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Targeting Aldosterone in the Treatment of Cardiorenal Diseases

November 2026

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Targeting Aldosterone in the Treatment of Hypertension and Cardiorenal Diseases

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

- Dysregulated aldosterone is the driver in 30% of uncontrolled and resistant hypertension (u/rHTN)
- Lorundrostat demonstrated meaningful 24-hour BP reduction and safety of once-daily dosing in participants with u/rHTN
  - Demonstrated benefit in HTN participants with CKD
  - Demonstrated benefit in HTN participants with moderate to severe OSA
- 20M u/rHTN patients in the United States
  - Increased market opportunity in comorbid CKD or OSA
- PDUFA target date Dec. 22, 2026

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Dysregulated Aldosterone In Hypertension and Related Comorbidities

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Abnormally Elevated Aldosterone Impacts Multiple Biological Pathways and is a Key Driver in 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.

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Lorundrostat Potential Benefit Across Spectrum of CRMS[1–5]

Targeting dysregulated aldosterone in overlapping CRMS conditions with high CV risk and large unmet need

OSA in the U.S.

Nighttime BP link to CV risk

70-80% prevalence of rHTN in OSA

~22M Moderate-to-Severe OSA



HTN in the U.S.

30% prevalence of dysregulated aldo in u/rHTN

Visceral adiposity link to dysregulated aldo

~20M u/rHTN patients

CKD in the U.S.

>25% increase in CV risk vs controlled HTN

Kidney injury link to u/rHTN & hyperperfusion of kidney

~23M HTN + CKD patients

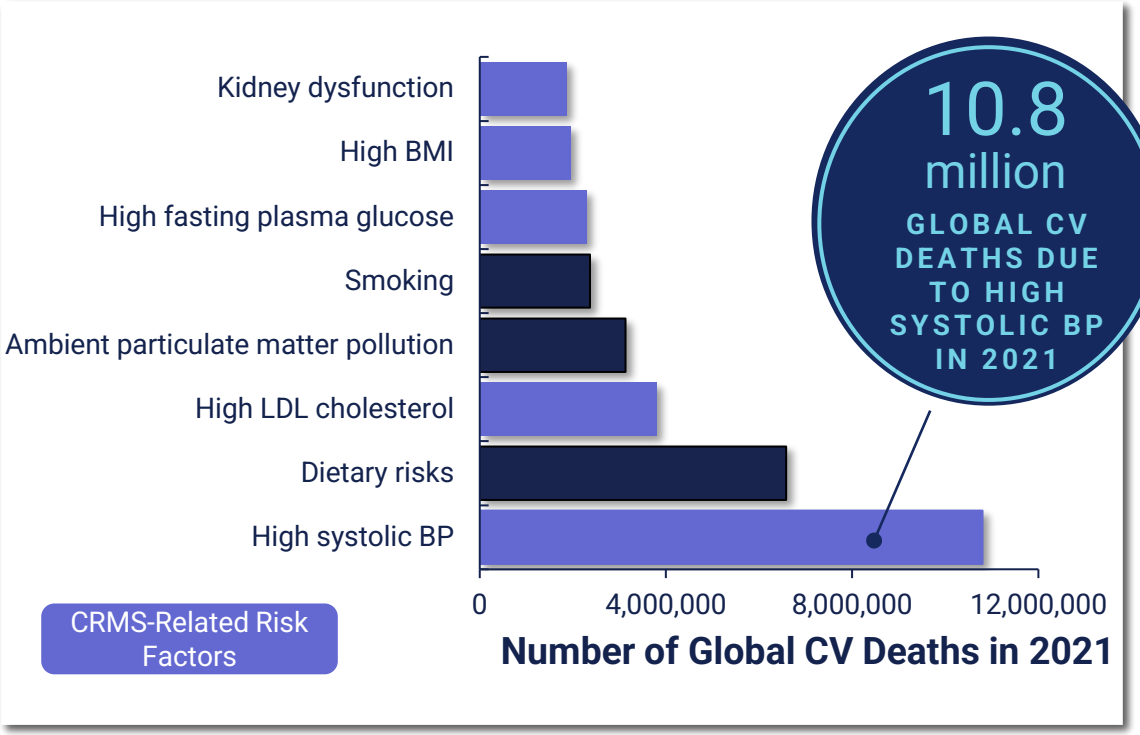
BP, blood pressure; CRMS, cardio-renal-metabolic syndrome; CKD, chronic kidney disease; CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HTN, hypertension.

