

Meet AZN Management: ESC 2025

Conference call and webcast
for investors and analysts

31 August 2025



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Meet AZN Management @ ESC – agenda

Furthering the AstraZeneca ambition

Ruud Dobber, EVP, BioPharmaceuticals Business

**Addressing unmet need in
cardiometabolic diseases**

Sharon Barr, EVP, BioPharmaceuticals R&D

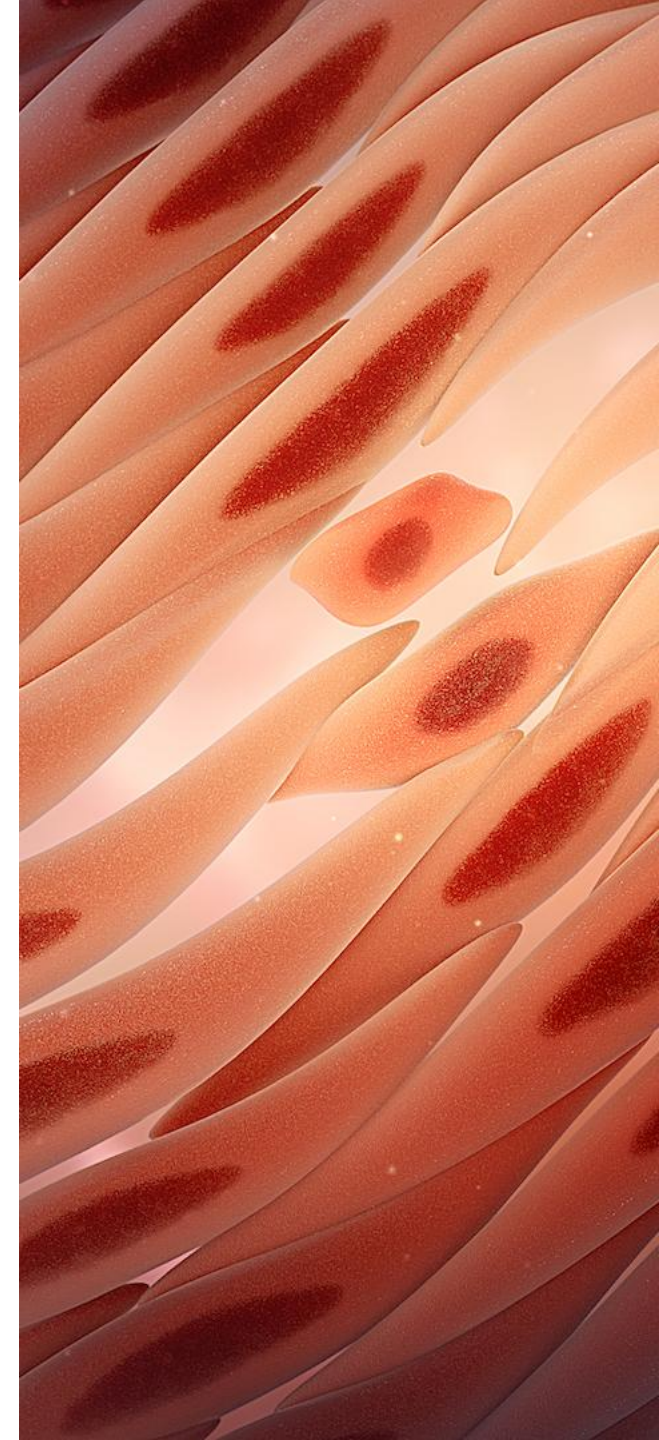
baxdrostat – Phase III BaxHTN:
baxdrostat in hard-to-control hypertension

Dr Bryan Williams, Chair of Medicine,
University College London

**Delivering next-wave of CVRM
growth with baxdrostat**

Sharon Barr, EVP, BioPharmaceuticals R&D
Ruud Dobber, EVP, BioPharmaceuticals Business

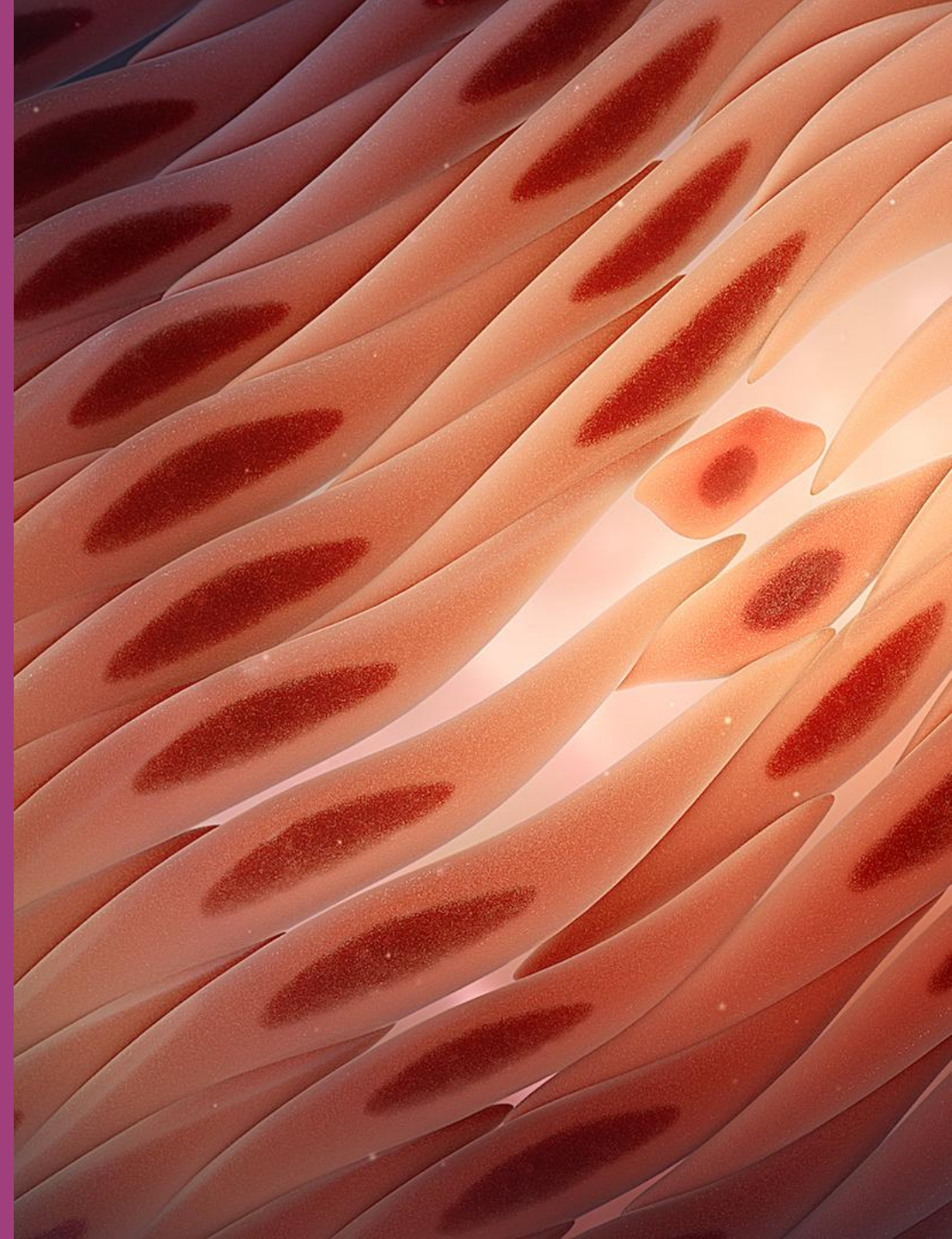
Closing remarks and Q&A session



Furthering the AstraZeneca ambition

Ruud Dobber

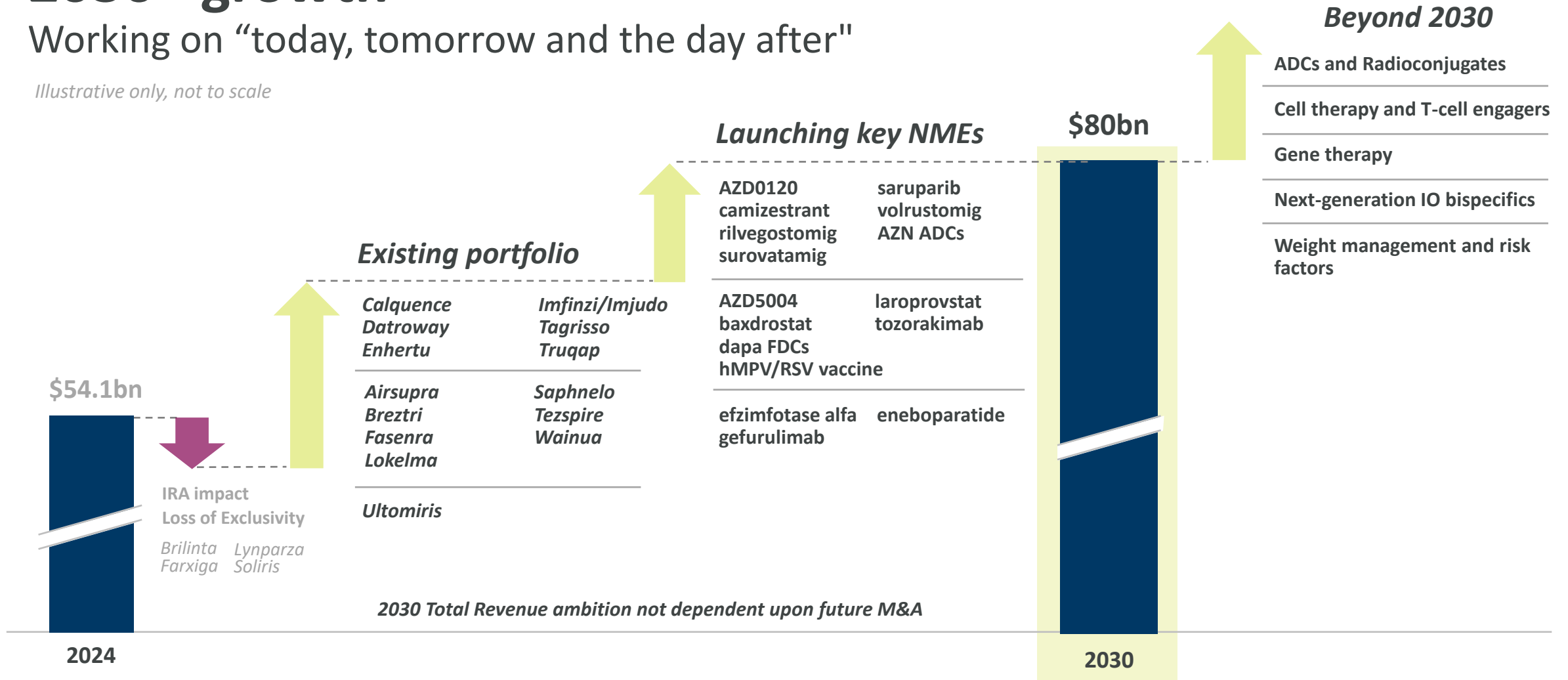
EVP, BIOPHARMACEUTICALS BUSINESS



Ambition – \$80bn Total Revenue by 2030 & sustained 2030+ growth

Working on “today, tomorrow and the day after”

