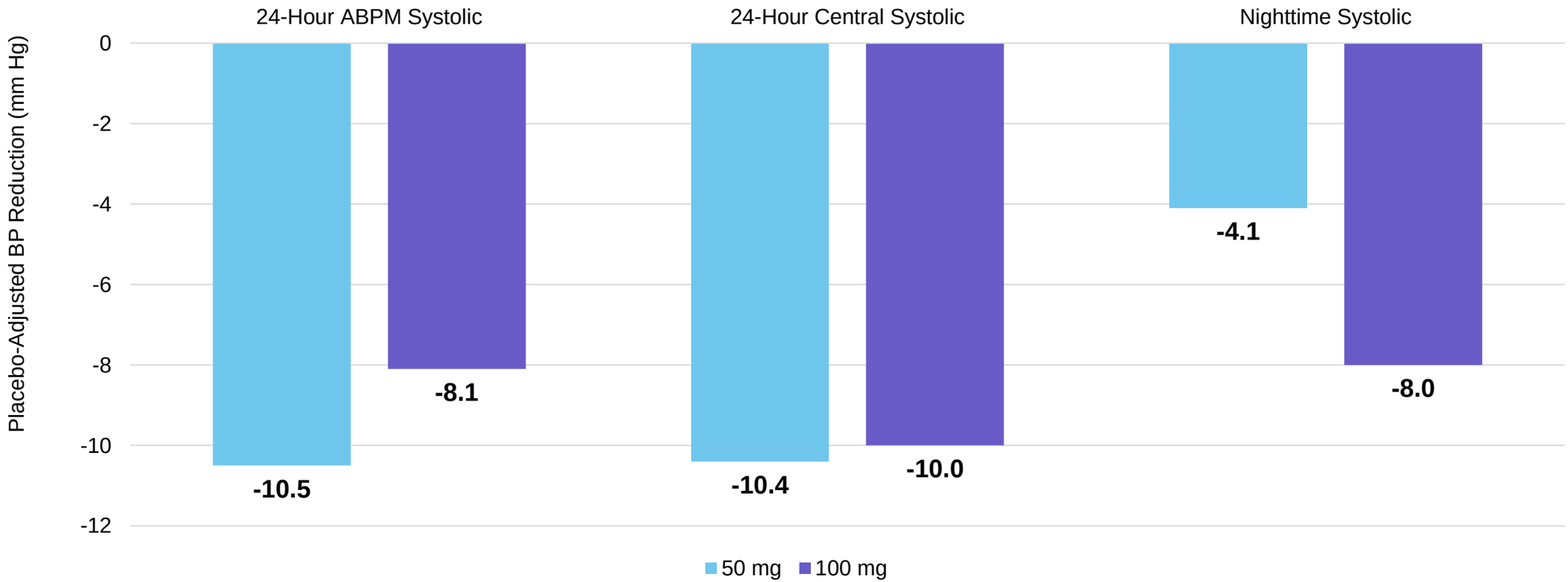
Obesity and diuretic use are determinants of enhanced response in systolic BP reduction



*Part 1 of Phase 2 Target-HTN Proof-of-Concept Trial.

Reductions in 24-Hour Average, Central and Nighttime Systolic BP Supportive of Primary Findings

Central BP and nighttime BP reductions may be a more accurate way of predicting cardiovascular benefit



Analysis of 24-hour ambulatory monitoring in subjects with baseline systolic BP >130 mm Hg by automated office and 24-hour ambulatory monitoring.

Lorundrostat Demonstrated a Well-Tolerated Profile

Individual Hyperkalemic Events – Number of Subjects (% of group size)

	Mean Change from Baseline to Wk 8	Mild 5.6-6.0 mmol/L	Moderate 6.1-6.5 mmol/L	Severe >6.5 mmol/L
50 mg QD (n=28)	+0.25 mmol/L	1 (3.6%)	0	1* (3.6%)
100 mg QD (n=61)	+0.29 mmol/L	8 (13.1%)	1 (1.6%)	1 (1.6%)
All active (n=164)		16 (9.8%)	4 (2.4%)	2* (1.2%)
Placebo (n=36)		0	0	0

6/164 (3.7%) of subjects with one or more observed episodes of serum K^+ >6.0 mmol/L; 5 of 6 judged not related to study medication.

* Measure in 1 subject was an isolated incident not verified by repeat measurement with study drug discontinuation (protocol deviation).