1. Ndumele CE, et al. *Circulation.* 2023;148:1606-1635. **2.** Buglioni A, et al. *J Am Heart Assoc*. 2015;4:e002505. **3**. Ebinger JE, et al. *Eur J Prev Cardiol*. 2023;30(10):960-968. **4**. Marassi M & Fadini GP. *Cardiovasc Diabetol*. 2023;22:195. **5.** Alterki A, et al. *Int J Mol Sci*. 2023;24:6807.

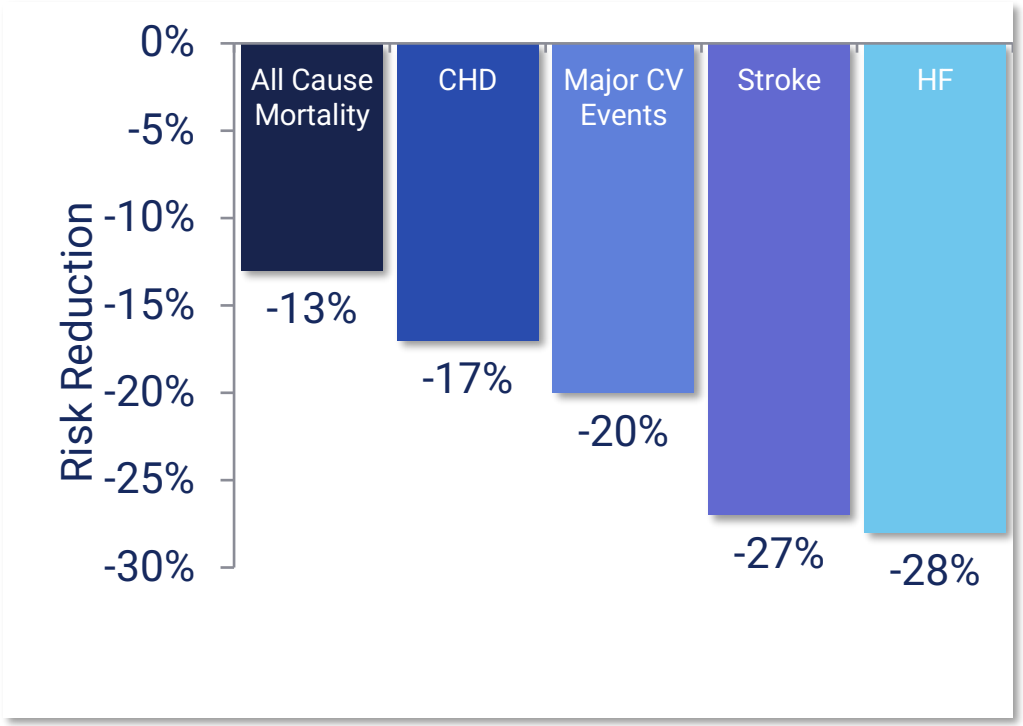
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Uncontrolled and Resistant Hypertension Is the Leading Global Modifiable Risk Factor for Cardiovascular Death

Top 8 Global Modifiable Risk Factors for CV Deaths in 2021[1]



Risk Reduction per 10mmHg Reduction in Systolic BP[2]



BMI, body mass index; BP, blood pressure; CRMS, cardio-renal-metabolic syndrome; CV, cardiovascular; LDL, low density lipoprotein.