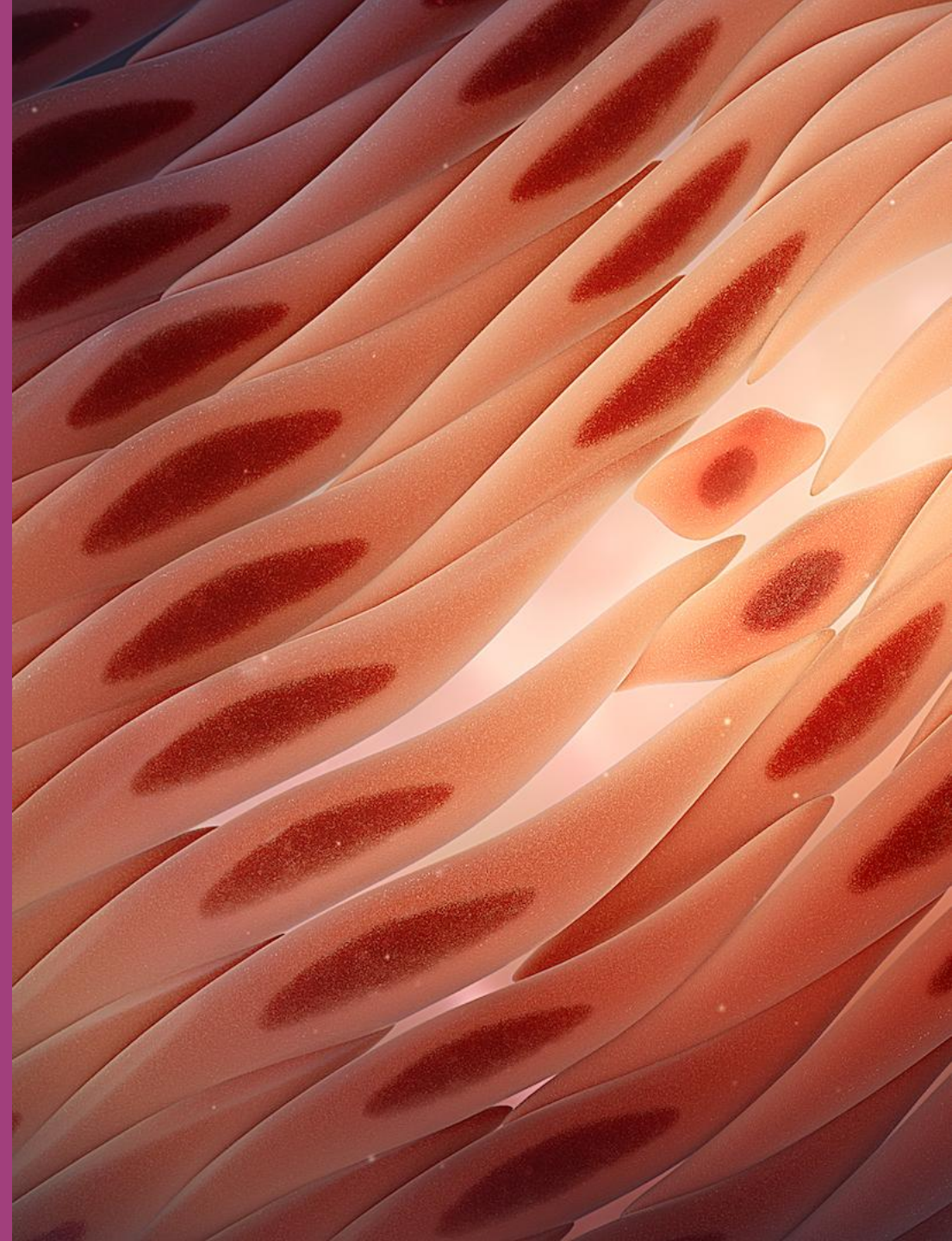
Illustrative only, not to scale



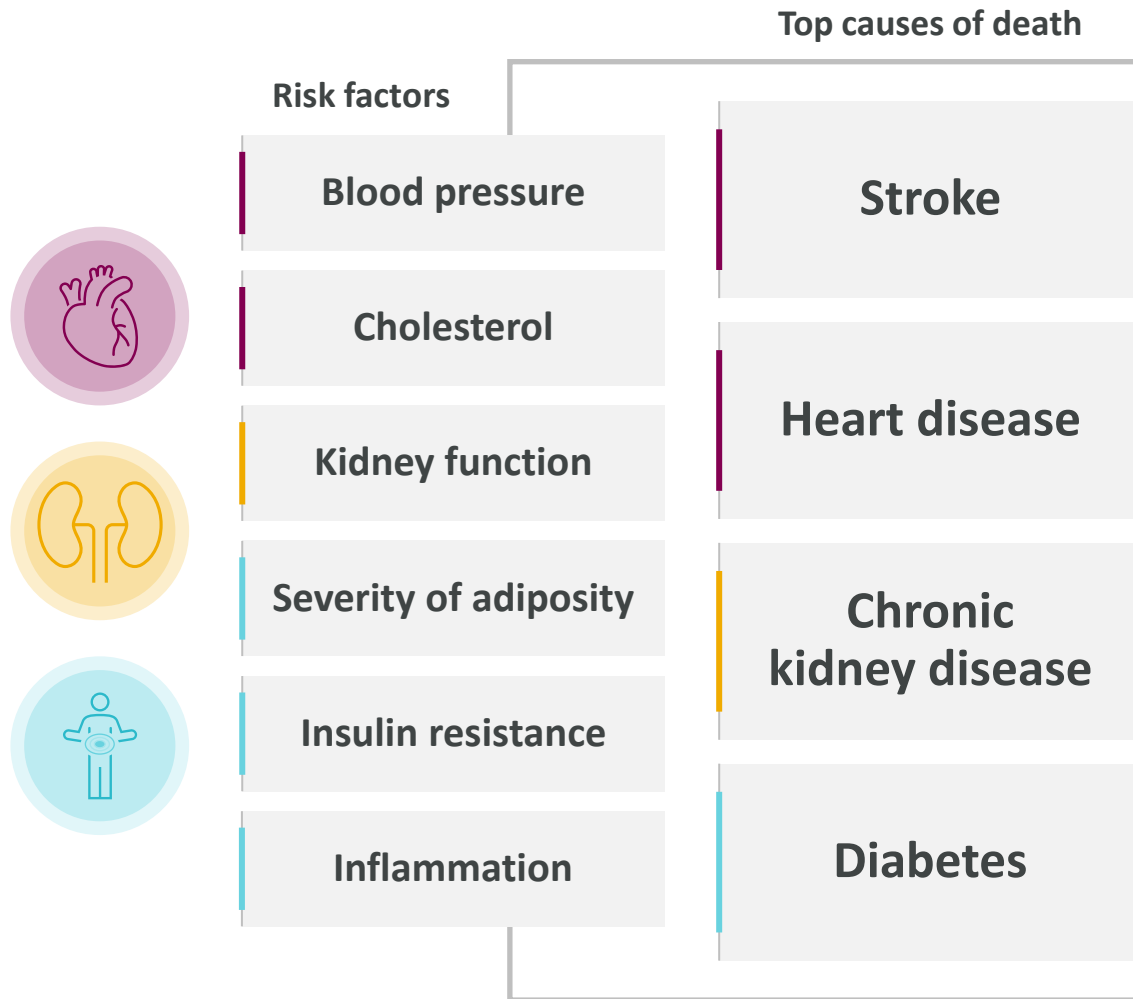
Addressing unmet need in cardiometabolic diseases

Sharon Barr

EVP, BIOPHARMACEUTICALS R&D



Uniquely positioned to address risk factors and interconnectedness of cardiometabolic disease



Increasing need for novel mechanisms and combination therapies to address multi-organ and multi-risk factor diseases

Up to 80%
of adults 65+
have two or more
chronic diseases¹

>50%
causes of death
globally by 2040²



Ambition to transform care across cardiometabolic diseases where large unmet need remains



