Theravance Biopharma

Ampreloxetine Investor Event

May 23, 2024

Theravance Biopharma®

Medicines That Make a Difference®

Welcome/Opening Remarks

Rick Winningham
Chairman and Chief Executive Officer

Forward Looking Statements

This presentation contains certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives, expectations and future events. Theravance Biopharma, Inc. (the “Company”) intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995.

Examples of such statements include statements relating to: the Company’s expectations regarding its future profitability, expenses and uses of cash; the Company’s goals, designs, strategies, plans and objectives; future growth of YUPELRI sales; future royalty payments; the ability to provide value to shareholders; the Company’s regulatory strategies and timing of clinical studies; safety, efficacy or differentiation of the Company’s product candidates; the status of patent infringement litigation initiated by the Company and its partner against certain generic companies in federal district courts; contingent payments due to the Company from the sale of the Company’s TRELEGY ELLIPTA royalty interests to Royalty Pharma; and expectations around the use of OHSA scores as endpoints for clinical trials. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of this press release and the conference call and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: factors that could increase the Company’s cash requirements or expenses beyond its expectations and any factors that could adversely affect its profitability; whether the milestone thresholds can be achieved; delays or difficulties in commencing, enrolling or completing clinical studies; the potential that results from clinical or non-clinical studies indicate the Company’s product candidates or product are unsafe, ineffective or not differentiated; risks of decisions from regulatory authorities that are unfavorable to the Company; dependence on third parties to conduct clinical studies; delays or failure to achieve and maintain regulatory approvals for product candidates; risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products; risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure; the ability of the Company to protect and to enforce its intellectual property rights; volatility and fluctuations in the trading price and volume of the Company’s shares; and general economic and market conditions.

Other risks affecting the Company are in the Company’s Form 10-Q filed with the SEC on May 15, 2024, and other periodic reports filed with the SEC. In addition to the risks described above and in Theravance Biopharma's filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma’s results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

Presenting KOL Disclosure

Drs. Biaggioni and Kaufmann are members of advisory committees supporting the CYPRESS clinical trial and paid consultants to Theravance Biopharma.

The views and opinions expressed by Drs. Biaggioni and Kaufmann are their own and do not necessarily reflect the views and opinions of Theravance Biopharma.

Agenda

10:00	**Welcome / Opening Remarks**	**Rick Winningham:** Chairman and Chief Executive Officer
10:10	**Neurogenic Orthostatic Hypotension in Multiple System Atrophy**	**Dr. Horacio Kaufmann:** Felicia B. Axelrod Professor of Dysautonomia Research, Department of Neurology at NYU Grossman School of Medicine
10:25	**Ampreloxetine as a Targeted Therapy for nOH in MSA**	**Dr. Italo Biaggioni:** Professor of Medicine and Pharmacology; Director, Vanderbilt Autonomic Dysfunction Center
10:35	**Ampreloxetine: Discovery Through CYPRESS Design and Execution**	**Dr. Áine Miller:** Senior Vice President, Head of Development
11:00	**Opportunity Analysis**	**Rhonda Farnum:** Senior Vice President, Chief Business Officer
11:10	**Closing Remarks / Q&A**	**Rick Winningham / All Presenters**

Theravance:
Built to Deliver Value

Theravance Biopharma aims to transform the treatment of specialty respiratory and neurologic diseases by developing and commercializing *Medicines that Make a Difference®* in patients' and caregivers' lives

Commercial Stage Company with Phase 3 Data in 2025

YUPELRI® revefenacin inhalation solution

Only FDA-approved, once-daily, nebulized LAMA maintenance medicine for COPD

Theravance hospital team co-promotes with VIATRIS™ community team (35% / 65% profit split)[1]

Last twelve months' US net sales of $229M (+12% Y/Y), with expanding margins[1]

Ampreloxetine

First-in-class norepinephrine transporter (NET) inhibitor for nOH in MSA

Top line Phase 3 data anticipated in 2025

Financial Strength

$100M cash and no debt[2]

Nearly $400M in potential future milestones plus royalties through partnerships

1. In the US, Viatris is leading the commercialization of YUPELRI, and Theravance Biopharma co-promotes the product under a profit and loss sharing arrangement (65% to Viatris; 35% to Theravance Biopharma). 2. Refer to our SEC filings for further information. COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic agent; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

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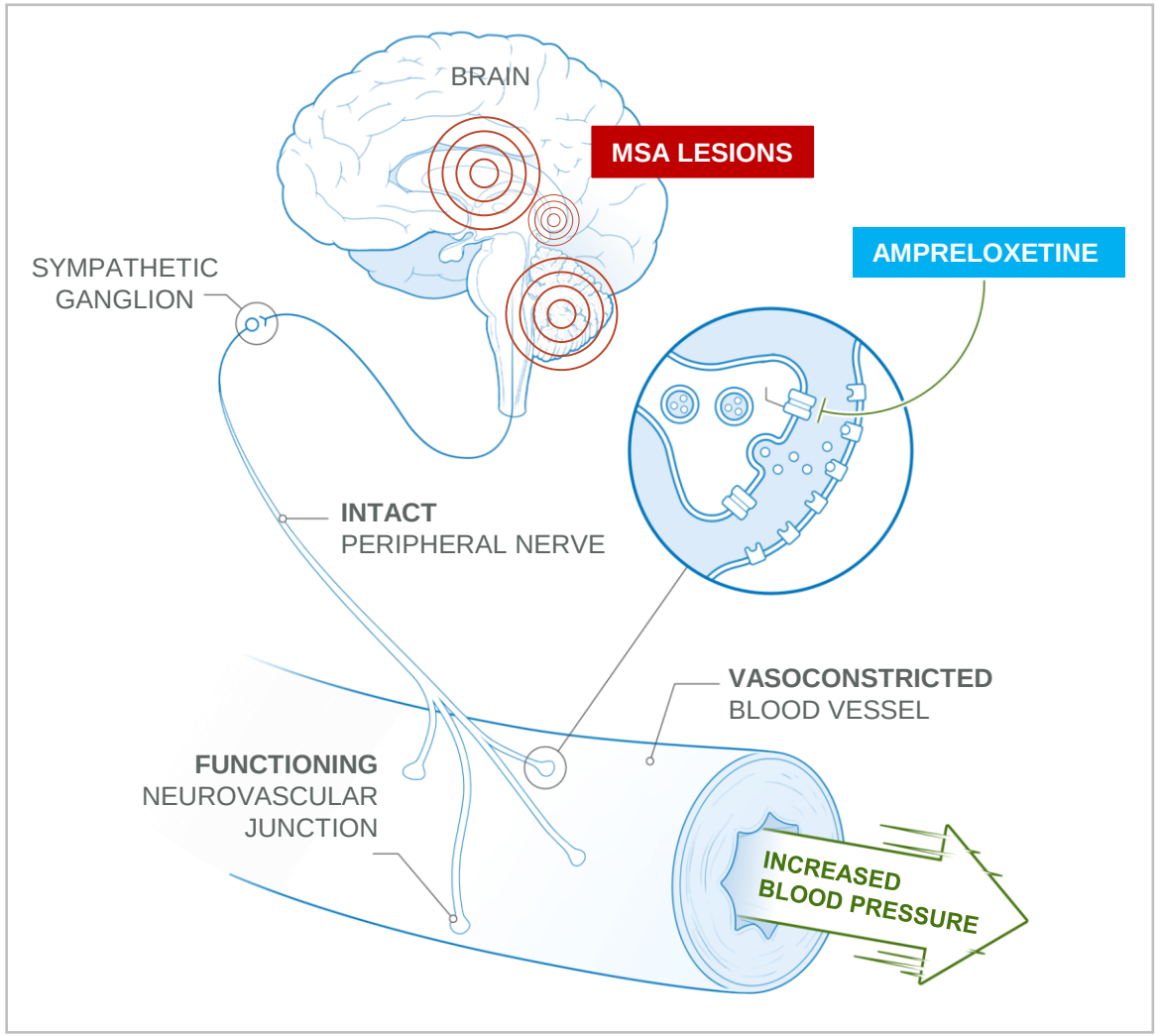
Ampreloxetine: a first in class NET inhibitor for nOH in MSA



Multiple System Atrophy (MSA) is a devastating, incurable neurodegenerative disease

MSA is caused by central nervous system degeneration associated with abnormal accumulation of a protein known as alpha-synuclein

Neurogenic Orthostatic Hypotension (nOH) is a frequent and often debilitating complication of MSA

Loss of autonomic signaling in MSA patients causes persistently low blood pressure upon standing, leading to significant symptom burden

NET inhibition is uniquely-suited to address nOH in MSA

Ampreloxetine, a selective NET inhibitor, increases NE delivery by intact peripheral nerves, improving vascular tone and mitigating symptoms of nOH

NE, norepinephrine; NET, norepinephrine transporter.

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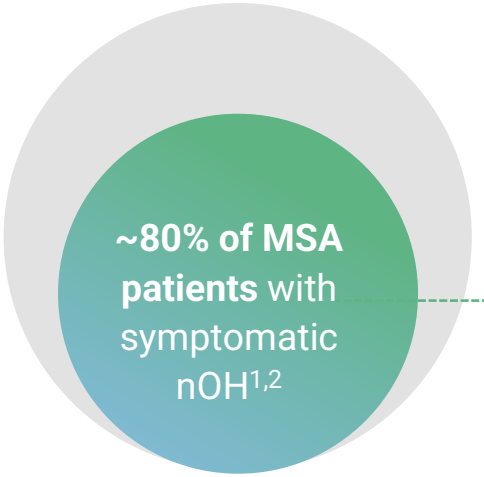
The Significant Unmet Need in nOH in MSA

40,000 MSA patients suffer from symptomatic nOH in the US

Ampreloxetine's addressable population:



~40K
MSA Patients w/ nOH

Treatment alternatives are significantly lacking

- Approved treatments have not demonstrated durable symptom benefits in well-controlled studies
- Commonly prescribed therapies carry significant risk of worsening supine blood pressure
- Population remains sub-optimally treated

Ampreloxetine appears safe and well-tolerated, with durable symptom benefits

- No observed signal for worsening supine hypertension
- Sustained benefits in MSA patients with nOH out to 22 weeks[3]

1. Kalra DK, et al. Clin Med Insights: Cardiol. 2020 (70%-90%);14:1179546820953415. 2. Delveinsight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy, CJ Mathias (1999). 3. Data from MSA patients at week 6 of the randomized withdrawal period of study 0170.
MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension

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Neurogenic Orthostatic Hypotension in Multiple System Atrophy

Horacio Kaufmann, MD FAAN
The F. B. Axelrod Professor of Neurology and Professor of Medicine at NYU Grossman School of Medicine

NYU Langone MEDICAL CENTER

Addressing the unmet need in nOH in MSA

Multiple System Atrophy

MSA is a debilitating disease that severely impairs the autonomic nervous system and causes neurogenic orthostatic hypotension (nOH)