- Treatment-emergent adverse events were hyperkalemia (defined as greater than 5.1 mmol/L), decreased glomerular filtration, urinary tract infection, diarrhea, hypertension, and COVID-19 infection
- Three subjects experienced serious adverse events, 2 were deemed unrelated and 1 was deemed related in a subject with worsening hyponatremia that reversed after drug discontinuation

Rapid Development Program for Lorundrostat with Near-Term Data Readouts

Lorundrostat

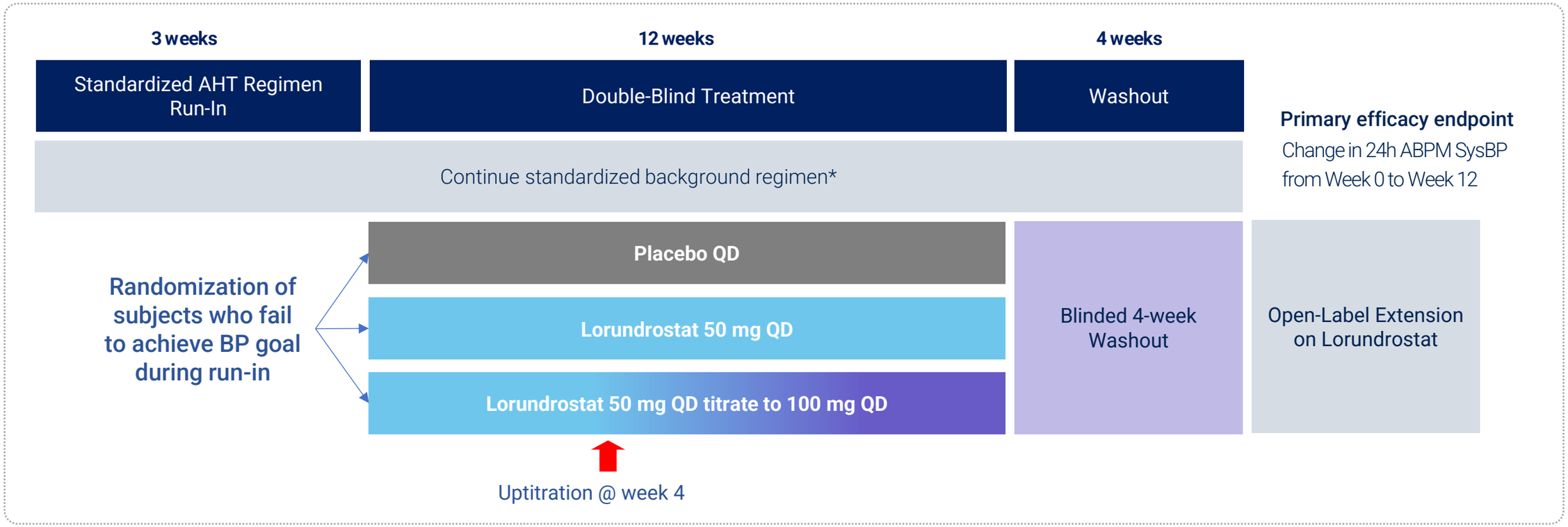
Trial	Safety	Proof of Concept	Pivotal	Top-line Data
Hypertension	uHTN & rHTN Standardized background AHT			March 2025
	uHTN & rHTN Existing background AHT			Mid 1H 2025
Chronic Kidney Disease (CKD)	CKD PoC & Profiling			2Q 2025
Open-Label Extension	uHTN & rHTN			

Advance-HTN Pivotal Study Design

ADVANCE-HTN

Confirmatory efficacy and safety trial of lorundrostat in uncontrolled and resistant hypertension, target 261 subjects

Inclusion Criteria:	24h ABPM 130-180 on ≥2 AHTs eGFR ≥ 45 Serum K+ ≤4.8
Stratification:	By number of background AHT meds
Baseline Demographics:	>50% Black or African American >66% BMI over 30 >40% female