Dyslipidaemia and ASCVD

Eliminate LDL-C as a cardiovascular risk factor

Hypertension

Address hard-to-control hypertension and advance cardiorenal risk reduction

Heart failure and amyloidosis

Drive prevention of end-stage disease

Kidney disease

Prevent or slow kidney failure across entire spectrum of disease

Weight management and diabetes

Reduce or reverse weight-related comorbidities and advance organ protection



2bn¹

c.70% not at LDL-C goal despite statin use²

1.3bn³

c.50% treated remain uncontrolled⁴

300-500k⁵
with 2- to 5-year average mortality post-ATTR-CM diagnosis⁶

Millions across distinct populations

30m | heart failure⁷
>50m | high proteinuria^{8,9}
600m | hypertension^{10,11}

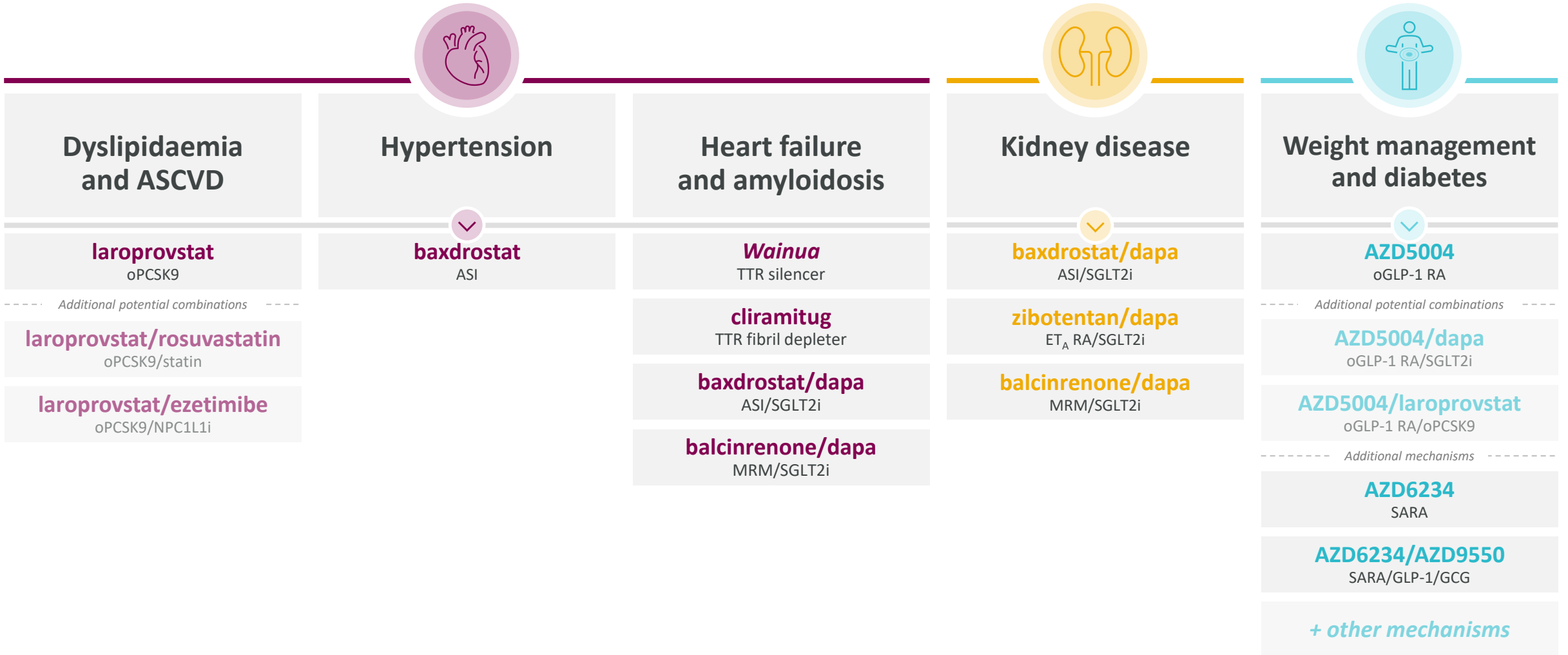
2.5bn¹²

majority of those suffering from obesity and overweight have at least one co-morbidity¹³

1. World Health Organization – Global Health Observatory Raised Cholesterol. 2. World Heart Federation. Cholesterol. 3. World Health Organization – Hypertension Fact Sheet. 4. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*. 2021 Sep 11;398(10304):957-980. doi: 10.1016/S0140-6736(21)01330-1. Epub 2021 Aug 24. 5. Ionis 2024 Annual Report. 6. Nativi-Nicolau JN, Karam C, Khella S, Maurer MS. Screening for ATTR amyloidosis in the clinic: overlapping disorders, misdiagnosis, and multiorgan awareness. *Heart Fail Rev*. 2022 May;27(3):785-793. 7. Lala et AL. The interplay between heart failure and chronic kidney disease; *Diabetes Obes Metab*. 2025;27:3568–3582. 8. LabCorp data. 9. Internal estimates. 10. Foti KE, Wang D, Chang AR, Selvin E, Sarnak MJ, Chang TI, Muntner P, Coresh J. Potential implications of the 2021 KDIGO blood pressure guideline for adults with chronic kidney disease in the United States. *Kidney Int*. 2021 Mar;99(3):686-695. doi: 10.1016/j.kint.2020.12.019. PMID: 33637204; PMCID: PMC7958922. 11. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Kidney Int*. 2019 Nov;96(5):1048-1050. doi: 10.1016/j.kint.2019.07.012. Epub 2019 Sep 30. PMID: 31582227. 12. World Health Organization – Obesity Fact Sheet. 13. TriNetX (US EHR data), November 2020 and Optum claims data. Obesity defined as ICD10 codes E66.0, E66.1, E66.2, E66.8, E66.9. Obesity defined as BMI > 30, Overweight as BMI 25-29.9. Appendix: [Glossary](#).



Addressing unmet need with novel mechanisms and combinations to drive next wave of growth



baxdrostat – potential first-in-class opportunity to set foundation in hard-to-control hypertension

Significant proportion of patients remain uncontrolled





1.3bn patients globally with hypertension¹



c.50% of those treated remain uncontrolled²

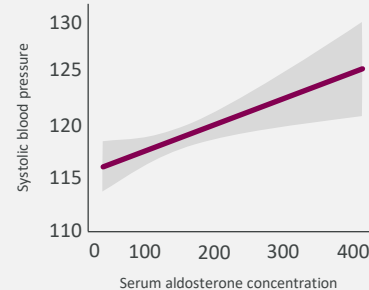
Addressing critical unmet need by targeting aldosterone dysregulation with baxdrostat

Highly selective, potent aldosterone synthase inhibition 

Robust safety and efficacy at low doses 

24-hour control supported by long half-life 

Higher aldosterone leads to higher blood pressure³



Once-daily dosing with no off-target hormonal effects



No clinically relevant drug-drug interactions



Ability to combine while maintaining efficacy at low doses



Early morning hypertension may cause increase in cardiac events

Bax24
H2 2025

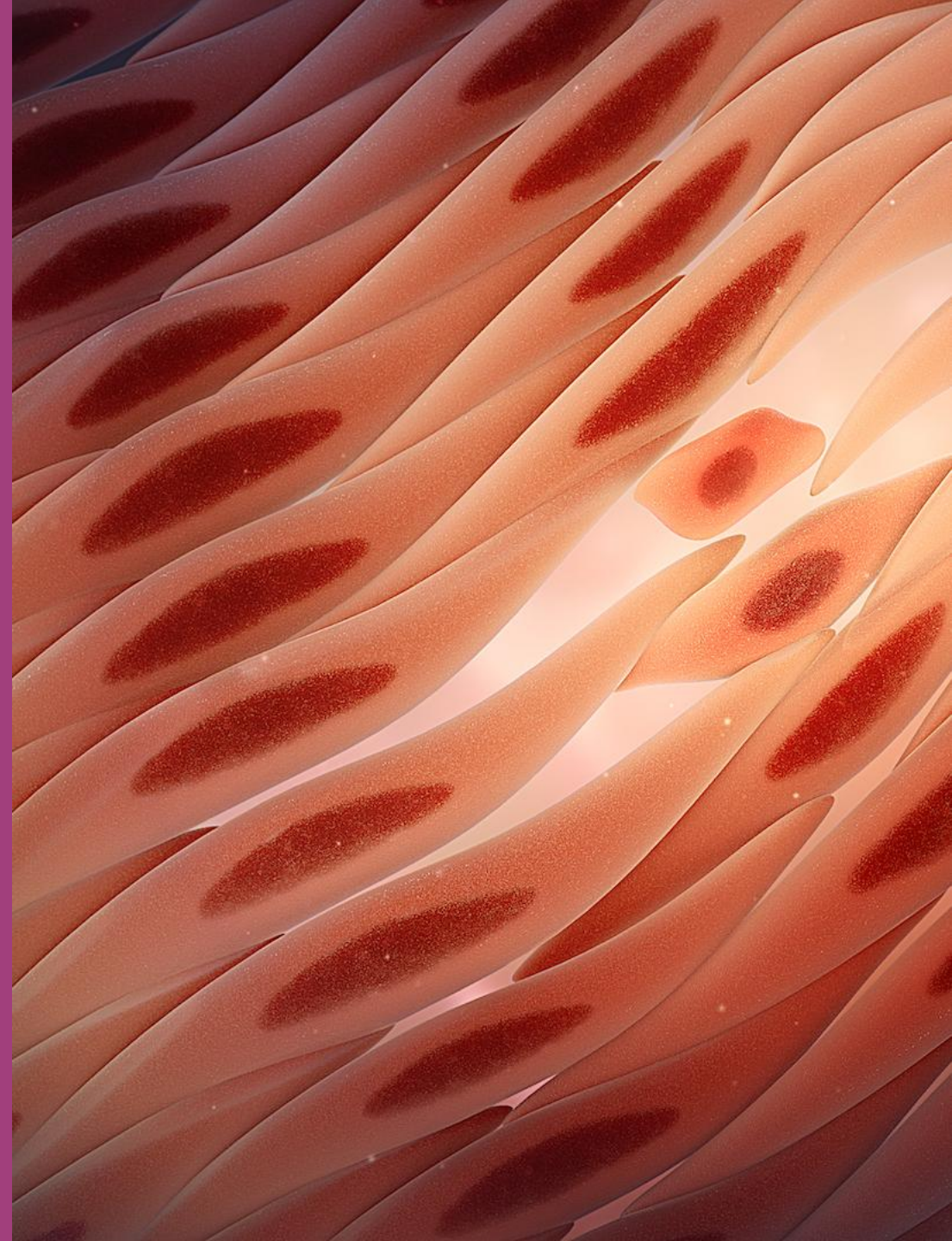
Extended half-life with potential to deliver 24-hour SBP control