Current standard of care in nOH in MSA

None of the drugs CURRENTLY available for nOH works well in patients with MSA

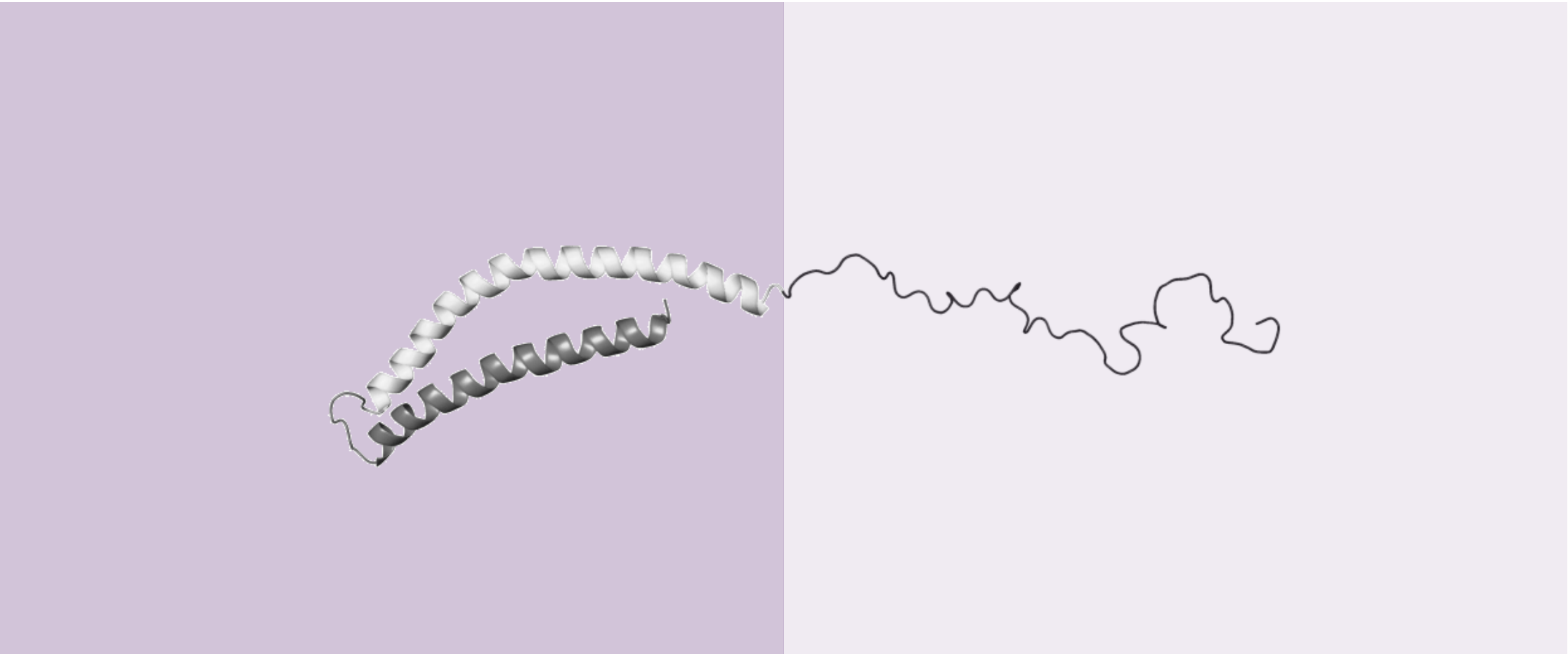
High unmet need

There is an urgent need for an effective treatment that can help these patients

Hope for patients

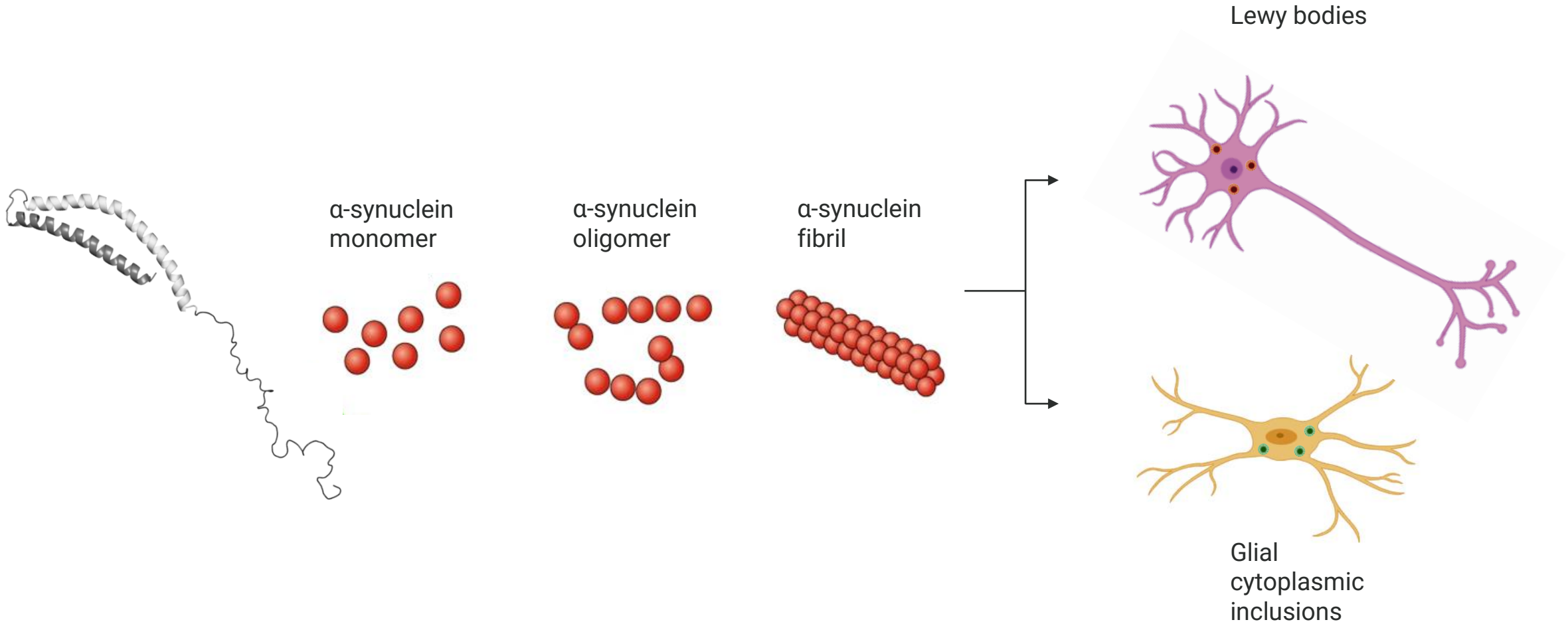
We now have an effective drug tailored for nOH in MSA

Synucleinopathies are caused by the abnormal buildup of the protein synuclein



Yu, 2020.

Synucleinopathies are caused by the abnormal buildup of the protein synuclein



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CNS synucleinopathies

Multiple System Atrophy (MSA)

Dementia with Lewy Bodies (DLB)

Parkinson's Disease (PD)

MSA is rare and rapidly-progressive

~50K patients in the United States

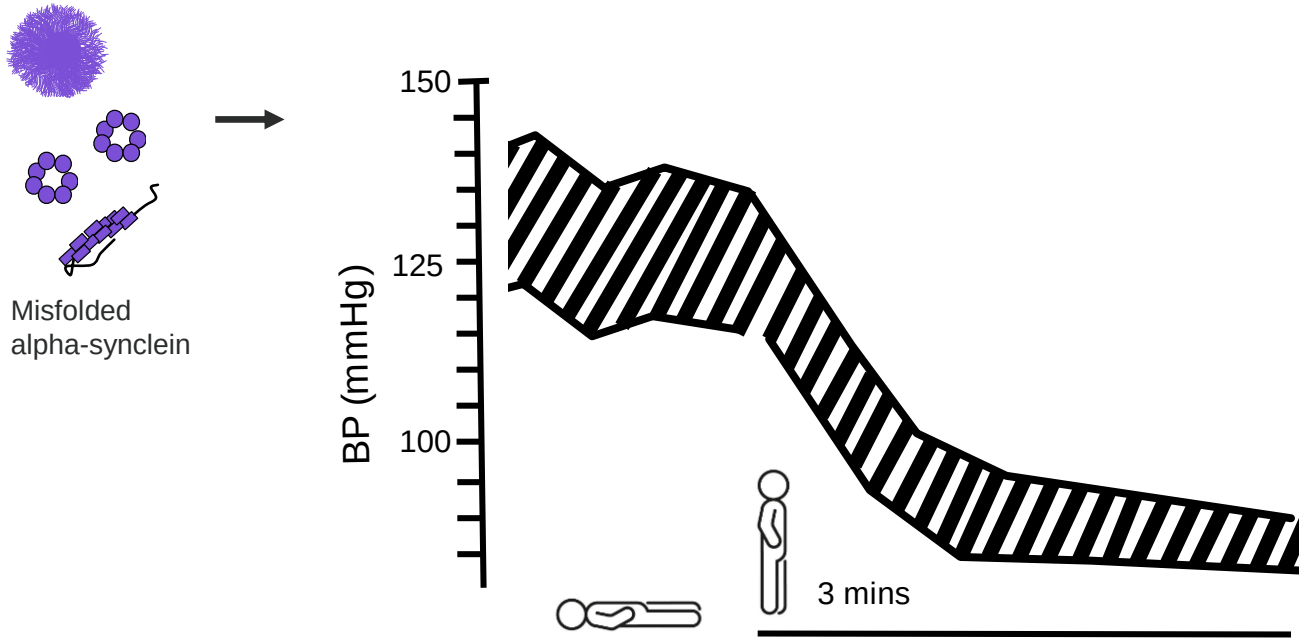
Severely impairs autonomic and motor functions

Average symptom onset in the sixth decade

Median survival is ~ 8 years

Abbreviations: MSA, multiple system atrophy.

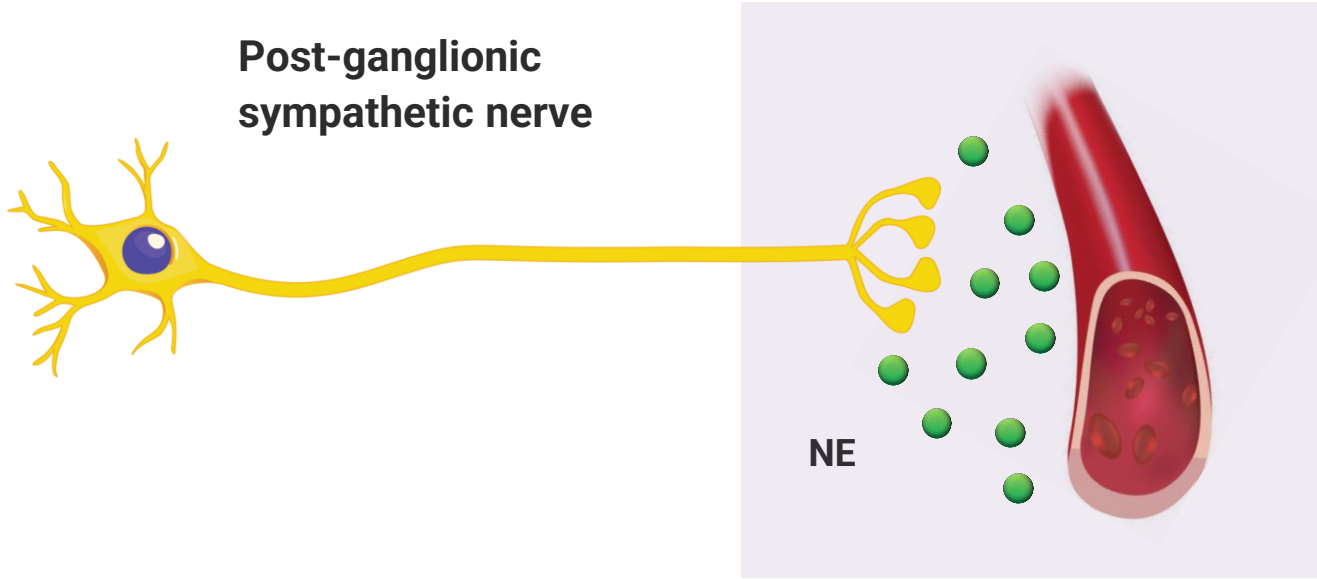
Neurogenic orthostatic hypotension (nOH)



- Occurs on standing
- Gravitational pooling of blood
- Blood pressure fall
- Caused by failure to release norepinephrine and insufficient vasoconstriction