1. Vaduganathan M, et al. *J Am Coll Cardiol*. 2022;80(25):2361-2371. **2.** *Ettehad D, et al. Lancet. 2016;387(10022):957-967.*

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The Unmet Need in u/rHTN is Largely Driven by Dysregulated Aldosterone

20-40% of hypertension patients have uncontrolled or resistant HTN

- Half of the treated HTN patients in the U.S. fail to achieve goal[1]
- Prevalence of apparent rHTN demonstrated to be ~20%[2]
- In optimized background treatment trials, 30-40% of participants fail to achieve goal[3]
- Kaiser optimized regimen trial – 20% of patients fail to achieve goal[4]

Aldosterone the primary culprit in u/rHTN

- Approximately 30% of all HTN patients have dysregulated aldosterone[5]
- Aldosterone breakthrough demonstrated in 30-40% of ACEi or ARB treated patients
- Obesity epidemic (visceral adiposity) linked to dysregulated or elevated aldosterone

1. millionhearts.hhs.gov 2, Prevalence of Apparent Treatment-Resistant Hypertension in the United States, Hypertension. 2019;73:424-431. DOI: 10.1161/ HYPERTENSIONAHA.118.12191.3. Identifying and treating resistant hypertension in PRECISION: A randomized long-term clinical trial with aprocitentan, DOI: 10.1111/jch.14517 4. Improved Blood Pressure Control Associated With a Large-Scale Hypertension Program, JAMA. 2013 August 21; 310(7): 699–705. doi:10.1001/jama.2013.108769. 5. Primary Aldosteronism and the Pathogenesis of Hypertension, Physiol Rev. 2018;98(1):103-137

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Lorundrostat Clinical Efficacy and Safety

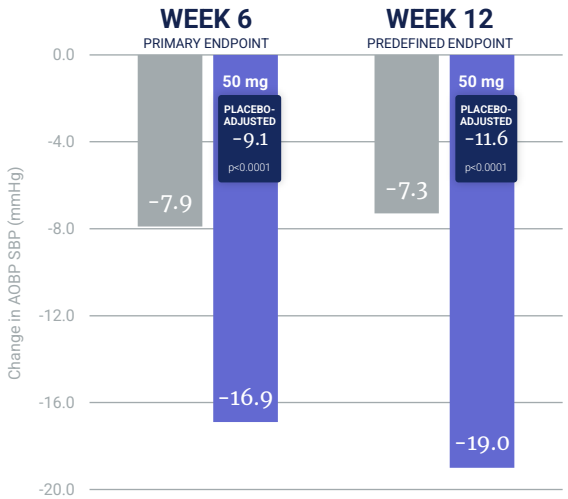
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Clinically Meaningful Efficacy across Participant Subgroups

Reductions in SBP of this magnitude have been linked to significant reduction in overall cardiovascular risk[1]

LAUNCH-HTN

u/r/HTN participants on prescribed regimen of 2-5 AHTs (n=1,083 randomized)

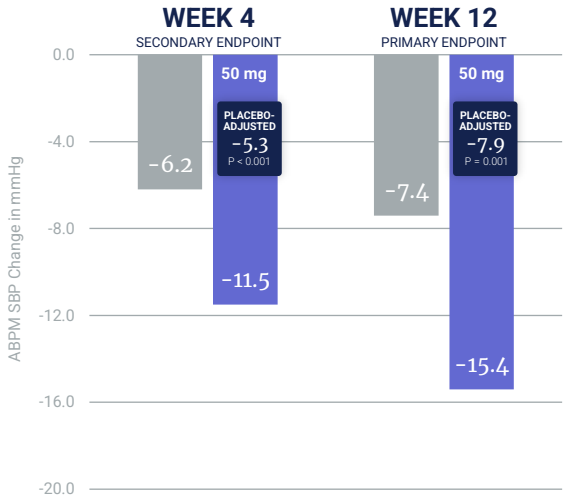


"Real World" - experience on 2 or more background medications

44% on lorundrostat and 24% on placebo achieved BP goal at week 6 (p=0.0033)

ADVANCE-HTN

Change in 24hr ABPM in mmHg (n=285 randomized)