baxdrostat – Phase III BaxHTN

Dr Bryan Williams

CHAIR OF MEDICINE,
UNIVERSITY COLLEGE LONDON



Background

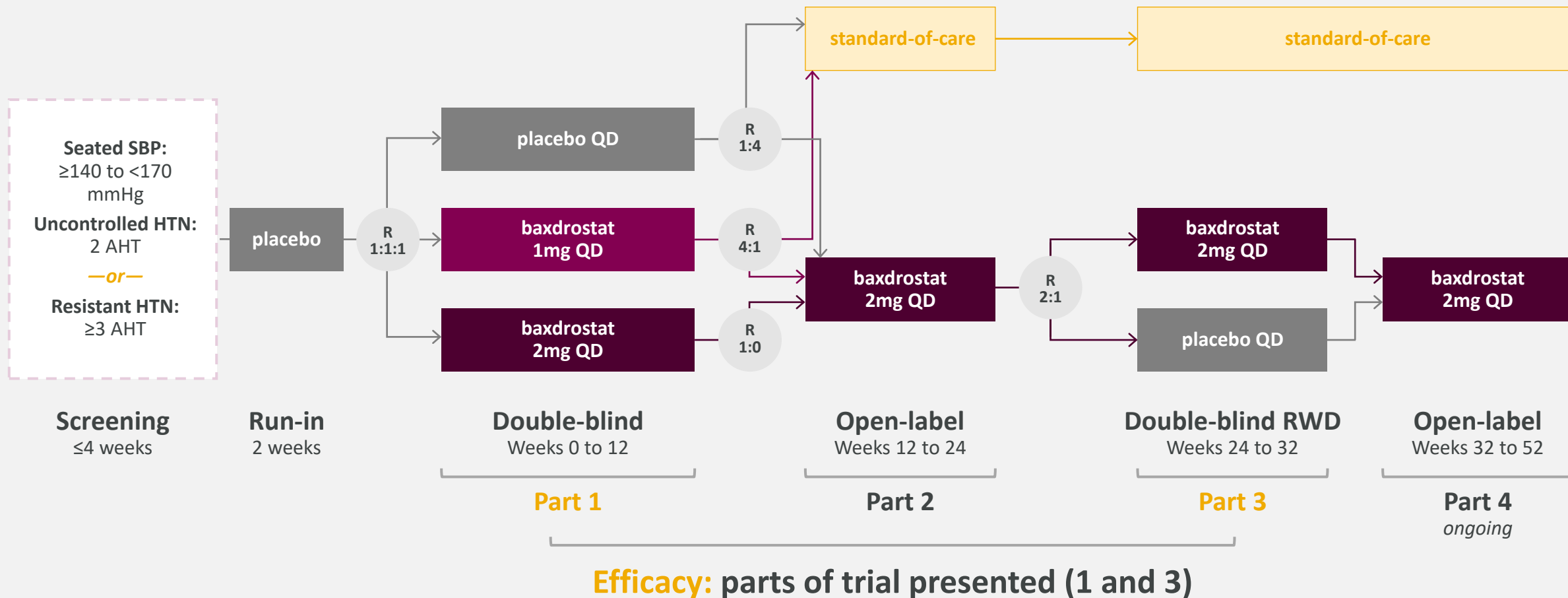
- Patients with uncontrolled and resistant hypertension are at high risk of cardiovascular morbidity and mortality and adverse renal outcomes¹⁻⁴
- Aldosterone dysregulation is a key driver of uncontrolled and resistant hypertension and hypertension-mediated organ damage⁵⁻⁷
- MRAs can block the mineralocorticoid receptor-mediated effects of aldosterone, but their clinical utility is limited by dose-dependent adverse effects⁸
- **baxdrostat is a highly selective and potent aldosterone synthase inhibitor^{9,10}**



BaxHTN Phase III trial objective: assess the efficacy and safety of baxdrostat in patients with uncontrolled or resistant hypertension



Phase III trial design



Trial population



Adults ≥ 18 years of age with uncontrolled or resistant hypertension



Key inclusion criteria

- Mean seated-SBP ≥ 140 and < 170 mmHg despite treatment with maximally tolerated doses of either 2 (uncontrolled HTN) or ≥ 3 (resistant HTN) anti-hypertensive medications, including a diuretic, for ≥ 4 weeks before screening
- eGFR ≥ 45 mL/min/1.73m²
- Serum potassium ≥ 3.5 and < 5 mmol/L



Key exclusion criteria

- Current use of MRAs or potassium-sparing diuretics
- Secondary hypertension (except for obstructive sleep apnoea or primary aldosteronism)
- Uncontrolled diabetes (HbA_{1c} $> 10\%$)
- Cardiovascular or cerebrovascular events within 6 months, or persistent atrial fibrillation

Seated office systolic BP at randomisation ≥ 135 mmHg



Trial endpoints



Primary endpoint: change in seated office systolic BP from baseline to Week 12

- 98% power to detect a mean (SD) difference of 6 (15) mmHg for a change from baseline in seated-SBP at Week 12 in favour of baxdrostat (1mg or 2mg versus placebo)

Secondary endpoints (hierarchical order):

- Change in seated-SBP from **RWD period** baseline (Week 24) to Week 32 (baxdrostat 2mg versus placebo)
- Change from baseline in seated-SBP at Week 12 in the **resistant hypertension subpopulation**
- Change from baseline in **seated-DBP** at Week 12
- **Achieving seated-SBP <130 mmHg** at Week 12

Exploratory endpoints:

- **Serum aldosterone concentrations and plasma renin activity**
- **Mean 24-hour and night-time ambulatory SBP**

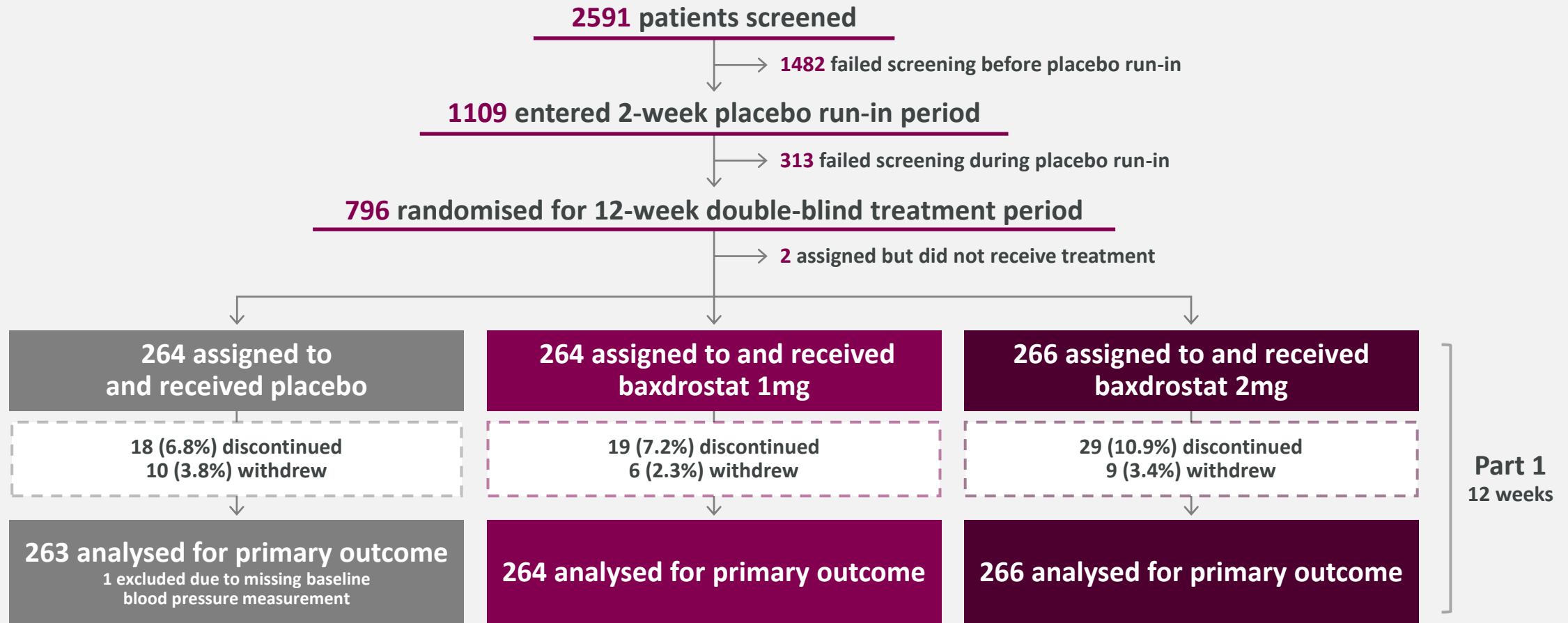
Safety endpoints:

- AEs, vital signs, laboratory tests, and adjudicated major adverse cardiovascular events
- AEs of special interest including hyperkalaemia requiring medical intervention



Trial disposition – primary outcome

12-week double-blind period



Participant characteristics



794 participants
 27% uncontrolled HTN
 73% resistant HTN

- Participants were 62% male and 63% White
 - 26% Asian; 7% Black
- Mean (SD) age was 61 (12) years
- Participants were from:
 - The Americas (27%)
 - Europe (43%)
 - Asia Pacific, Middle East, and Africa (30%)