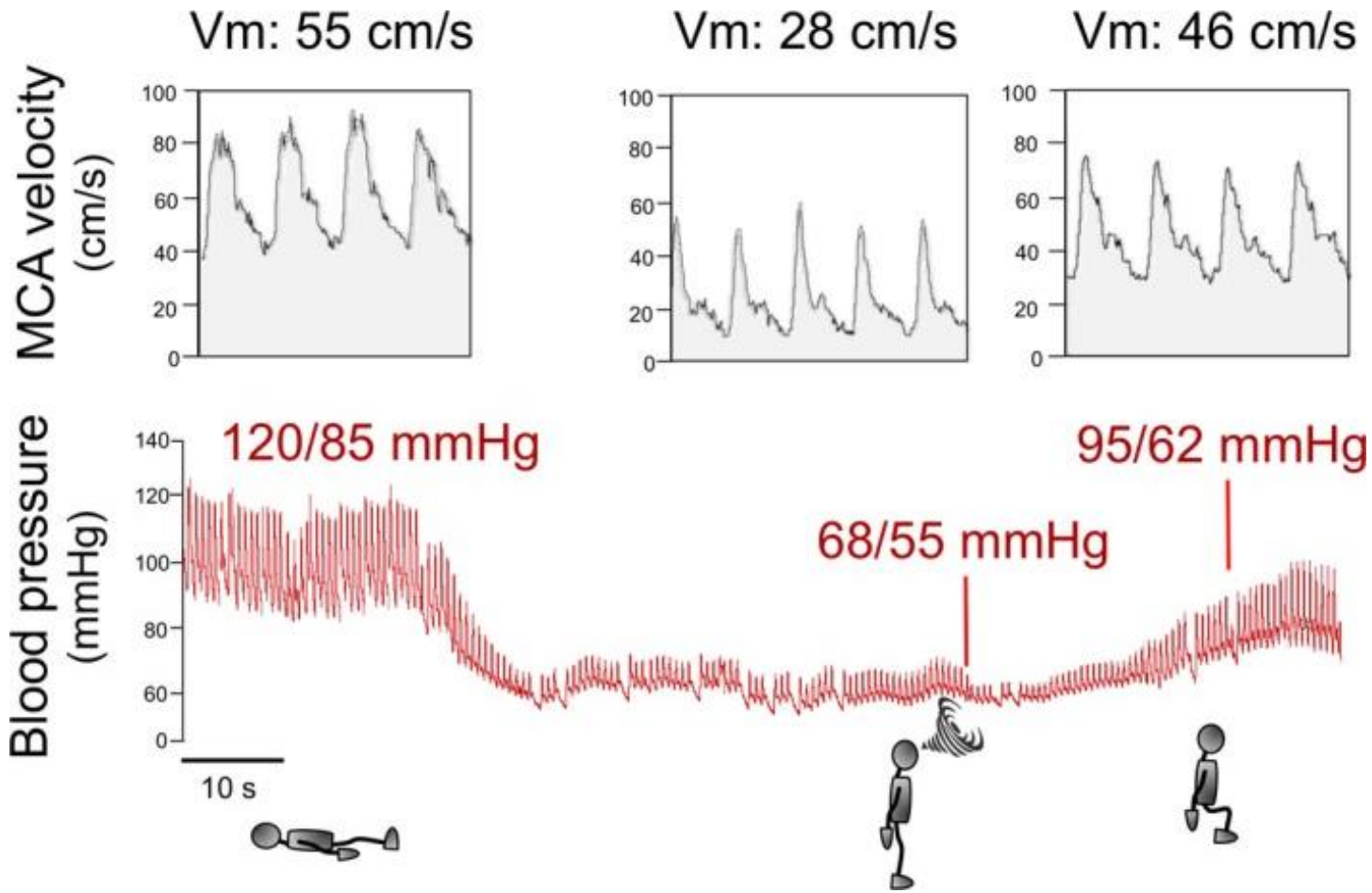
Abbreviations: BP, blood pressure; mmHg, millimeters of mercury.

Neurogenic orthostatic hypotension (nOH), cont.



Adapted from Palma JA, Kaufmann H. Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension. Mov Disord Clin Pract. 2017 May-Jun;4(3):298-308. Abbreviations: NE, norepinephrine.

Symptomatic orthostatic hypotension causes organ hypoperfusion



Palma JA, Kaufmann H. Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension. Mov Disord Clin Pract. 2017 May-Jun;4(3):298-308.
Abbreviations: MCA, middle cerebral artery; Vm, MCA velocity; mmHg, millimeters of mercury.

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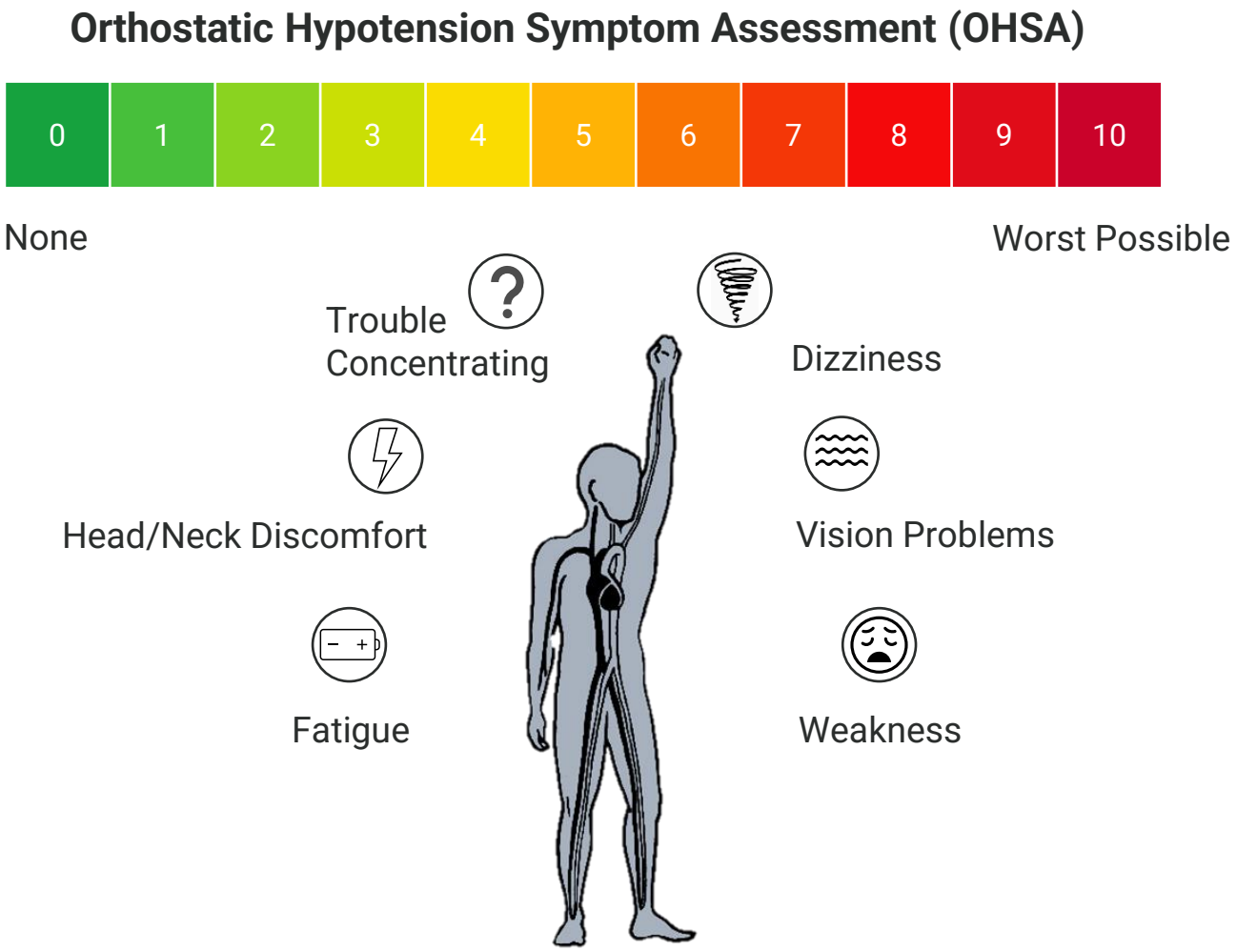
Symptoms of nOH are debilitating, persistent, and measurable



OHSA: patient reported measure of broad symptom burden of nOH

- Questionnaire called the OHQ
- Validated
- Accepted by the FDA as an outcome measure for drug approval
- 1 point change considered clinically meaningful

Abbreviations: nOH, neurogenic orthostatic hypotension; OHQ, orthostatic hypotension questionnaire.

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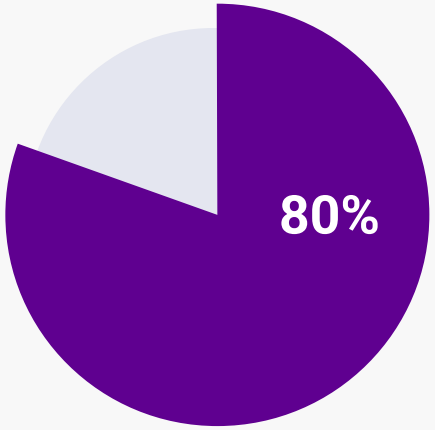
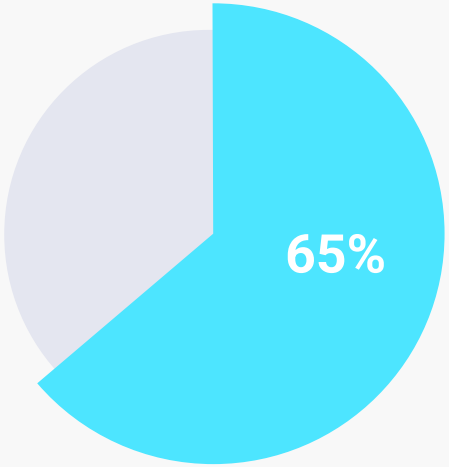
Symptomatic nOH is very frequent in MSA



80% of MSA patients suffer from symptoms of nOH



65% of MSA patients remain symptomatic despite treatment

MSA Natural History Statistics, NYU September 2019. Abbreviations: MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

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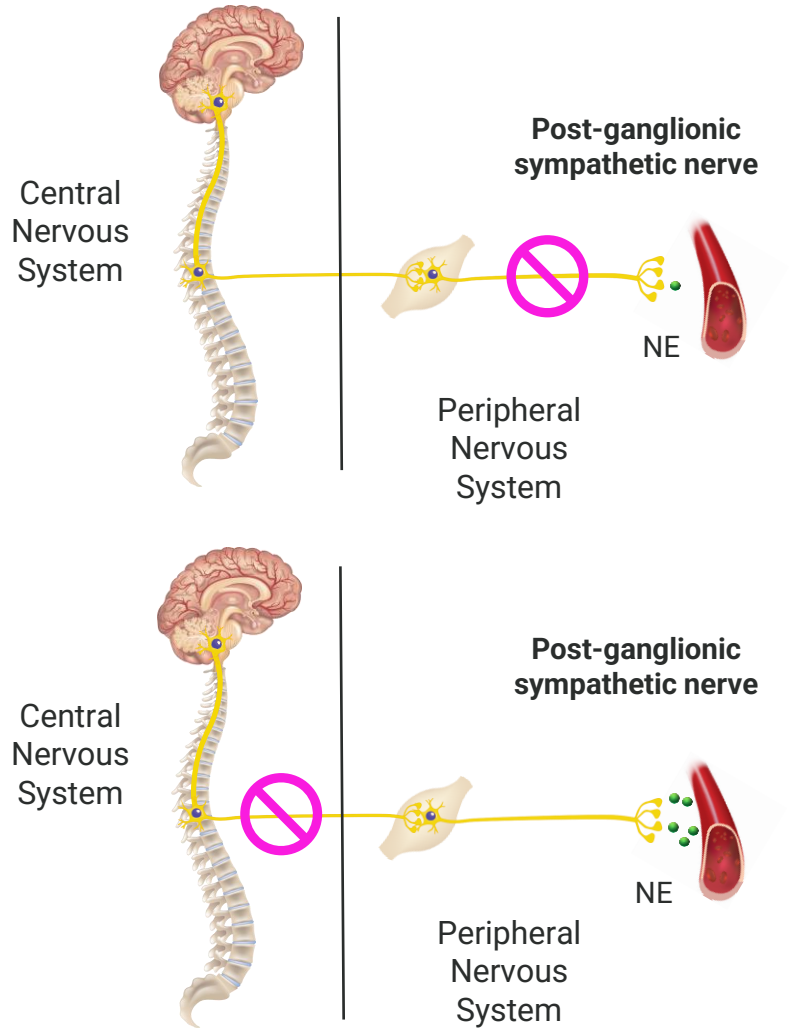
Commonly used therapies for nOH offer limited benefits

Fludrocortisone	Midodrine	Droxidopa
Off label use / not approved Raises supine blood pressure greater than standing	Modest efficacy: most patients remain symptomatic 3x/day dosing	Not effective in MSA based on meta-analysis Titrated, 3x/day dosing