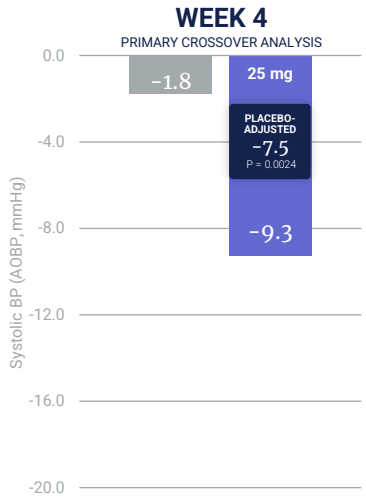


"Cardiologist" Setting for Patients with Confirmed u/rHTN

41% of lorundrostat and 18% of placebo achieved BP goal at week 4 (p<0.001)

EXPLORE-CKD

Change in AOBP in mmHg (n=59 randomized)

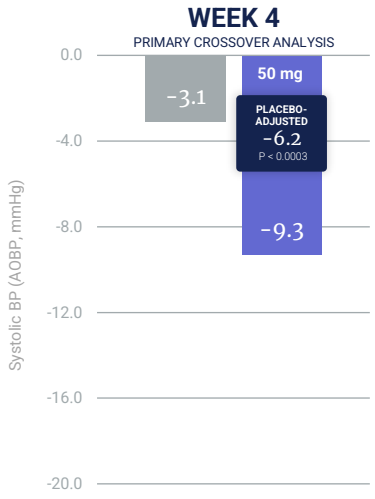


"Nephrologist" setting for u/rHTN with CKD on an SGLT2i

Lorundrostat reduced UACR by 31% at 4 weeks (p<0.0001)

EXPLORE-OSA

Change in AOBP in mmHg (n=48 randomized)