Characteristic	placebo (n=264)	baxdrostat 1mg (n=264)	baxdrostat 2mg (n=266)
Age, mean ± SD, years	61.9 ± 11.6	59.8 ± 11.8	61.8 ± 11.7
Male sex, n (%)	162 (61.4)	169 (64.0)	163 (61.3)
Race, n (%)¹			
White	167 (63.3)	165 (62.5)	168 (63.2)
Black	15 (5.7)	23 (8.7)	21 (7.9)
Asian	72 (27.3)	65 (24.6)	72 (27.1)
Native Hawaiian or Pacific Islander	1 (0.4)	1 (0.4)	0 (0.0)
Other	9 (3.4)	10 (3.8)	5 (1.9)



Participant characteristics

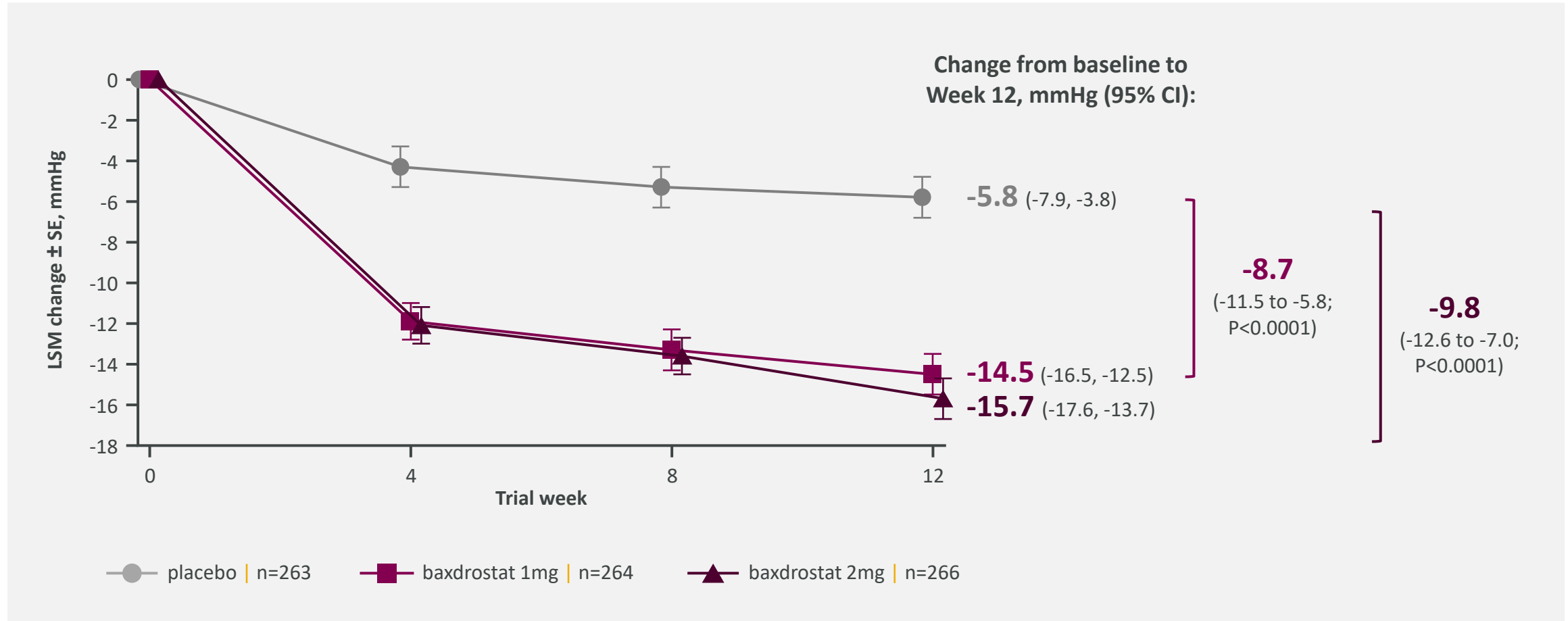
- Clinical characteristics at baseline were similar across treatment arms
- Baseline BP: 149/87 mmHg
 - Median number of background AHT medications: 3 (for each treatment group)
 - Almost all on a diuretic (99.6%)
 - 90% on an ACEi or ARB
 - 70% on a calcium channel blocker
 - 34% on a beta blocker
- 52% had obesity, 38% had diabetes
- Baseline potassium: 4.2 mmol/L
- Baseline eGFR: 85.0 mL/min/1.73m²

Characteristic	placebo (n=264)	baxdrostat 1mg (n=264)	baxdrostat 2mg (n=266)
Seated BP, mmHg*			
Systolic, mean ± SD	149.0 ± 8.7	149.7 ± 10.1	149.1 ± 9.1
Diastolic, mean ± SD	85.8 ± 10.5	88.0 ± 10.5	85.8 ± 10.5
eGFR, mL/min/1.73m²			
Mean	84.1 ± 18.0	86.6 ± 18.5	84.3 ± 17.9
<60, n (%)	29 (11.0)	27 (10.2)	30 (11.3)
Serum sodium, mmol/L			
Mean ± SD	139.6 ± 2.5	139.9 ± 2.6	139.8 ± 2.5
Serum potassium, mmol/L			
Mean ± SD	4.2 ± 0.5	4.2 ± 0.4	4.2 ± 0.4
Serum aldosterone, ng/dL[†]			
Median (IQR)	7.5 (4.2,10.3)	7.9 (4.7, 10.8)	7.2 (4.5, 10.9)
PRA, ng/mL/h[‡]			
Median (IQR)	1.4 (0.6, 4.0)	1.8 (0.7, 4.7)	1.5 (0.6, 5.0)