Abbreviations: MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

Post-ganglionic sympathetic nerves are spared in MSA



Parkinson's Disease, Dementia of Lewy Body

Multiple System Atrophy

Abbreviations: MSA, multiple system atrophy; NE, norepinephrine

Ampreloxetine as a Targeted Therapy for nOH in MSA

Dr. Italo Biaggioni

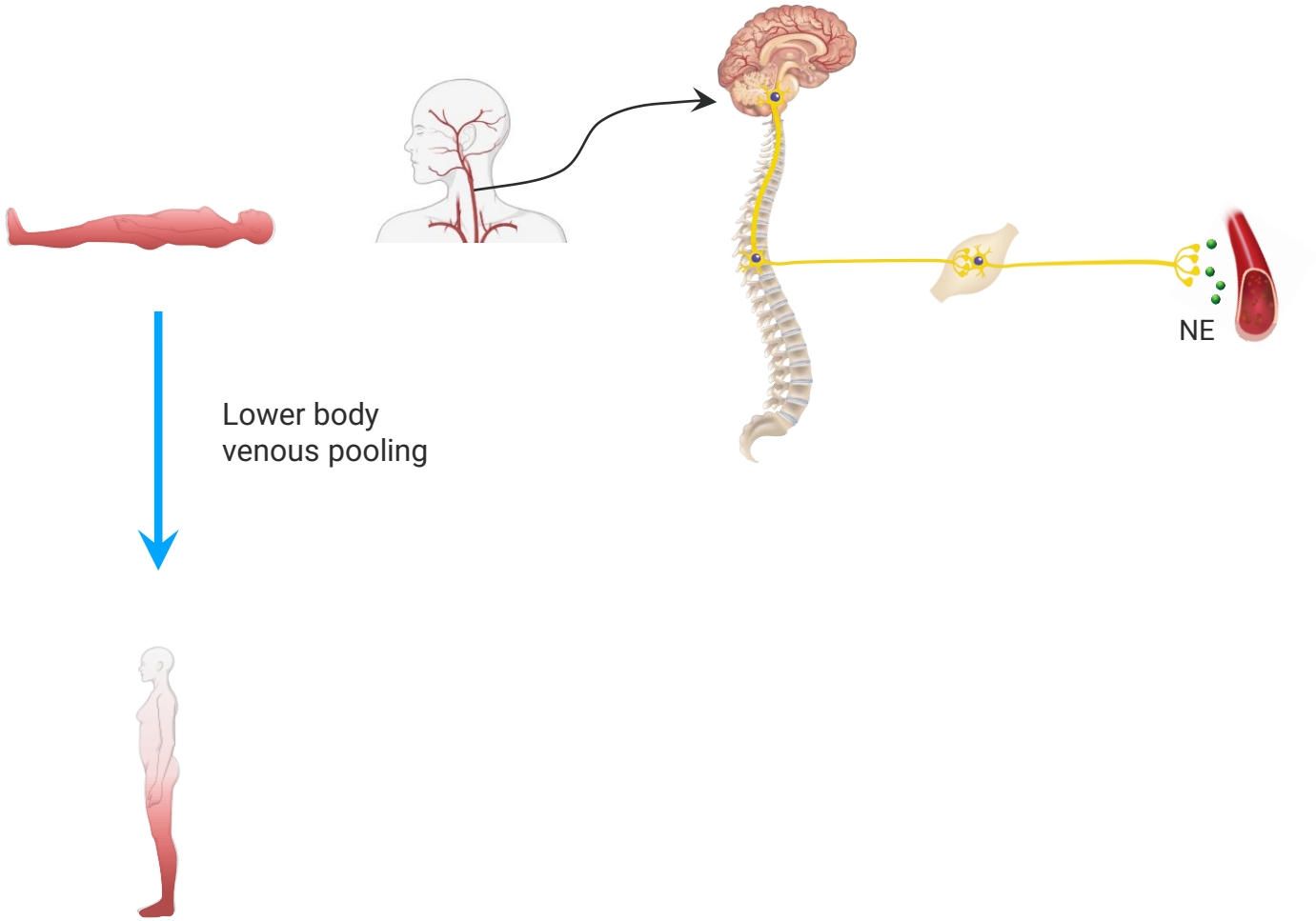
Professor of Medicine, Division of Clinical Pharmacology at Vanderbilt University Medical Center

David Robertson Professor of Autonomic Disorders

Director, Autonomic Dysfunction Center

Vanderbilt Autonomic Dysfunction Center

Increased NE “delivery” prevents hypotension upon standing



Upon standing, there is gravitational volume shifts, with pooling of blood in the lower body

NE, norepinephrine.

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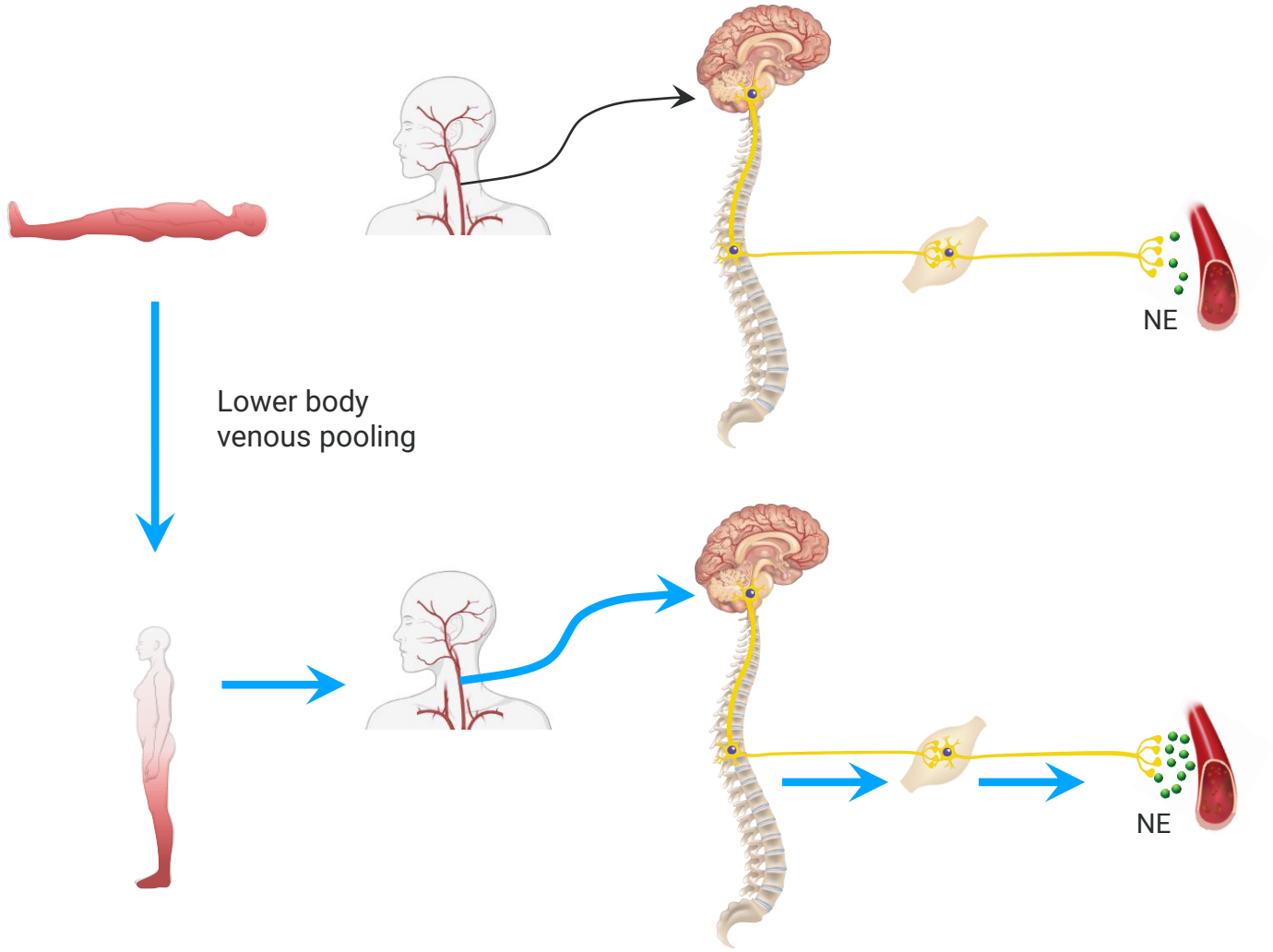
Increased NE “delivery” prevents hypotension upon standing



Upon standing, there is gravitational volume shifts, with pooling of blood in the lower body

This is sensed by baroreceptors, which trigger compensatory sympathetic activation

NE, norepinephrine.

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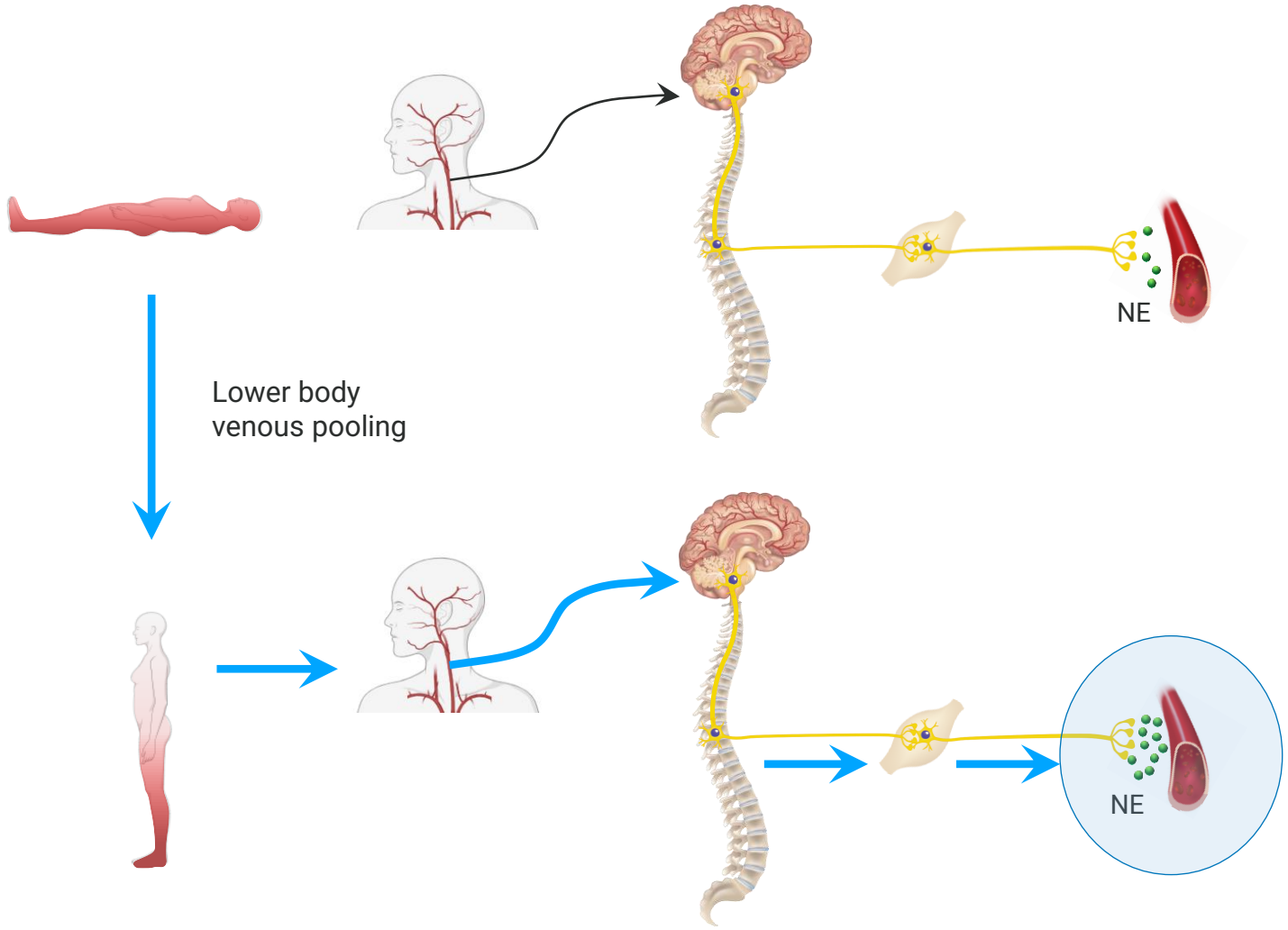
Increased NE “delivery” prevents hypotension upon standing



Upon standing, there is gravitational volume shifts, with pooling of blood in the lower body

This is sensed by baroreceptors, which trigger compensatory sympathetic activation