"Sleep Specialist" setting for u/rHTN with OSA

No evidence of benefit on AHI; clinically meaningful reduction in BP

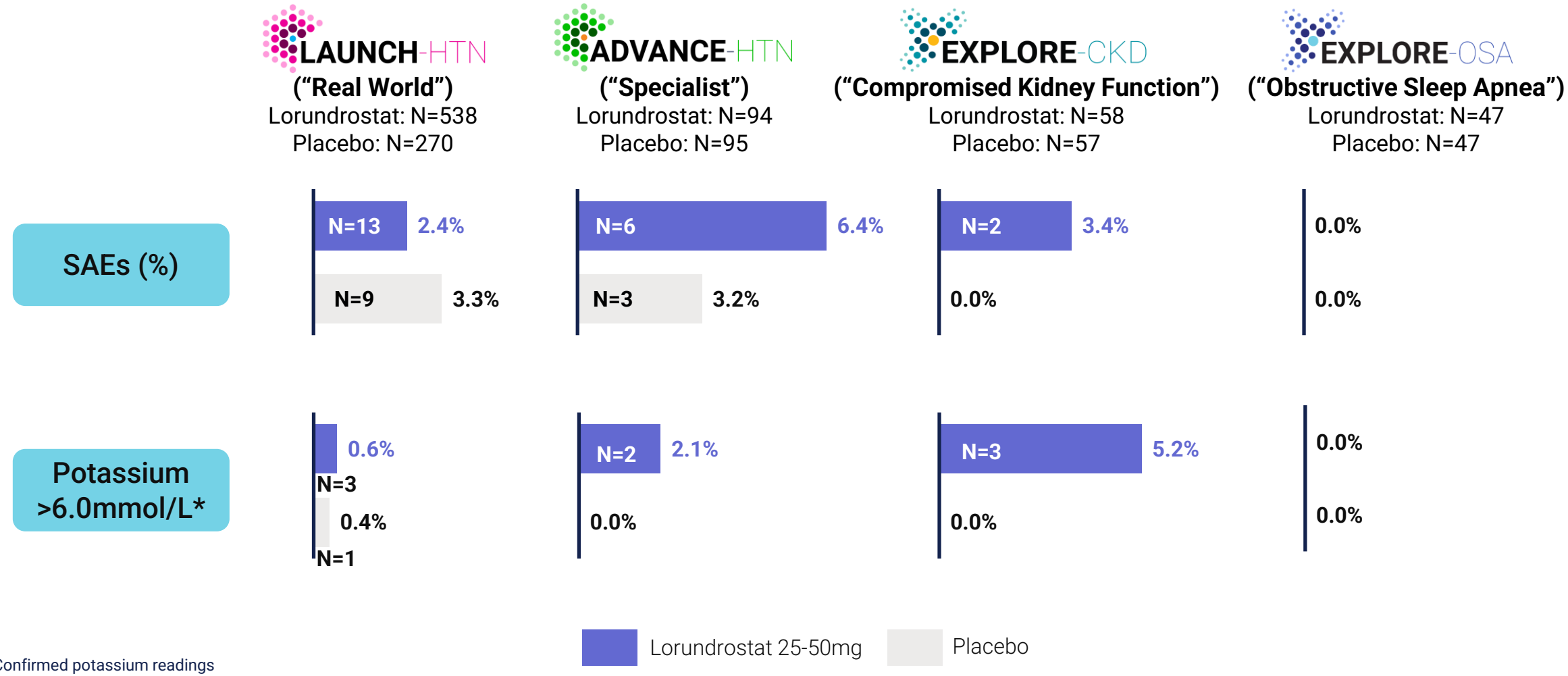
Lorundrostat 25-50mg Placebo

1. Whelton PK, Carey RM, AronowWS, et al. 2017 *Hypertension*. 2018;71(6):1269-1324.

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Favorable Safety and Tolerability Profile across Patient and Prescriber Types

Very low rates of serious adverse events and treatment discontinuations



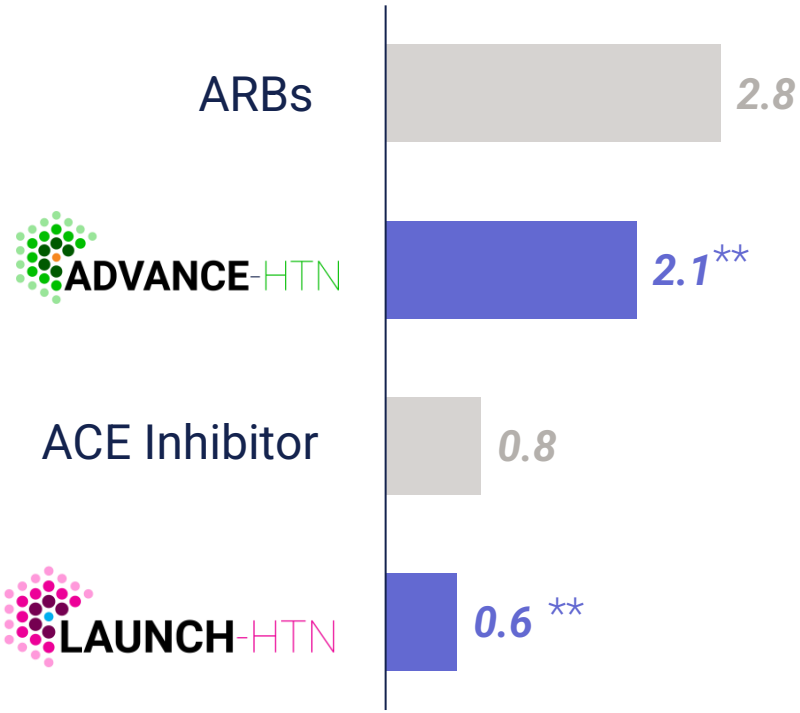
* Confirmed potassium readings

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Lorundrostat Potassium Profile Similar to ACE Inhibitor and ARBs – Predictable and Modest

- Lorundrostat potassium levels are **very mild and consistent with observed levels of ACE inhibitors and ARBs today***
  - Potassium levels were mild even in Advance-HTN trial with high-dose ARB background
- Change in potassium is an on-mechanism response **for any RAAS inhibitor**

Hyperkalemia (K^+ > 6.0) at Study Visit and Repeat Test (%)



Mild Potassium Profile, Increase Typically Resolves Within Two Weeks

* Sadjadi, et al Pathology and Laboratory Medicine International 9 July 2009
** Confirmed potassium readings