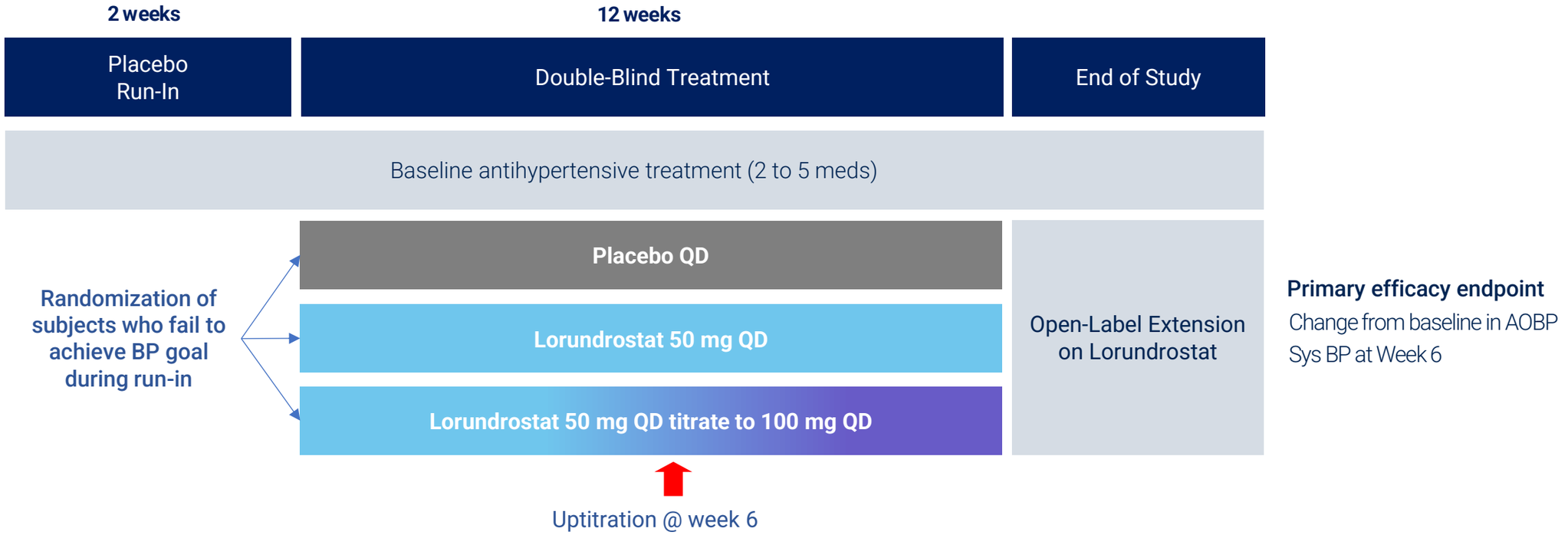
*Start standardized drug background regimen. 2 AHTs = ARB + Diuretic / 3-5 AHTs = ARB + Diuretic + CCB

Launch-HTN Pivotal Study Design

Efficacy and safety trial of lorundrostat in uncontrolled and resistant hypertension, ~1,000 subjects

Inclusion criteria:

- AOBP SysBP 135-180 on 2 to 5 AHTs
- eGFR ≥ 45
- Serum K+ ≤4.8



Primary efficacy endpoint

Change from baseline in AOBP Sys BP at Week 6

CKD Proof-of-Concept and Profiling Trial

EXPLORE-CKD

Proof-of-Concept in hypertensive subjects with stage 2-3b CKD with albuminuria

Inclusion criteria:

- Existing or naïve to SGLT2 inhibitor treatment
- AOBP SysBP ≥135 on an ACE inhibitor or an ARB
- eGFR 30-89 mL/min/1.73m^2
- Serum K+ ≤4.8

Primary efficacy endpoint

Change in AOBP Sys BP @ wk 4 compared to placebo

Exploratory endpoints

Change in UACR @ wk 4 compared to placebo

Safety and PK

Mineralys Leadership Team

Agile and experienced in developing novel, leading therapies

Jon Congleton

Chief Executive Officer

30+ years of experience: Marion, HMR, Aventis, Teva, Nivalis, Impel Pharma

David Rodman, MD

Chief Medical Officer

15+ years of academic experience and 15+ years of industry experience: Novartis, Vertex, ProQR

Adam Levy

Chief Financial Officer

15+ years of banking experience: Merrill Lynch, Jefferies, BAML; and 7+ years of industry experience: Miragen, Brickell, Sanifit

Minji Kim, PhD.

Chief Business Officer

20+ years of experience: Affamed, Jounce, Curis, Hoffman-LaRoche, Genentech

Cindy Berejikian

Executive Vice President, Operations

25+ years of experience: Amgen, Otonomy, Forty Seven

Financial Summary

Balance sheet supports activities to execute on upcoming milestones

Nasdaq	**MLYS**
Q3 2024 Cash Balance*	**$264mm**
Shares of common stock outstanding†	**49,768,669**

Research Analyst Coverage:	
BofA Securities	Charlie Yang
Evercore ISI	Umer Raffat / Mike DiFiore
Goldman Sachs	Richard Law
Stifel	Annabel Samimy
Guggenheim Securities	Seamus Fernandez
Wells Fargo Securities	Mohit Bansal
LifeSci Capital	Rami Katkhuda
HC Wainwright	Matthew Caufield

*Includes cash, cash equivalents, and investments..
†As of November 4, 2024 and excludes 549,755 pre-funded warrants.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