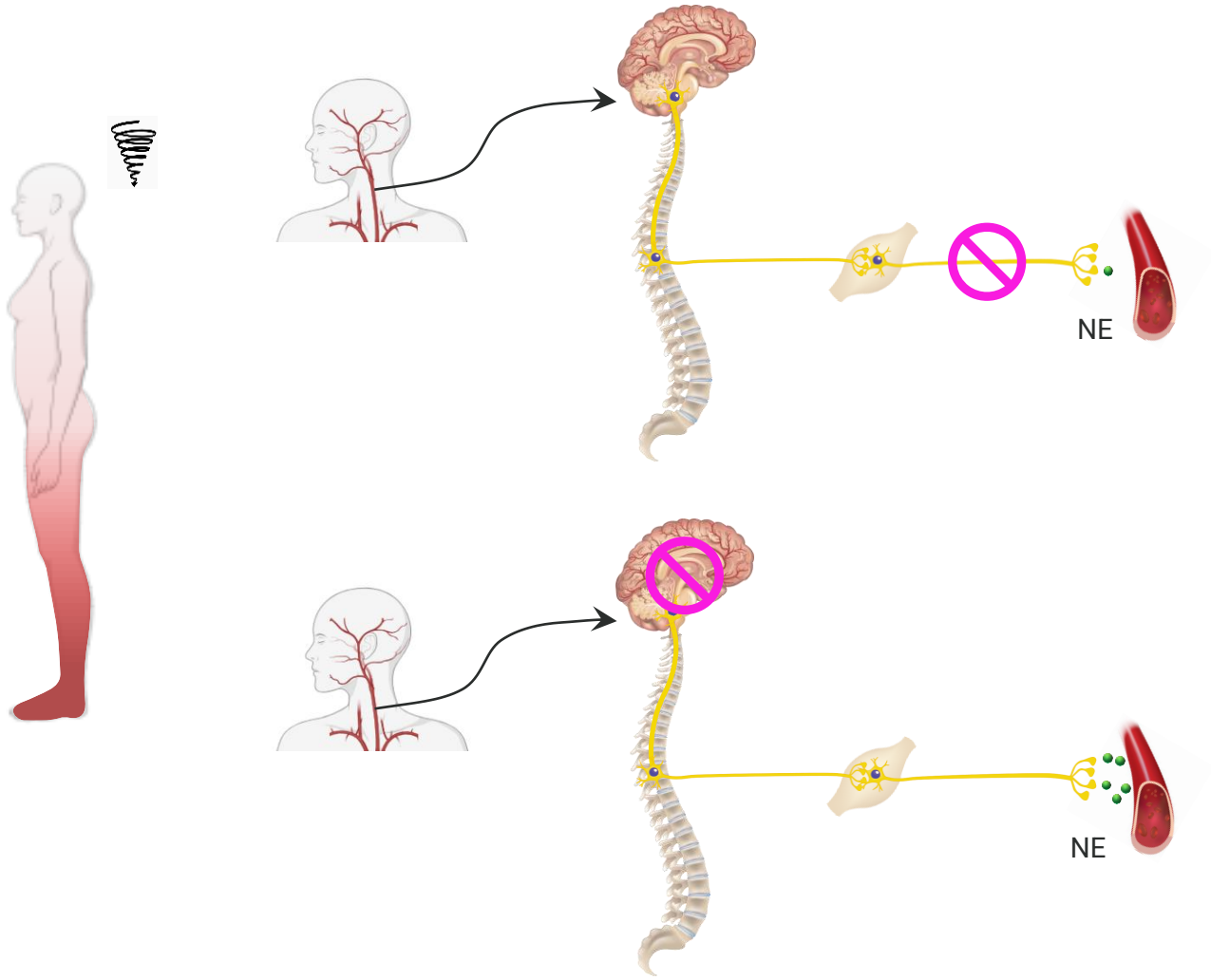
NE is released from sympathetic noradrenergic neurons and acts on receptors in the vascular system….

… to restore stroke volume, increase heart rate, and maintain blood pressure

Plasma NE ~doubles
Supine: 220 pg/ml
Standing: 480 pg/ml

NE, norepinephrine.

Neurogenic OH is a failure of NE delivery because of…



Peripheral loss of noradrenergic pathways:
Parkinson's Disease, Dementia of Lewy Body,
Pure Autonomic Failure

Central loss of autonomic regulation:
Multiple System Atrophy

NE, norepinephrine.

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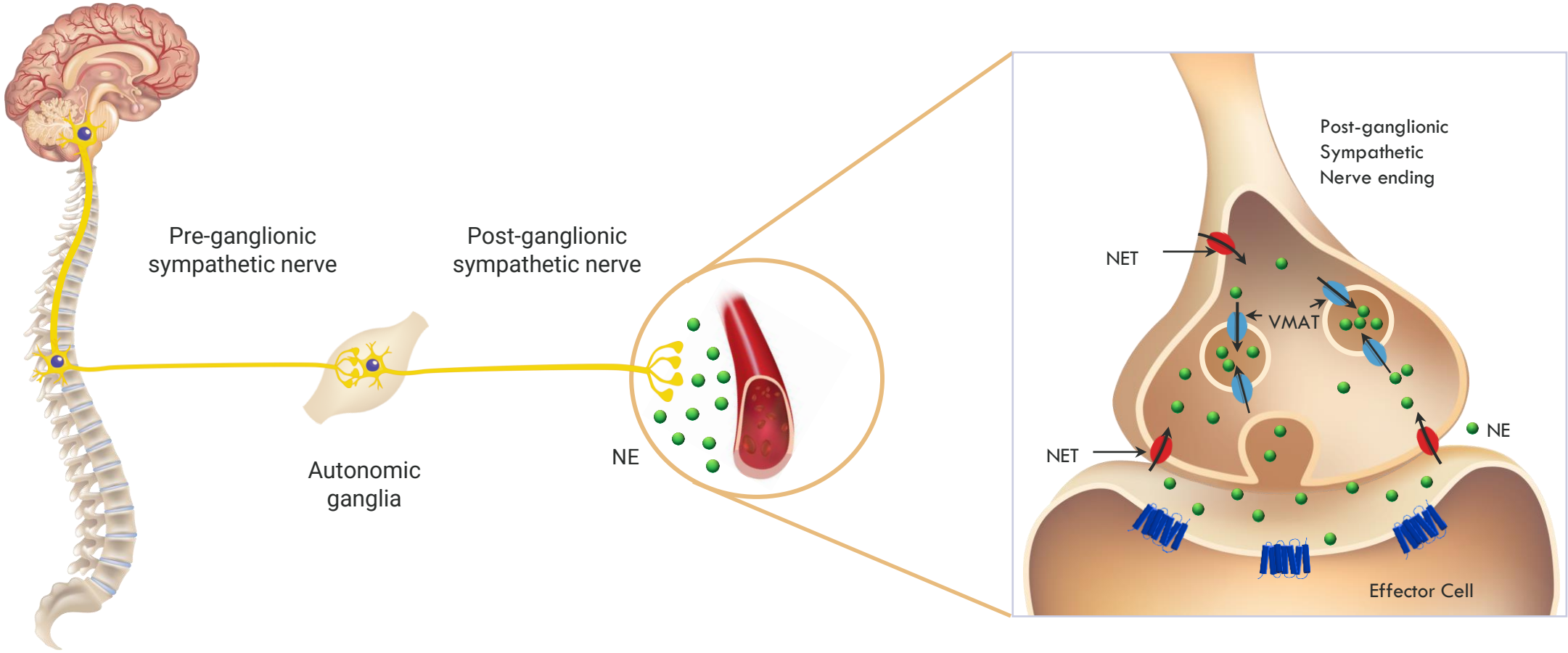
Therefore, NE is essential to sympathetic cardiovascular regulation



Post-ganglionic sympathetic neurons rely on NE to regulate cardiovascular tone

NE, norepinephrine; NET, norepinephrine transporter; VMAT, vesicular monoamine transporter.

Increasing NE “delivery” via reuptake (NET) blockade

Sympathetic activation

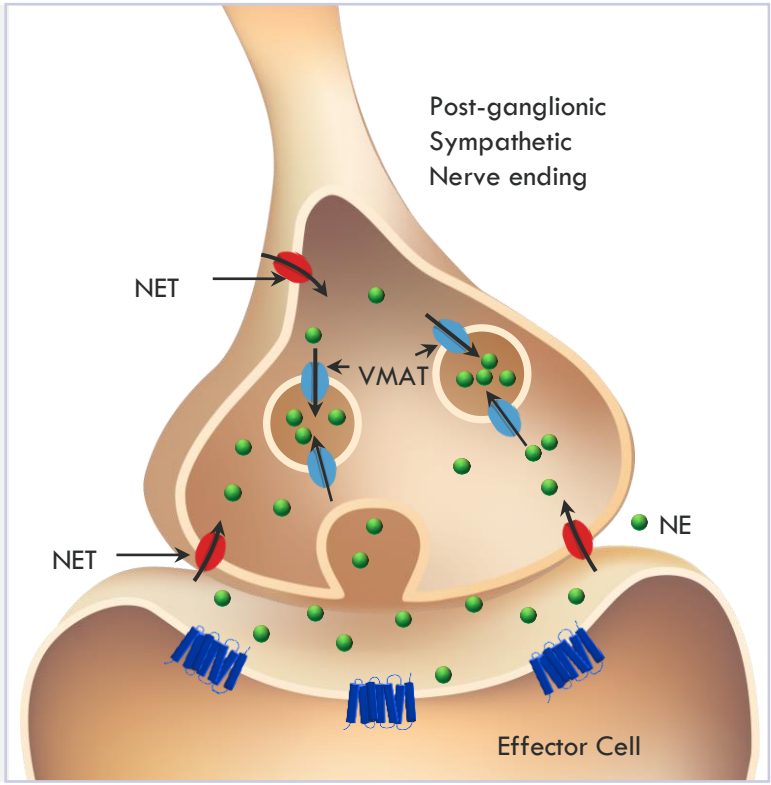
↓

NE release into the synapse

↓

Activation of adrenergic
α receptors (vasoconstriction)

β receptors (increase heart rate)



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Activation of adrenergic
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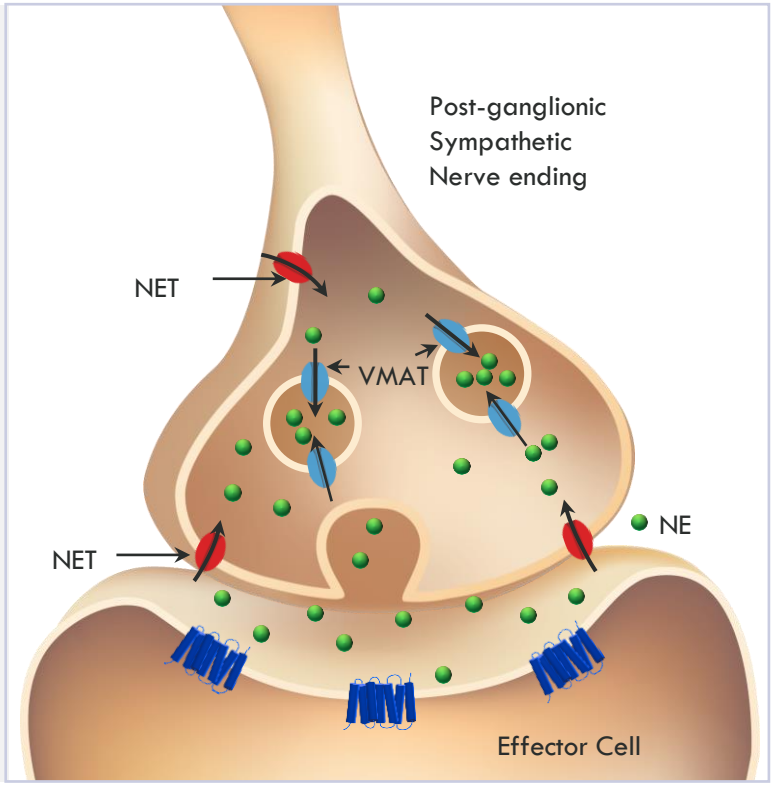
β receptors (increase heart rate)