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

	Trial	Safety	Proof of Concept	Pivotal	Status
Hypertension	TARGET-HTN	u/rHTN Existing background AHT			Completed
	ADVANCE-HTN	u/rHTN Optimized background AHT			Completed
	LAUNCH-HTN	u/rHTN Existing background AHT			Completed
	TRANSFORM-HTN	Open-Label Extension*			Ongoing
Hypertension + CKD	EXPLORE-CKD	HTN + CKD			Completed
Hypertension + OSA	EXPLORE-OSA	HTN + OSA			Completed

*Randomized Treatment Withdrawal Substudy Completed

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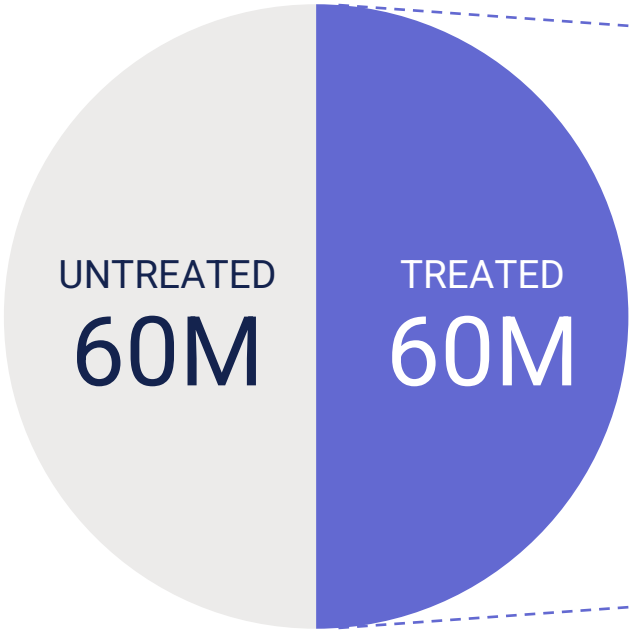
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Significant Commercial Opportunity in CRMS

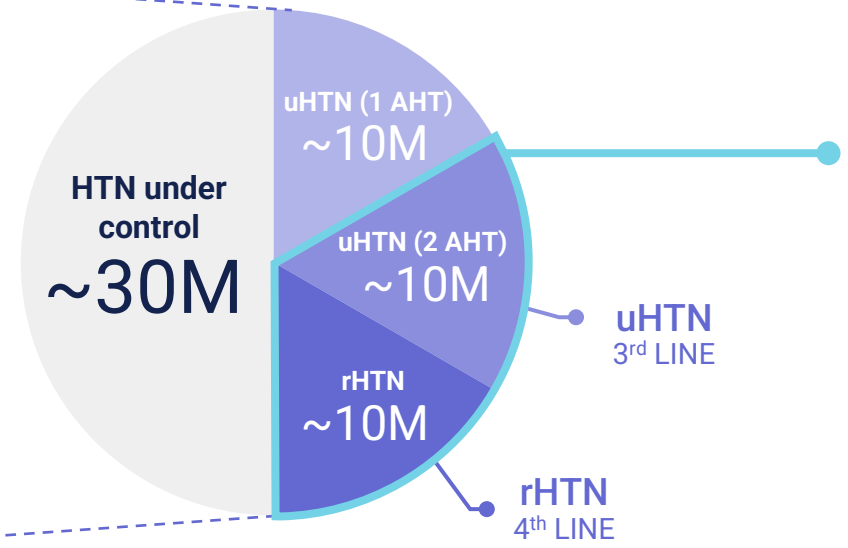
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Large Total Addressable Market: 20M People in U.S. with Uncontrolled or Resistant Hypertension and Related Comorbidities

~120M
HTN PATIENTS IN THE U.S.