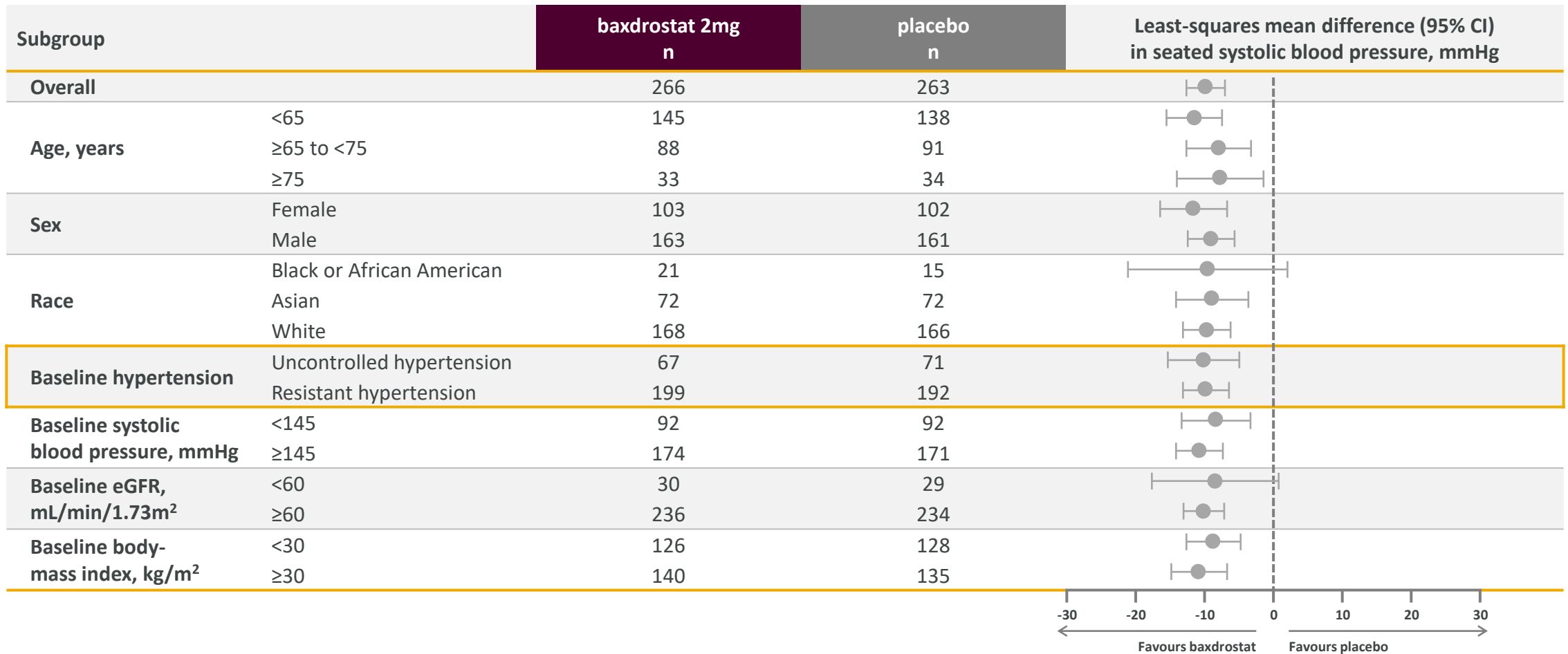


Primary outcome – change in seated-SBP

baxdrostat versus placebo, baseline to Week 12

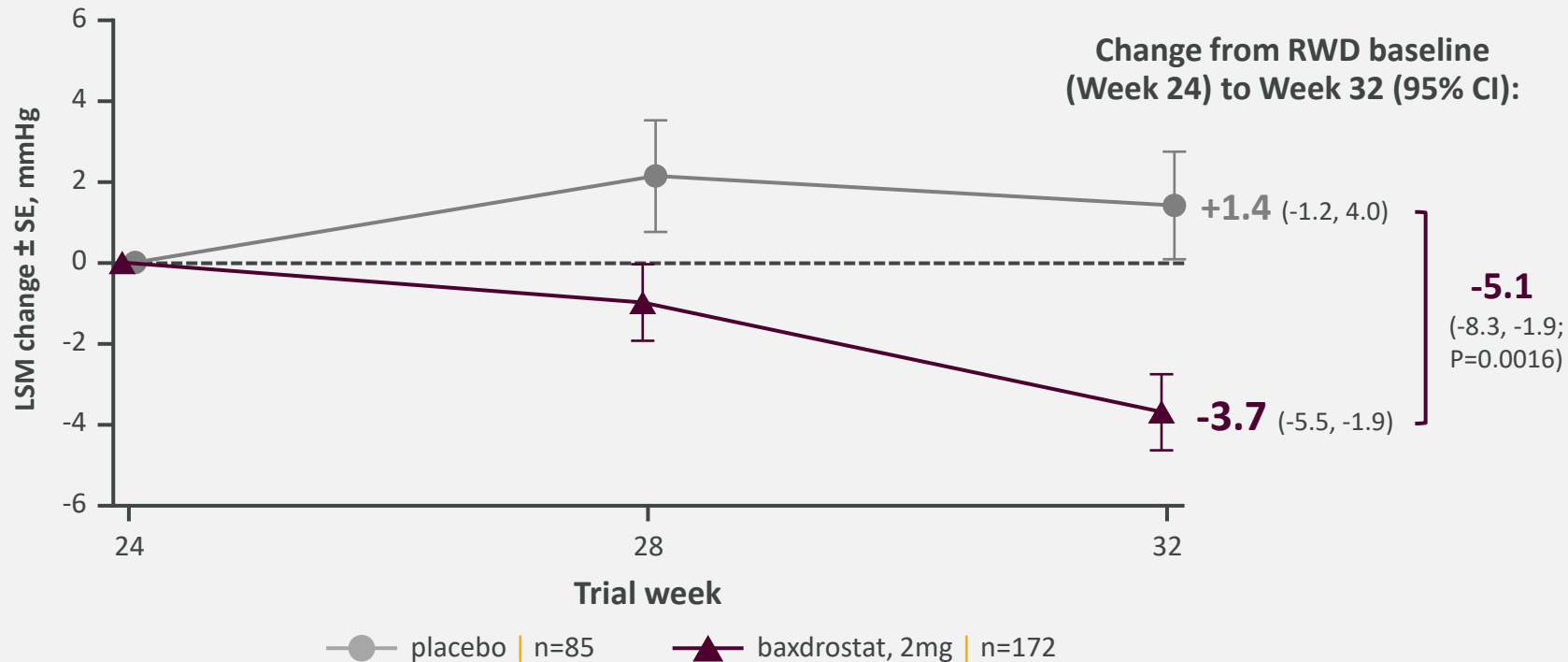


Changes in seated SBP at Week 12 were consistent across all pre-specified subgroups with baxdrostat 2mg



Impact of 8-week randomised withdrawal period of baxdrostat 2mg on seated SBP

Seated-SBP at the start of the RWD period (Part 3): **133 mmHg** in both groups



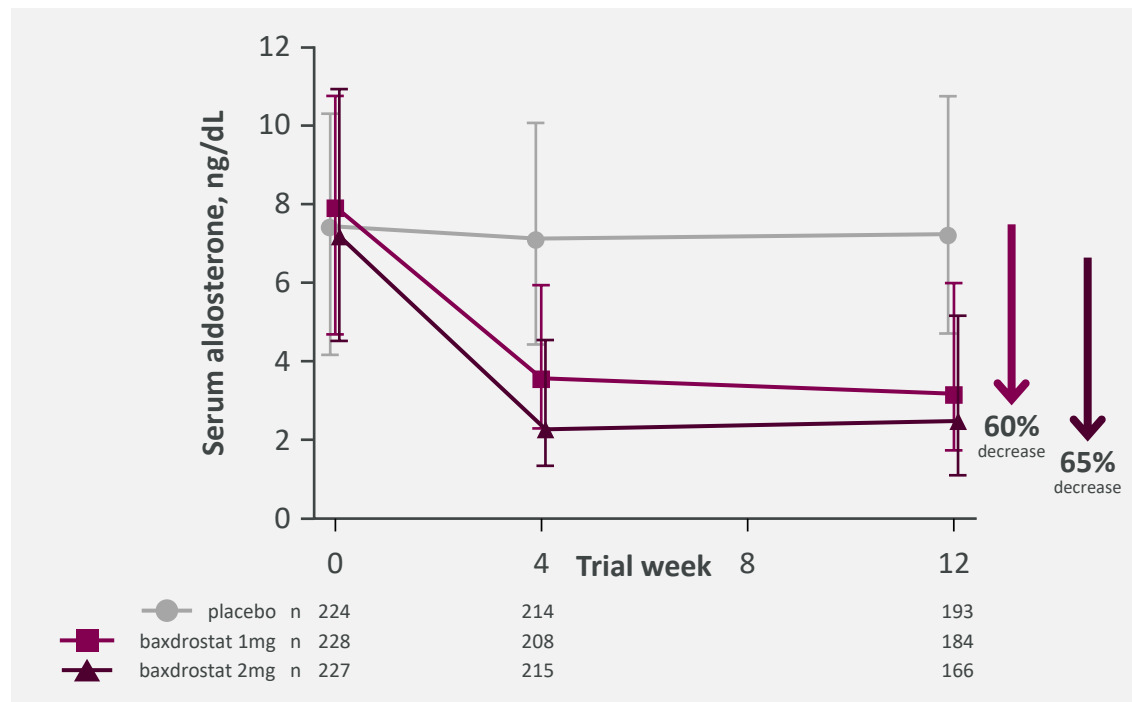
Slow offset of effect on baxdrostat on SBP

Continued BP lowering with baxdrostat 2mg out to 32 weeks

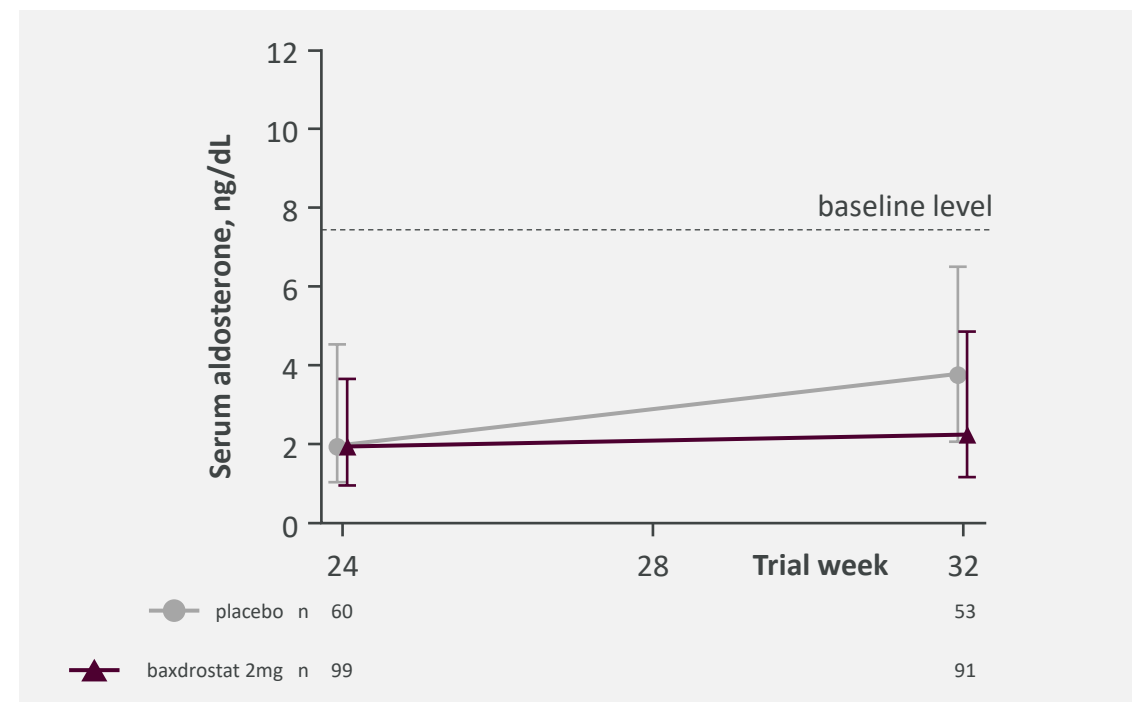


Impact on serum aldosterone concentrations during Part 1 and Part 3 (randomised withdrawal period)

Part 1: double-blind period



Part 3: double-blind RWD period

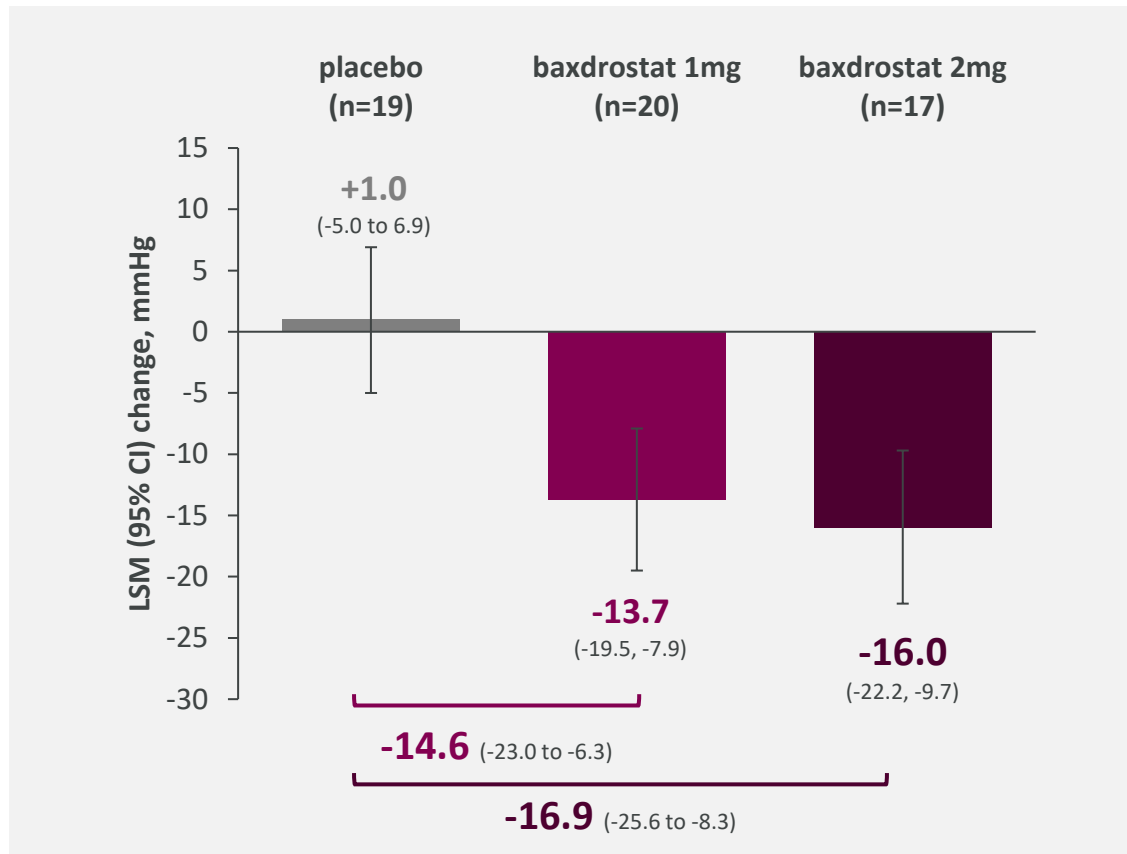


Serum aldosterone concentration (median) decreased from baseline to Week 12 with:
 baxdrostat 1mg from 7.9 to 3.2 ng/dL: 60% decrease | baxdrostat 2mg from 7.2 to 2.5 ng/dL: 65% decrease