↓

Up to 80% of NE is recaptured by NET for recycling



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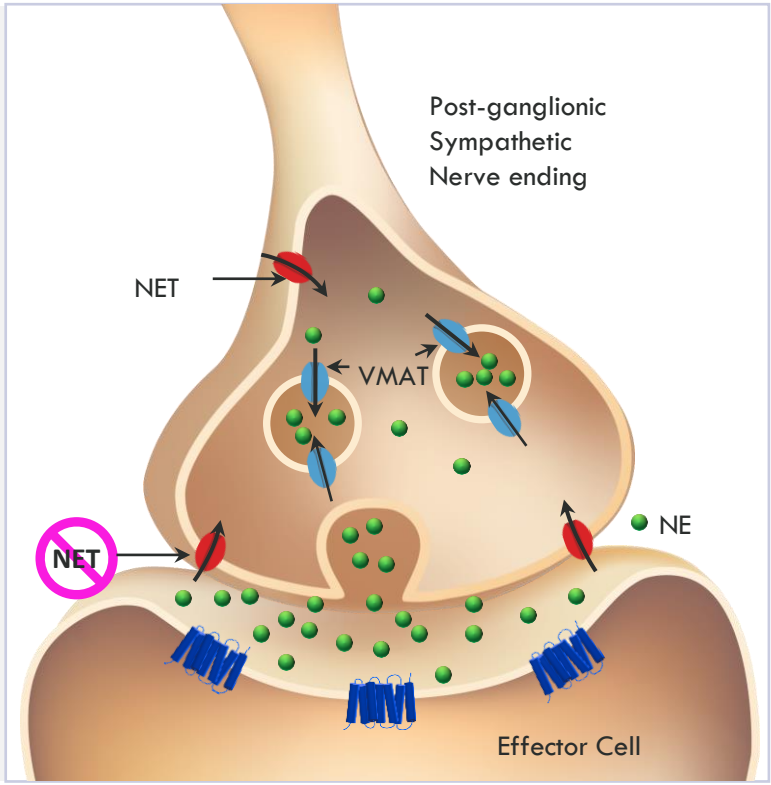
Up to 80% of NE is recaptured by NET for recycling

NET blockers increase intrasynaptic NE concentrations and actions



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↓

Activation of adrenergic
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β receptors (increase heart rate)

↓

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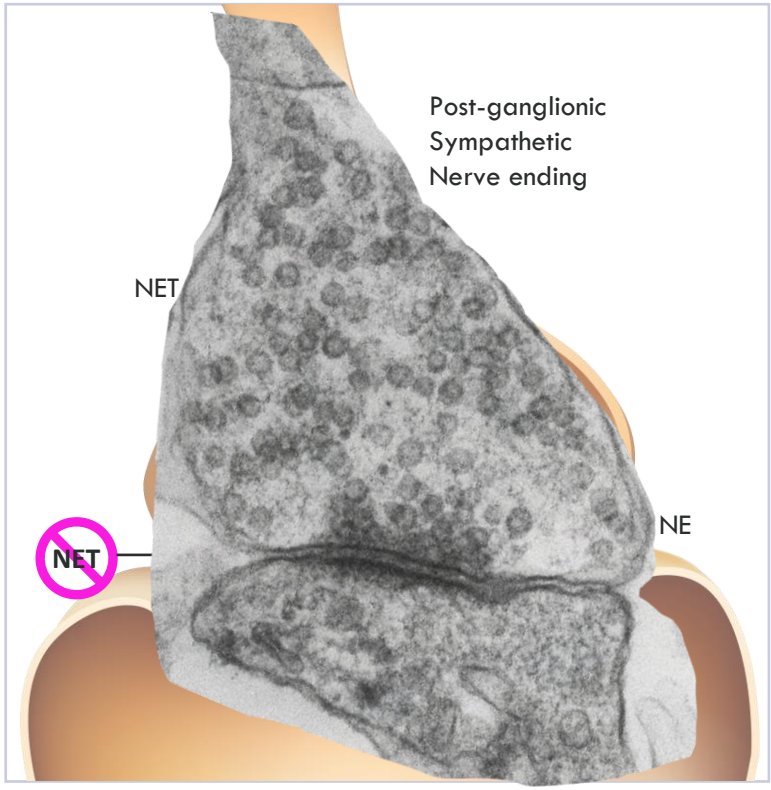
NET blockers increase intrasynaptic NE concentrations and actions

Precisely where it is needed



NE, norepinephrine; NET, norepinephrine transporter; VMAT, vesicular monoamine transporter.

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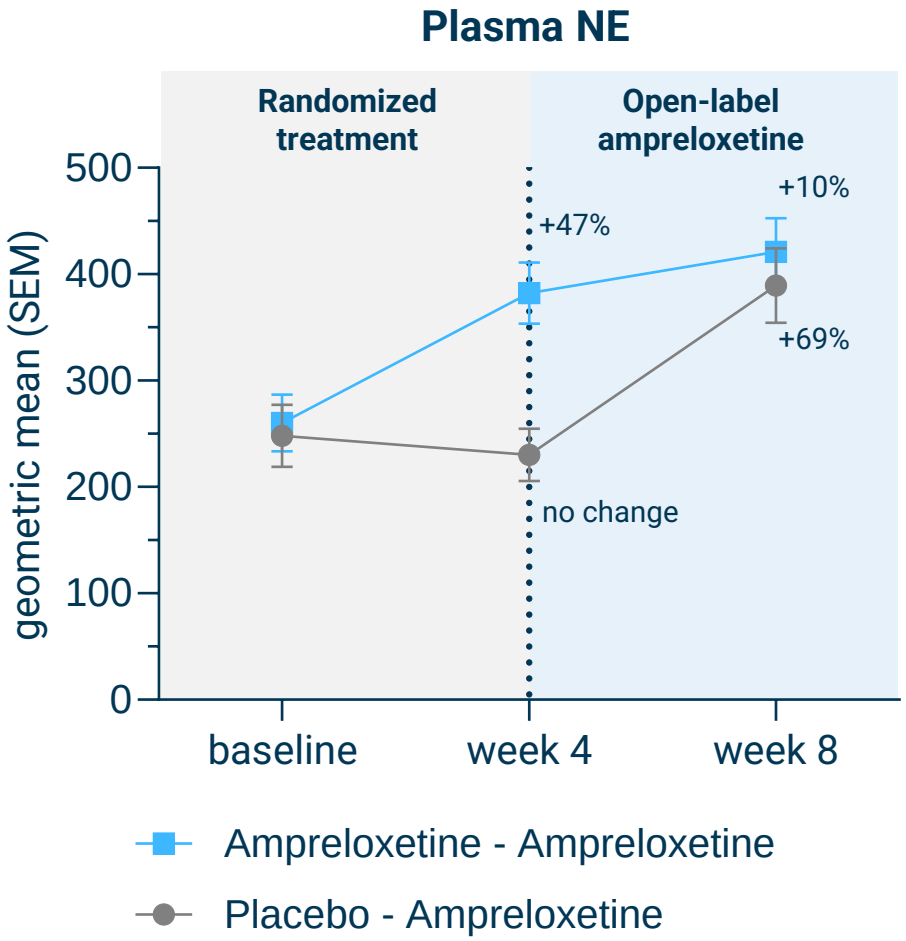
Ampreloxetine raised plasma NE levels durably in nOH



Ampreloxetine raised plasma significantly in patients with symptomatic nOH out to eight weeks

Greatest increases in plasma NE seen in patients with MSA (+57% at 4 weeks)

Data from 0169 and 0170 studies; ampreloxetine 10mg dose administered once per day.
Data labels indicate geometric mean ratio vs previous visit.
SEM, standard error of geometric mean; MSA, multiple system atrophy; NE, norepinephrine, nOH, neurogenic orthostatic hypotension.

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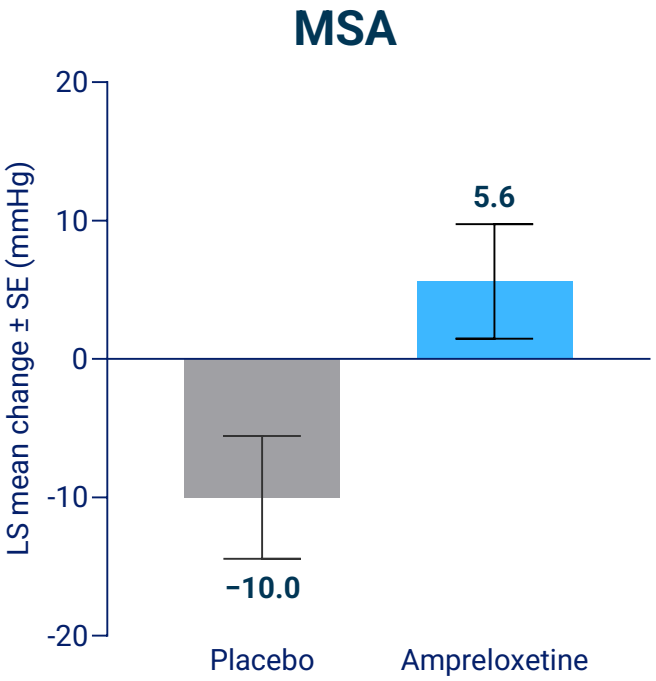
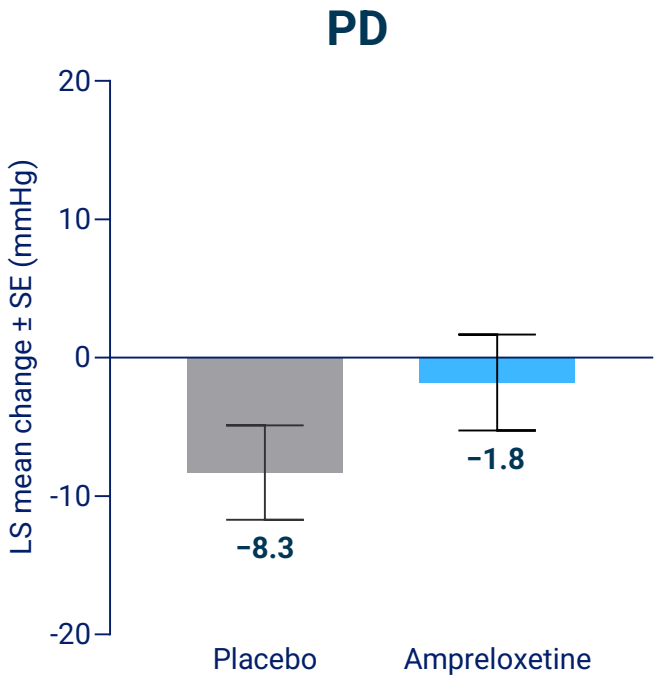
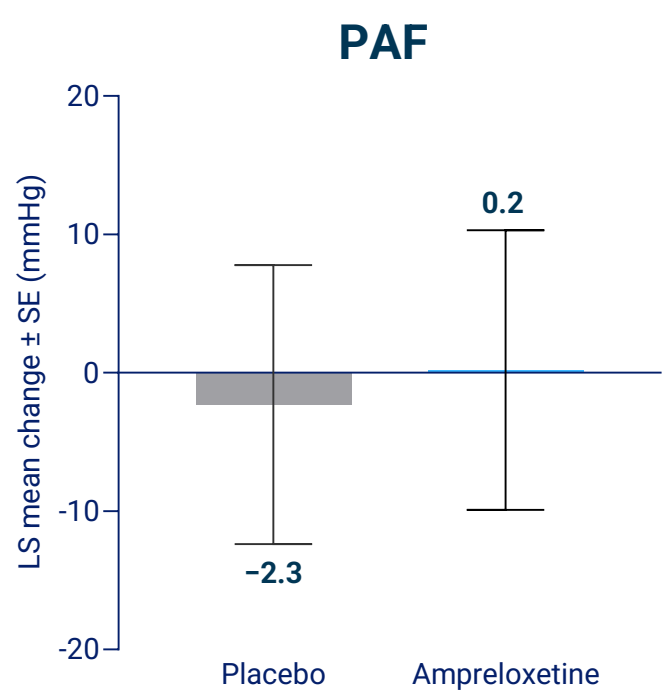
Ampreloxetine preferentially improved standing systolic blood pressure in MSA



Treatment difference:
15.7 mmHg (*P*<0.05)



Treatment difference:
6.5 mmHg



Treatment difference:
2.5 mmHg

Data taken from randomized withdrawal period in Study 0170.
LS, least squares; mmHg, millimeters of mercury; MSA, multiple system atrophy; PAF, pure autonomic failure; PD, Parkinson's Disease; SE, standard error.