PATIENT POPULATION BREAKDOWN IN THE U.S



Addressable Market 20M u/rHTN

- ~3M have HTN + CKD
- ~6M have HTN + OSA

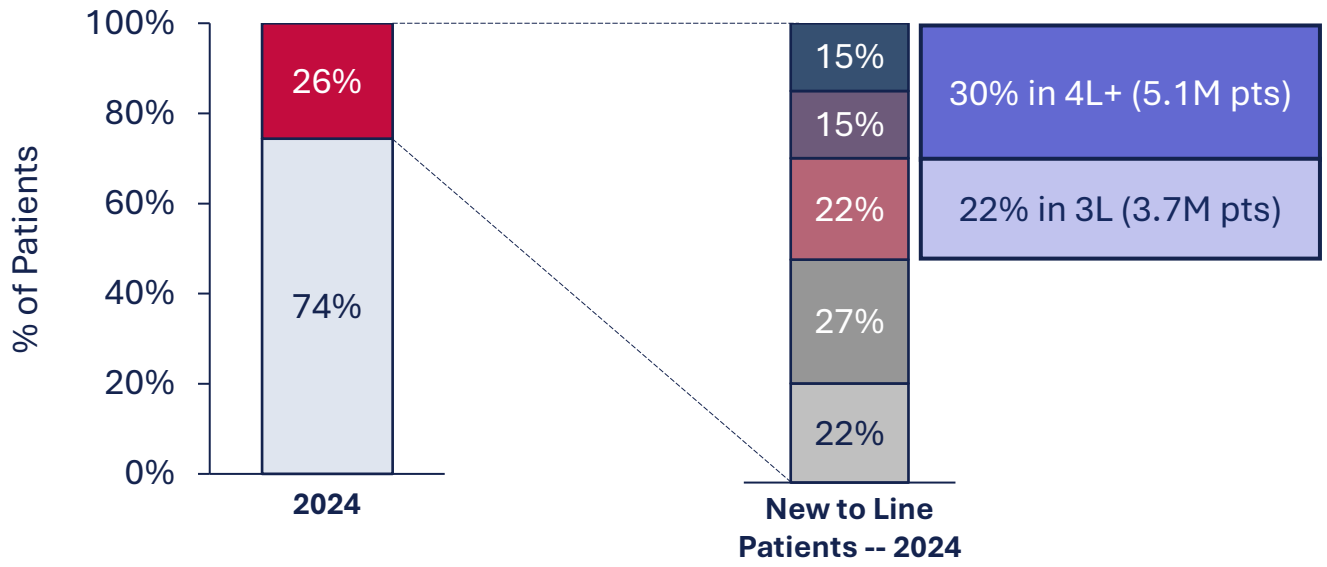
Millionhearts.hhs.gov
IQVIA data project May 2024

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8.8 Million u/rHTN Patients per Year Try New Treatments – an Opportunity for Lorundrostat

More than half of new-to-line patients each year would be eligible for lorundrostat 3L+ treatment

New-to-Line vs Existing Patient Distribution



New-to-Line Patient Line of Therapy Distribution

Eligible New Patient Pool per year

65M
Treated HTN patients

✖

26%
New-to-Line patients

✖

52%
3rd Line+

=

8.8M
3L & 4L+ New-to-Line patients with HTN

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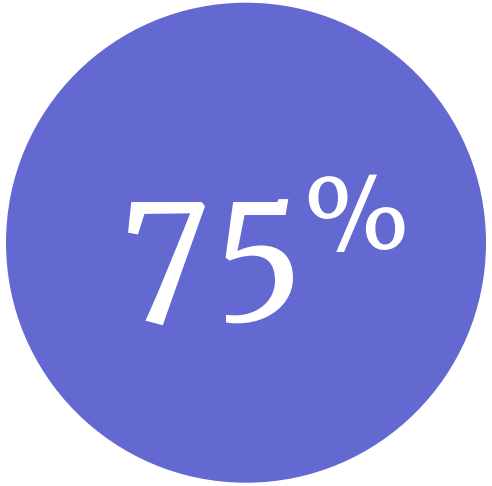
Per Market Research, the Majority of PCPs, Cardiologists and Nephrologists Are Likely to Prescribe Lorundrostat Based on Efficacy and Safety Profile

Likelihood to prescribe lorundrostat for u/rHTN



Based on Launch-HTN & Advance-HTN efficacy & safety data[1]

Likelihood to prescribe lorundrostat for u/rHTN with CKD



Based on Explore-CKD efficacy & safety data in u/rHTN with CKD[2]