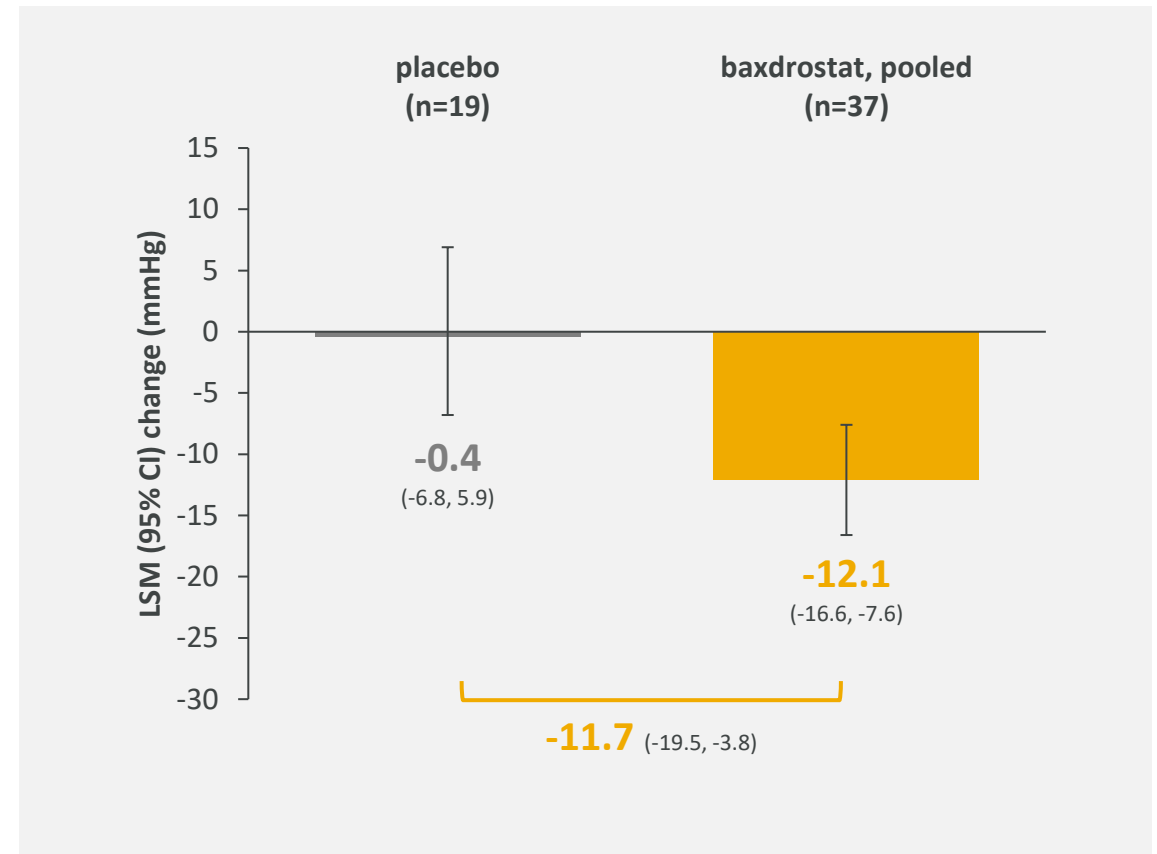


ABPM sub-study – baxdrostat impact on mean 24-hour and night-time SBP versus placebo at Week 12

Ambulatory 24-hour average SBP



Ambulatory night-time average SBP



Safety data – Part 1 to 12 weeks

- AEs were mostly mild
- One death in the placebo group
- No reports of adrenal insufficiency
- Most common AEs – numerically higher for baxdrostat versus placebo:
 - Hyperkalaemia
 - Hyponatraemia
 - Hypotension
 - Muscle spasms
 - Dizziness
- There were low rates of:
 - Confirmed serum potassium >6.0 mmol/L
 - Hyperkalaemia leading to discontinuation

n (%)	placebo (n=264)	baxdrostat 1mg (n=264)	baxdrostat 2mg (n=266)
Any adverse event	109 (41.3)	125 (47.3)	119 (44.7)
Moderate/severe	23 (8.7)	27 (10.2)	37 (13.9)
Severe	5 (1.9)	3 (1.1)	7 (2.6)
Any adverse event leading to discontinuation	5 (1.9)	7 (2.7)	12 (4.5)
Hyperkalaemia leading to discontinuation	0 (0.0)	2 (0.8)	4 (1.5)
Any serious adverse event¹	7 (2.7)	5 (1.9)	9 (3.4)
Death	1 (0.4)	0 (0.0)	0 (0.0)
Adverse event of special interest²			
Hyperkalaemia	0 (0.0)	7 (2.7)	21 (7.9)
Hyponatraemia	1 (0.4)	2 (0.8)	6 (2.3)
Hypotension	2 (0.8)	5 (1.9)	6 (2.3)
Serum potassium – mmol/L			
>5.5 mmol/L	1/260 (0.4)	16/262 (6.1)	29/261 (11.1)
>6.0 mmol/L	1/262 (0.4)	6/262 (2.3)	8/263 (3.0)
Confirmed >6.0 mmol/L ³	0/262 (0.0)	3/262 (1.1)	3/263 (1.1)



Summary

- In participants with uncontrolled or resistant hypertension, the addition of baxdrostat 1mg or 2mg once daily to background anti-hypertensive therapy led to **placebo-adjusted reductions in seated-SBP of 8.7 mmHg and 9.8 mmHg**, respectively, after 12 weeks of treatment
- BP responses were consistent across **all pre-specified subgroups**
- Efficacy of baxdrostat persisted up to **at least 32 weeks**
- **Ambulatory 24-hour and night-time SBP were reduced** substantially with baxdrostat
- baxdrostat was generally **well tolerated**, with no unanticipated safety findings
- Rates of **confirmed serum potassium >6.0 mmol/L** were low (1% in both baxdrostat groups)



The Phase III **BaxHTN** trial demonstrated the efficacy and safety of baxdrostat for reducing BP in a broad population of patients with uncontrolled and resistant hypertension



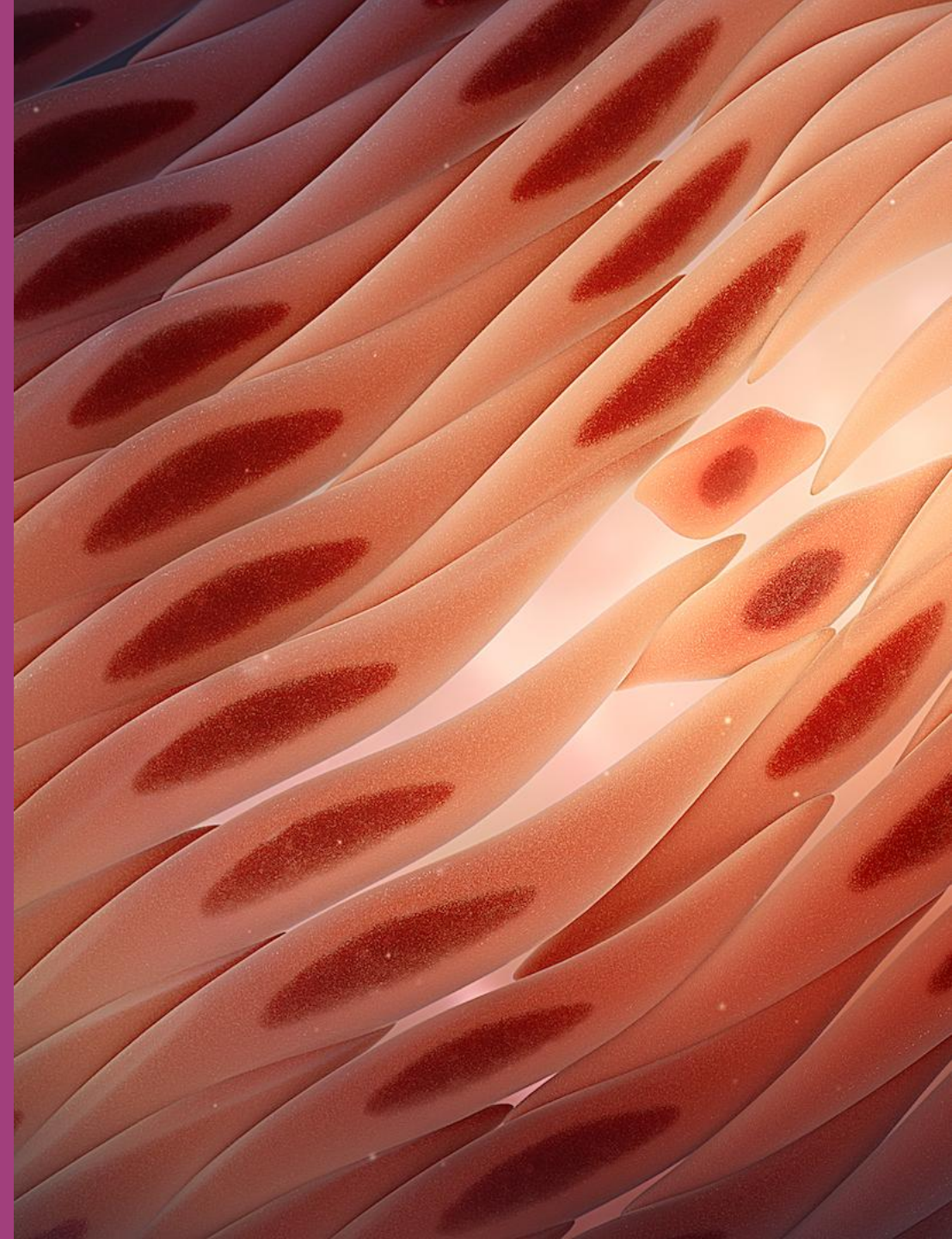
Delivering next-wave of CVRM growth with baxdrostat