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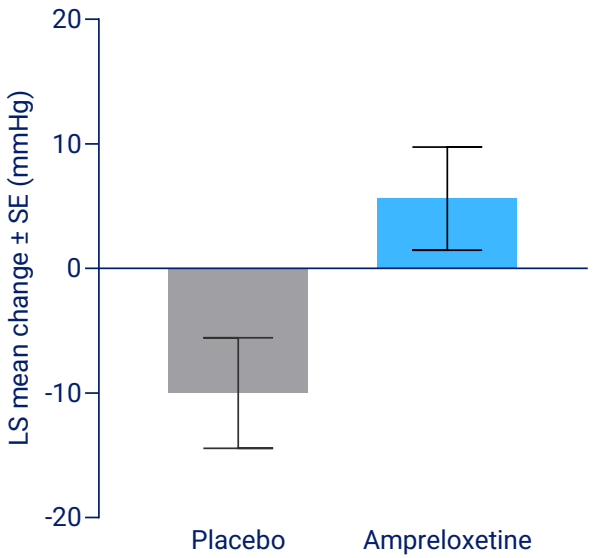
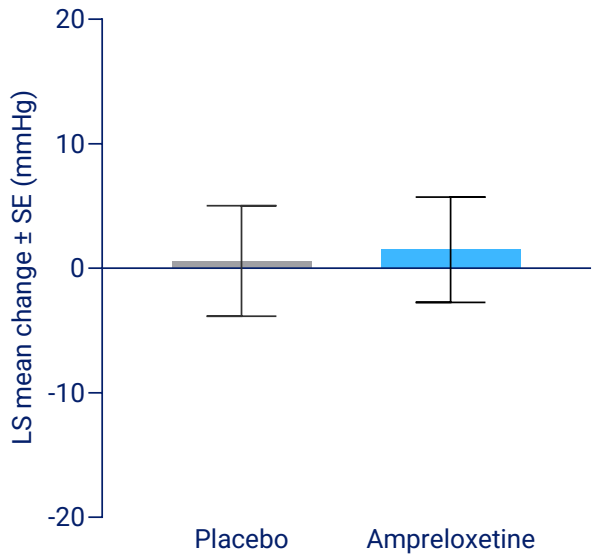
Ampreloxetine improved upright blood pressure “physiologically”

Standing SBP



Improvement

Supine SBP



No Difference

- Standing blood pressure improved without evidence of increasing supine blood pressure
- Approved therapies increase supine > standing blood pressure

Data from MSA patients at week 6 of the randomized withdrawal period of study 0170. Standing SBP measured at 3 min and supine SBP measured at 10 min. Line represents the mean +/- standard deviation.
MSA, multiple system atrophy; SBP, systolic blood pressure; SD, standard deviation.

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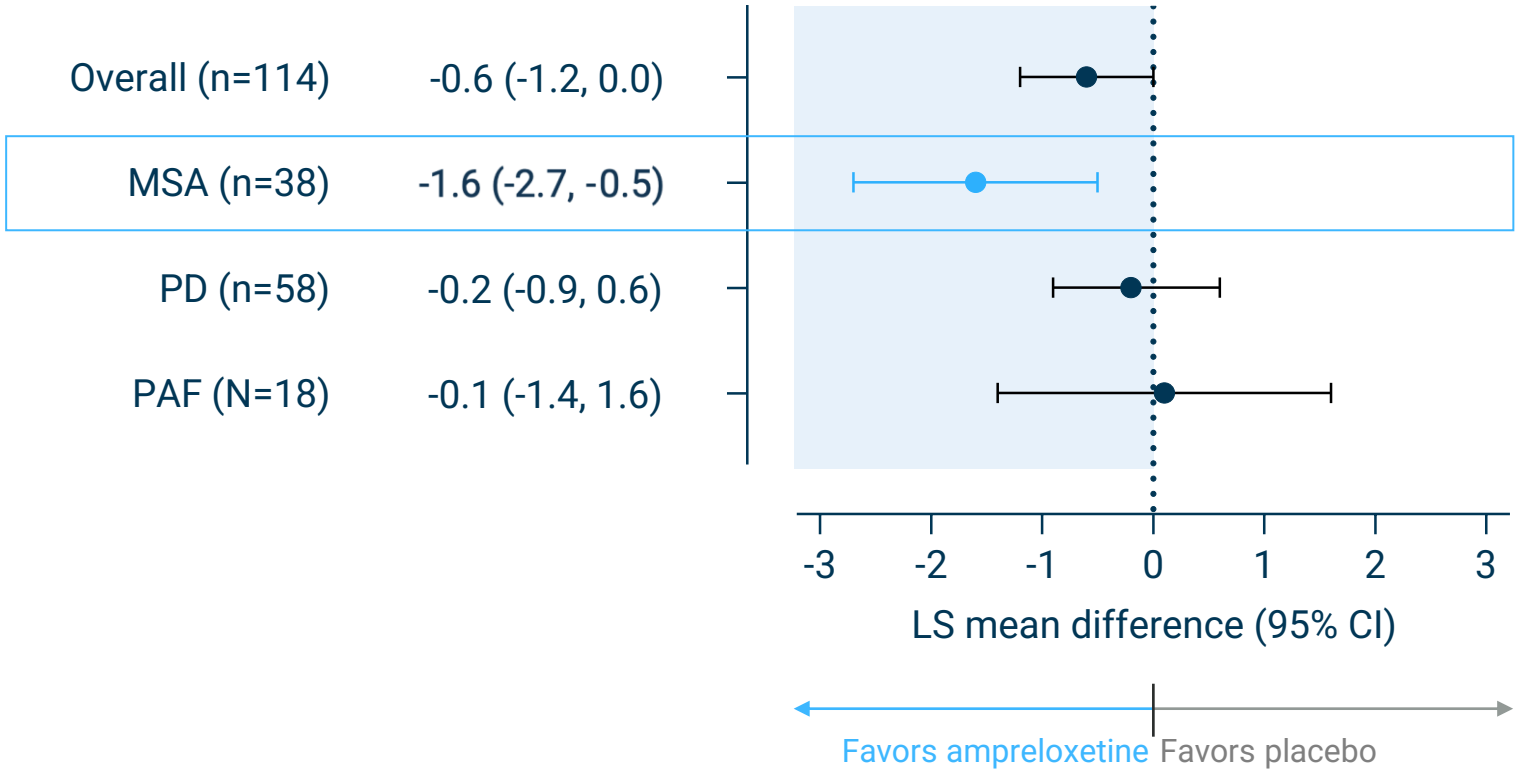
Ampreloxetine provided symptomatic benefit in MSA



- In Study 0170, patients reported a 1.6 point improvement in symptoms relative to placebo
- Symptomatic improvements consistent with changes in NE levels and standing 3- minute SBP
- Results are consistent with the NET hypothesis in nOH and support the design of CYPRESS

OHSA data taken from week 6 of randomized withdrawal period in Study 0170. CI, confidence interval; LS, least squares; MSA, multiple system atrophy; NE, norepinephrine; NET, norepinephrine transporter; nOH, neurogenic orthostatic hypotension; OHSA, orthostatic hypotension symptom assessment; PAF, pure autonomic failure; PD, Parkinson's Disease.

Ampreloxetine is a smart drug for nOH in MSA

MSA patients have spared noradrenergic neurons and residual sympathetic tone

Ampreloxetine increased NE levels in MSA patients

Ampreloxetine harnesses this residual sympathetic tone by increasing synaptic NE

Enhanced vasoconstriction, improved BP, alleviated symptoms

Potentiates sympathetic activity only when stimulated by upright posture

Mechanism of action is tailored to MSA

Vanderbilt Autonomic Dysfunction Center

BP, blood pressure; MSA, multiple system atrophy; NE, norepinephrine, nOH, neurogenic orthostatic hypotension.

Ampreloxetine: Discovery Through CYPRESS Design and Execution

Dr. Áine Miller
Theravance Biopharma SVP, Head of Development

Ampreloxetine: designed to address nOH in MSA

Discovery/Early Development » Ampreloxetine has a desirable PK/PD profile and has been safe and well tolerated in the clinic

CYPRESS Design and Execution » Pivotal CYPRESS study designed to confirm the clinically meaningful results seen in Study 0170 in MSA patients

Regulatory Preparation » Theravance Biopharma is positioned to capitalize rapidly and efficiently upon CYPRESS's potential success

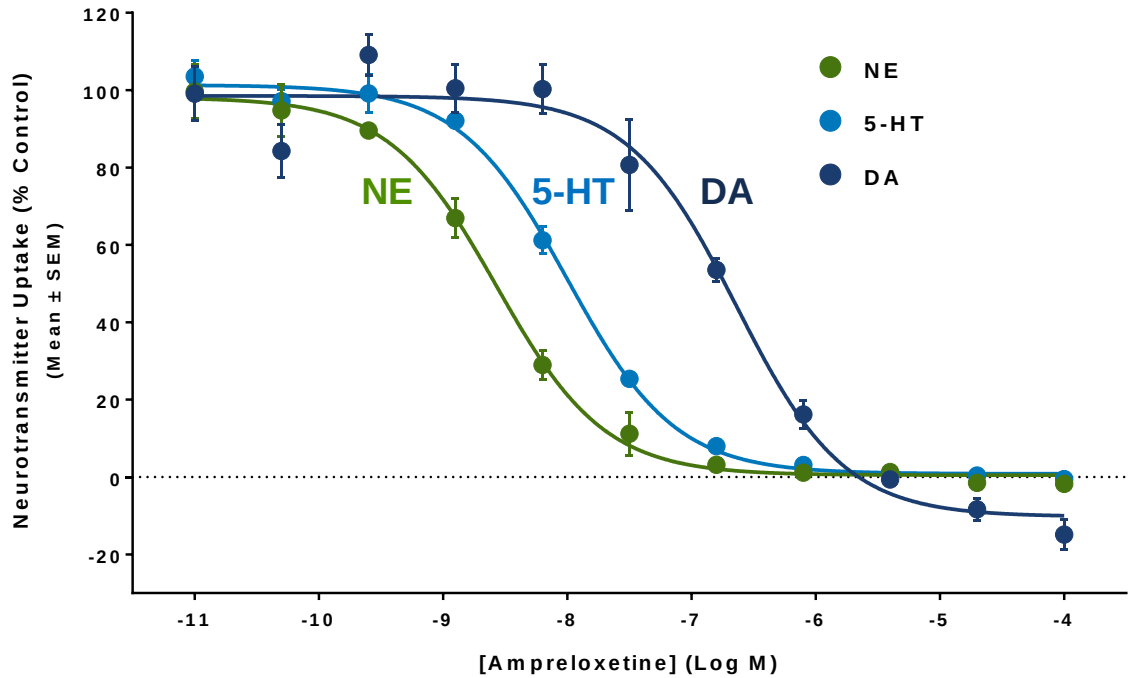
MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; PK/PD, pharmacokinetics/pharmacodynamics.

Ampreloxetine is a potent and selective inhibitor of the NE transporter (NET)

Ampreloxetine was designed to target and correct the norepinephrine imbalance

- Novel chemical entity, discovered and developed at Theravance Biopharma
- Potent and high-affinity NET inhibitor
- Orally bioavailable with half life that supports QD dosing
- Mechanism of action consistent with durability of effect

Pre-clinical studies confirmed ampreloxetine as a selective and potent inhibitor of NE transport



Rat spinal cord

Smith JA, et al. Int J Neuropsychopharmacol. 2014;18(2):pyu027. Hegde S et al. 2018 International Congress of Parkinson's Disease and Movement Disorders. Abstract 1612.
5-HT, serotonin; DA, dopamine; NE, norepinephrine.

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10 mg clinical dose selectively inhibits reuptake of NE

Ampreloxetine Dose (mg)	Projected Mean % NET Occupancy	Projected Mean % SERT Occupancy
10	> 90	< 50

Occupancy estimated using PK/PD model constructed from Phase 1 PET study and population pharmacokinetics of ampreloxetine in human trials

- 10 mg dose level achieves selective inhibition of NET over SERT (serotonin transporter)
- High levels of NET target engagement consistent with increases in NE observed in ampreloxetine clinical trials
- Low levels of SERT target engagement are consistent with the low incidence of serotonergic side effects (e.g., nausea, sleepiness, agitation) seen in ampreloxetine clinical trials

Kanodia et al., Clin Pharmacokinetic, 2021.
Smith et al., Intl J Neuropsychopharmacol. 2015.
NE, norepinephrine; NET, norepinephrine transporter; SERT, serotonin transporter.

Ampreloxetine: from discovery through CYPRESS, an investigational medicine for symptomatic nOH in patients with MSA

Indication Selection	Phase 2 PoC	Initial Phase 3	Pivotal Phase 3
NET inhibitor discovered at Theravance Biopharma	Demonstrated sustained, clinically meaningful symptom improvement for up to 5 months in nOH	Proposed indication of symptomatic nOH in patients with MSA	Refocused to patients with MSA
nOH in MSA caused by NE deficiency	nOH symptom improvements associated with increases in standing SBP	Expanded to broader synucleinopathies based on input from FDA	Designed to confirm benefit seen in MSA in previous Phase 3 program
NET inhibition particularly well suited to MSA pathophysiology		Revealed compelling, durable benefit in patients with MSA	FDA on path to full approval with positive CYPRESS data
Significant unmet need		SEQUOIA, REDWOOD, OAK	CYPRESS

MSA, multiple system atrophy; NE, norepinephrine; NET, norepinephrine transporter; nOH, neurogenic orthostatic hypotension; SBP, systolic blood pressure; SERT, serotonin transporter.