Those surveyed preferred lorundrostat vs baxdrostat, based on Launch-HTN and BaxHTN efficacy & safety profiles[3]

67%

PCPs

66%

Cardiologists

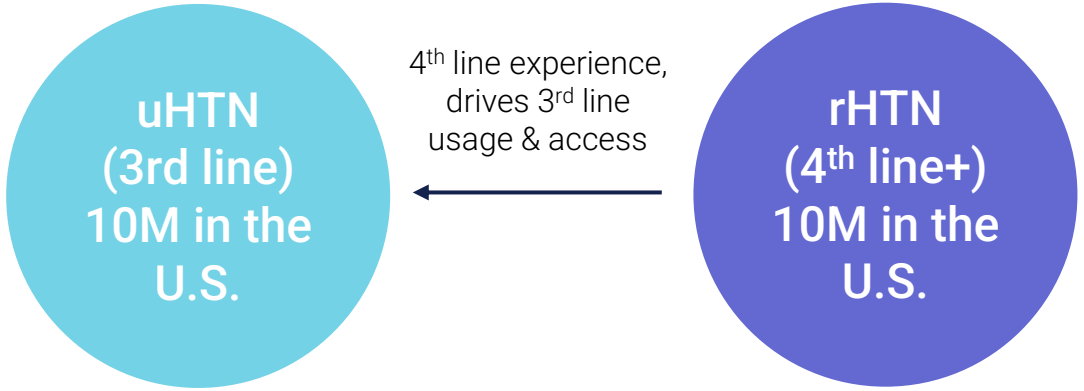
1. SERMO survey, March 2025, 212 PCPs and 101 cardiologists. 2. First Word Pharma survey, June 2025, 133 HCPs 3. SERMO survey, September 2025, 52 PCPs and 50 cardiologists

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Launch Plan Builds Upon u/rHTN Opportunity and Addresses Additional Areas of Unmet Clinical Need

Inclusion of ASI in AHA hypertension treatment guidelines

Potential best-in-class SBP reductions & safety in u/rHTN informs general prescribing
(Launch-HTN)



Generalists
High-volume PCPs

Specialists
Cardiologists
Nephrologists
High-volume PCPs

Confirmed u/rHTN
Advance-HTN: Only ASI studied in confirmed hypertension

Hypertensive nephropathy (<1g protein)
Explore-CKD: BP & Proteinuria reduction on SoC SGLT2i

u/rHTN, complicated by OSA & Obesity
Explore-OSA: Reduction of BP

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Financial Summary

Nasdaq	MLYS
September 30, 2026 Cash Balance*	$625M
Shares of common stock outstanding†	89,106,852

*Includes cash, cash equivalents and investments.
†As of October 29, 2026, and includes 549,755 shares underlying pre-funded warrants.

Research Analyst Coverage

BofA Securities	Jason Gerberry
Evercore ISI	Umer Raffat/Mike DiFiore
Goldman Sachs	Richard Law
Stifel	Annabel Samimy
Guggenheim Securities	Seamus Fernandez
Wells Fargo Securities	Mohit Bansal
Jefferies	Dennis Ding
LifeSci Capital	Rami Katkhuda
HC Wainwright	Matthew Caufield
TD Cowen	Tara Bancroft
UBS	Alice Nettleton

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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



Adam Levy

Chief Financial Officer

15+ years of banking experience: Merrill Lynch, Jefferies, BAML; and 10 years of industry experience: Miragen, Brickell, Sanifit



Eric Warren

Chief Commercial Officer

30+ years of experience: Merck, Genzyme, Pfizer, Sanofi, Nabriva, Esperion



Jessica Ibbitson

EVP Operations

20+ years of experience: ProQR, Vertex, TransTech, Nova Scotia Health Authority



Jeff Munsie

Chief Legal Officer

25+ years of experience: Orbital Therapeutics, Concert, Merrimack



Terry Ferguson, MD

Chief Medical Officer

20+ years of academic medicine and 15+ years industry experience: AstraZeneca, Amgen, Matinas Bio, Cadrenal Therapeutics

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