Sharon Barr

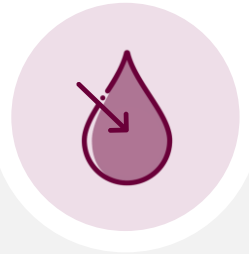
EVP, BIOPHARMACEUTICALS R&D

Ruud Dobber

EVP, BIOPHARMACEUTICALS BUSINESS



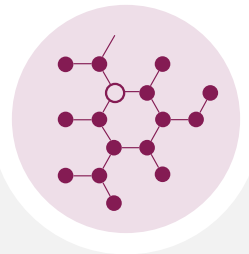
baxdrostat – potential first- and best-in-class aldosterone inhibitor to address hard-to-control hypertension



Largest mmHg reduction reported in primary analysis

Robust Hg reduction in hard-to-control population at Week 12¹

9.8 mmHg reduction with 2mg
8.7 mmHg reduction with 1mg



Differentiated profile

Powerful aldosterone synthase inhibition
with 60-65% plasma aldosterone reduction

Favourable tolerability profile
with no off-target hormonal effects or clinically relevant drug-drug interactions



Additional supportive analyses

Long half-life for potential 24-hour control
BaxHTN encouraging exploratory data
Bax24 trial ongoing | H2 2025



Leveraging existing foundation to transform hard-to-control hypertension globally with baxdrostat

Significant unmet need across regions

US: >20m

2L+ hypertension patients remain uncontrolled

ex-US: >75m

2L+ hypertension patients remain uncontrolled

Maximising strength of AstraZeneca in specialty and primary care to reach more patients with baxdrostat



c.85%

of 2L+ hypertension patients managed by primary care physicians and specialists^{1,2}



primary care



specialist



>90%

of cardiologists and majority of primary care physicians reached with current AstraZeneca CVRM presence^{1,2}



>115

countries currently reached with *Forxiga* and *Lokelma*



\$5bn+ potential with baxdrostat across monotherapy and combination opportunities



Monotherapy

to address aldosterone-driven diseases

BaxHTN

hard-to-control hypertension

Primary and all secondary endpoints met



Bax24

24-hour control in resistant hypertension

H2 2025

BaxPA

primary aldosteronism

Initiating



Combination with dapagliflozin

to transform treatment paradigm and further improve cardiorenal outcomes

BaxDUO-Arctic

CKD and hypertension
(eGFR slope)

BaxDUO-Pacific

CKD and hypertension
(outcomes)

PREVENT-HF

heart failure prevention

Ongoing Phase III with data anticipated >2026



Q&A Session

Key External Expert



Dr Bryan Williams

CHAIR OF MEDICINE,
UNIVERSITY COLLEGE LONDON

AstraZeneca Leadership



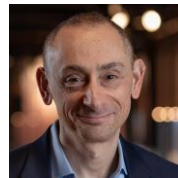
Sharon Barr

EVP, BIOPHARMACEUTICALS R&D



Ruud Dobber

EVP, BIOPHARMACEUTICALS
BUSINESS



Mikhail Kosiborod

SVP, LATE CVRM R&D

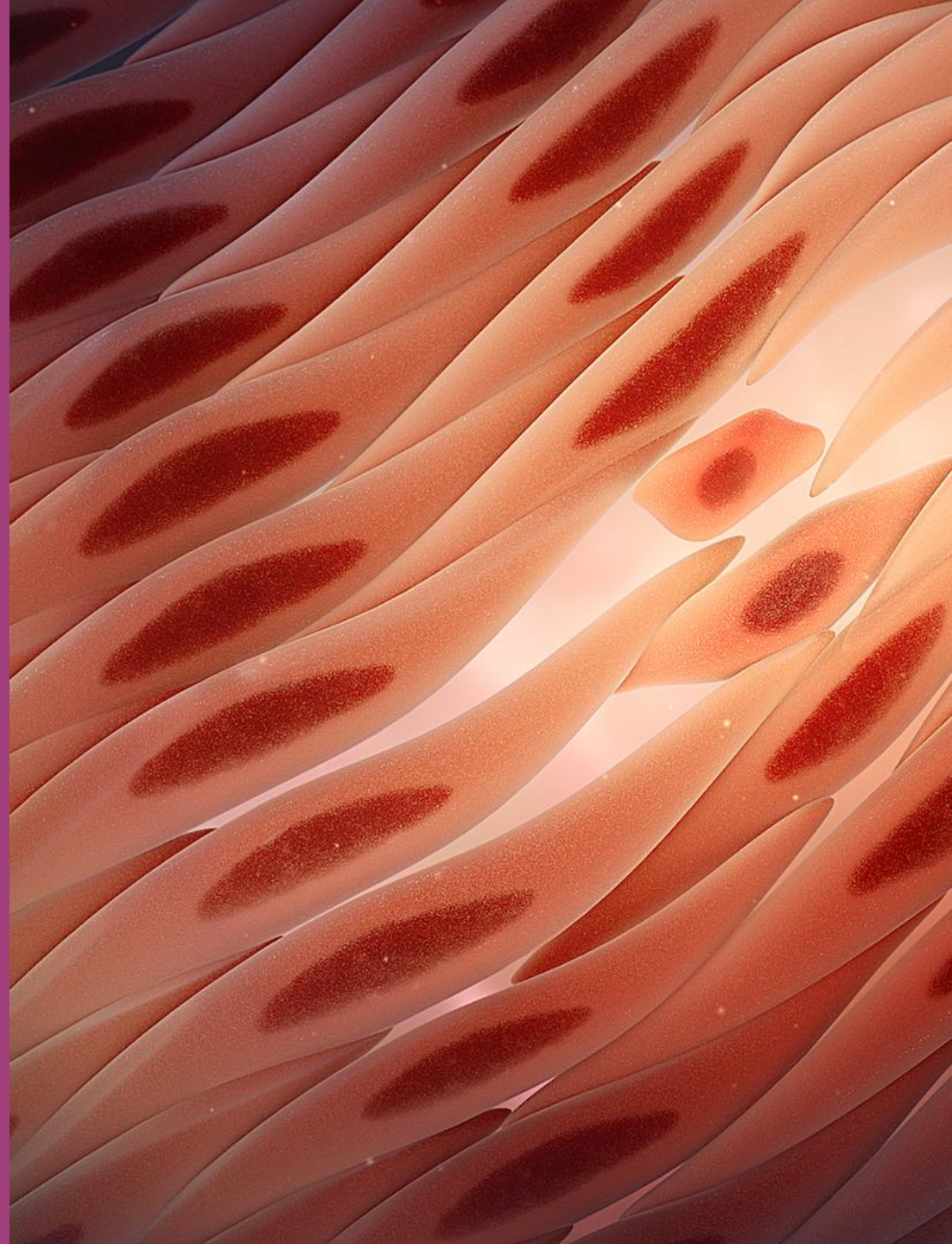


Mina Makar

SVP, GLOBAL CVRM BUSINESS



Appendix



Glossary

2L+	second-line plus
ABPM	ambulatory blood pressure monitoring
ACEi	angiotensin-converting enzyme inhibitor
ADC	antibody-drug conjugate
AE	adverse event
AHT	anti-hypertensive medication
ARB	angiotensin-receptor blocker
ASCVD	atherosclerotic cardiovascular disease
ASI	aldosterone synthase inhibitor
ATTR-CM	transthyretin amyloid cardiomyopathy
BP	blood pressure
CI	confidence interval
CKD	chronic kidney disease
CVRM	cardiovascular, renal and metabolism
DBP	diastolic blood pressure
eGFR	estimated glomerular filtration rate
ESC	European Society of Cardiology
ETA	endothelin A
GCG	glucagon
GLP-1	glucagon-like peptide-1
HbA_{1c}	glycated hemoglobin
hMPV/RSV	human metapneumovirus/respiratory syncytial virus
HTN	hypertension
IO	immuno-oncology

IQR	interquartile range
IRA	Inflation Reduction Act
LDL-C	low-density lipoprotein cholesterol
LSM	least-squares mean
M&A	mergers and acquisitions
MRA	mineralocorticoid receptor antagonist
MRM	mineralocorticoid receptor modulator
NME	new molecular entity
NPC1L1i	Niemann-Pick C1-like 1 protein
oGLP-1	oral glucagon-like peptide-1
oPCSK9	oral proprotein convertase subtilisin/kexin type 9
PRA	plasma renin activity
QD	once-daily
R	randomised
RA	receptor agonist
RWD	randomised withdrawal
SARA	selective amylin receptor agonist
SBP	systolic blood pressure
SD	standard deviation
SE	standard error
SGLT2i	sodium-glucose cotransporter 2 inhibitor
TTR	transthyretin



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