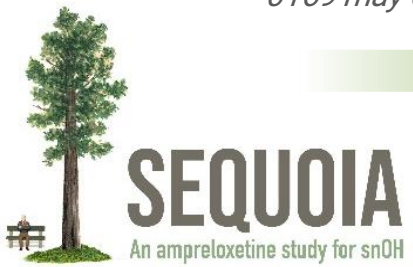
Initial Phase 3 program design

Phase 3 Registrational Program

Extension Study

Study 0169: 4 weeks
Randomized, double-blind, placebo controlled, parallel group (n=188)

All patients who complete 0169 may enroll into 0170



Study 0170: 22 weeks
Randomized 16-week open label, 6-week randomized, double-blind, placebo-controlled withdrawal (n=154)

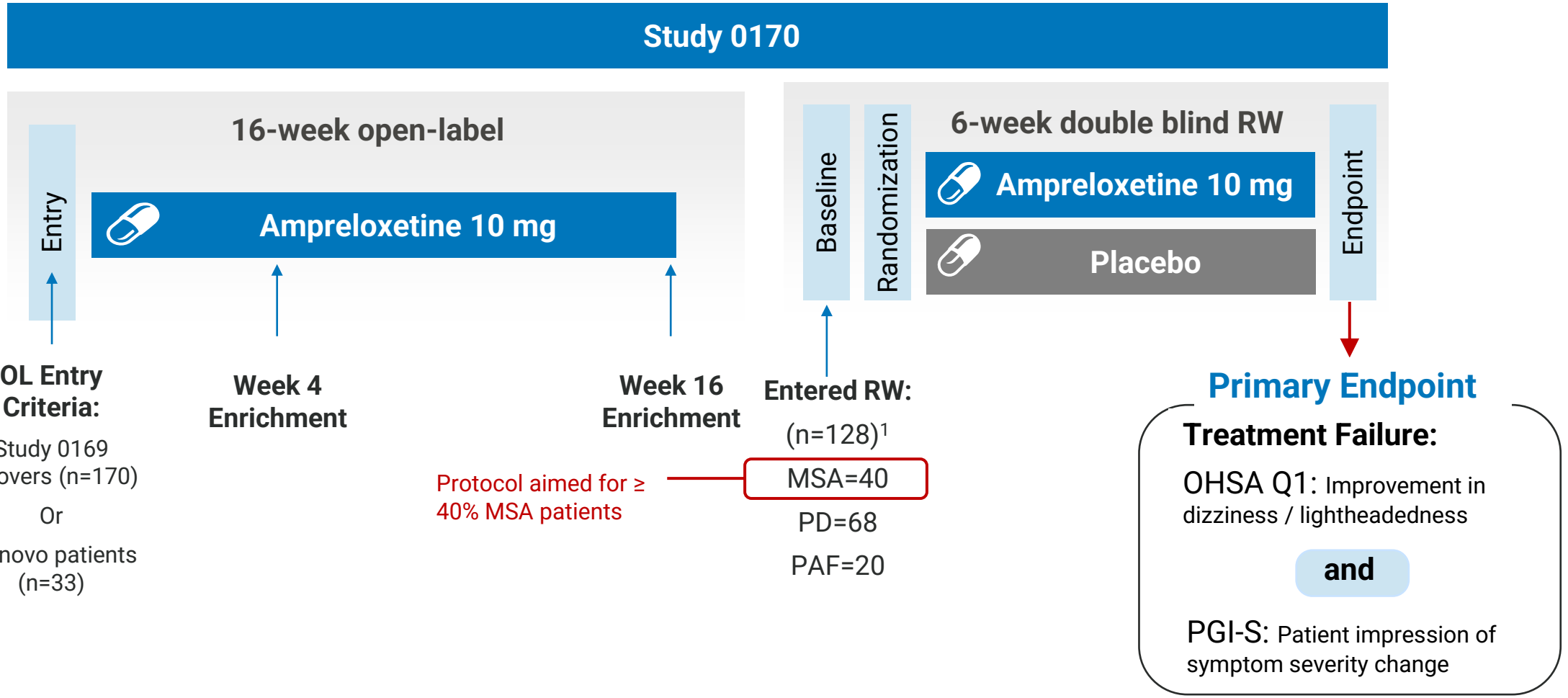
All patients who complete 0170 may enroll into 0171

Study 0171: 3.5 years
Long-term, open-label extension study

Synucleinopathies with nOH (prespecified subgroup analysis by disease)

snOH, symptomatic neurogenic orthostatic hypotension; nOH, neurogenic orthostatic hypotension.

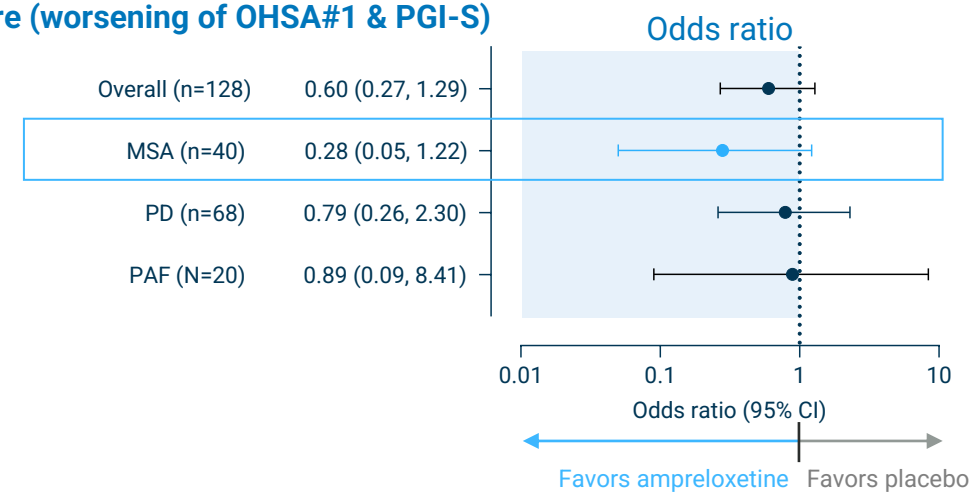
Study 0170 designed to assess durability



1. Study 0170 was terminated early because of negative results from Study 0169 (n=128 vs. 154 anticipated).
MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; OL, open label; PAF, pure autonomic failure; PD, Parkinson's disease; PGI-S, patient global impression of severity; RW, randomized withdrawal.

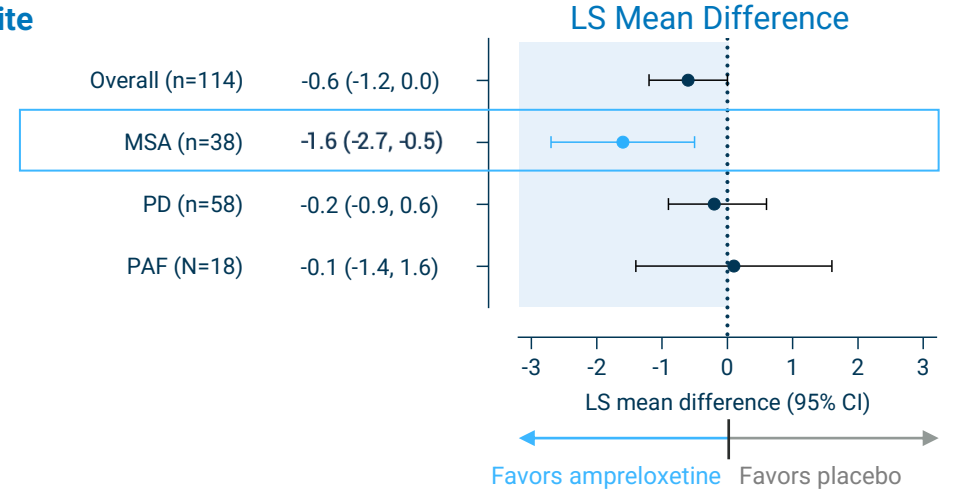
Study 0170 by-disease analyses demonstrated ampreloxetine's effects in MSA

Treatment Failure (worsening of OHSA#1 & PGI-S)



- Numerical, non-significant benefit in Treatment Failure endpoint primarily driven by MSA cohort

OHSA composite



- Compelling, 1.6-point benefit demonstrated in MSA cohort on OHSA Composite endpoint

The number of analyzable patients differ between analyses due to missing data. Missing data is imputed as treatment failure for the primary endpoint. Missing data for OHSA composite, OHSA#1 and OHDAS composite scores are assumed missing at random and analyzed through a mixed model repeated measures analysis. n=128; n=number of subjects enrolled in the randomized withdrawal period. CI, confidence interval; LS, least squares; MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; PAF, pure autonomic failure; PD, Parkinson's disease; PGI-S, patient global impression of severity.

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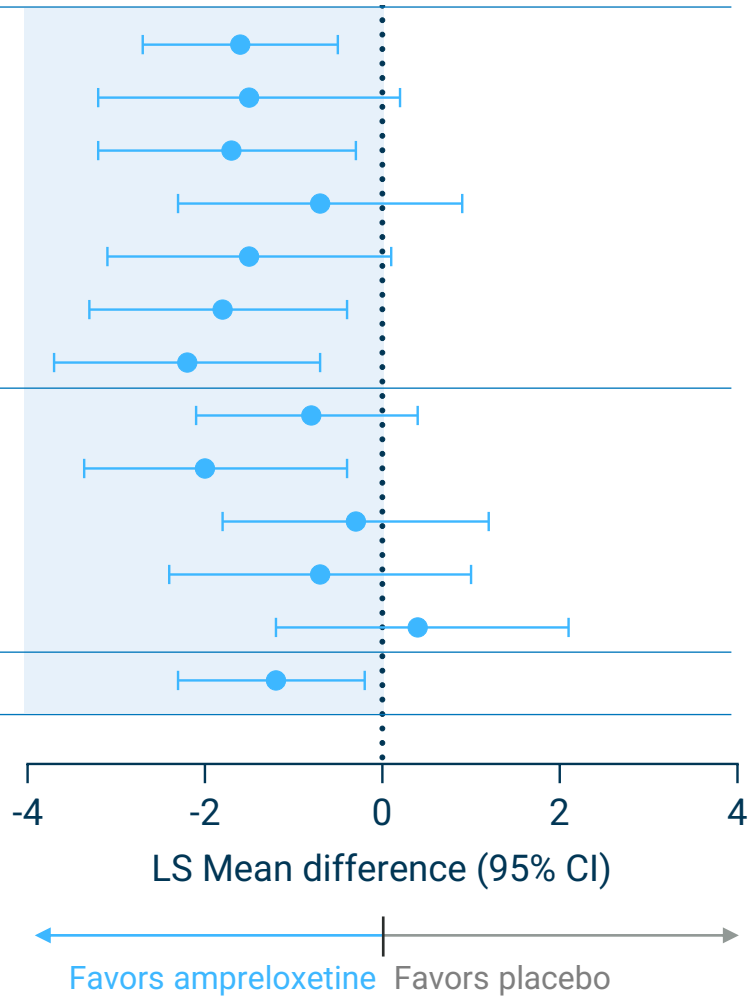
Study 0170 OHQ questionnaire composite score and individual items in MSA

OHSA	Symptom composite score	-1.6 (-2.7, -0.5)
	- Dizziness	-1.5 (-3.2, 0.2)
	- Vision	-1.7 (-3.2, -0.3)
	- Weakness	-0.7 (-2.3, 0.9)
	- Fatigue	-1.5 (-3.1, 0.1)
	- Trouble concentrating	-1.8 (-3.3, -0.4)
	- Head/neck discomfort	-2.2 (-3.7, -0.7)
OHDAS	Daily activities composite score	-0.8 (-2.1, 0.4)
	- Standing short time	-2.0 (-3.6, -0.4)
	- Standing long time	-0.3 (-1.8, 1.2)
	- Walking short time	-0.7 (-2.4, 1.0)
	- Walking long time	0.4 (-1.2, 2.1)
OHQ composite score		-1.2 (-2.3, -0.2)



Individual item score analyses are post-hoc, except for dizziness.
CI, confidence interval; LS, least squares; MSA, multiple system atrophy; OHDAS, orthostatic hypotension daily activity scale; OHQ, orthostatic hypotension questionnaire; OHSA, orthostatic hypotension symptom assessment.

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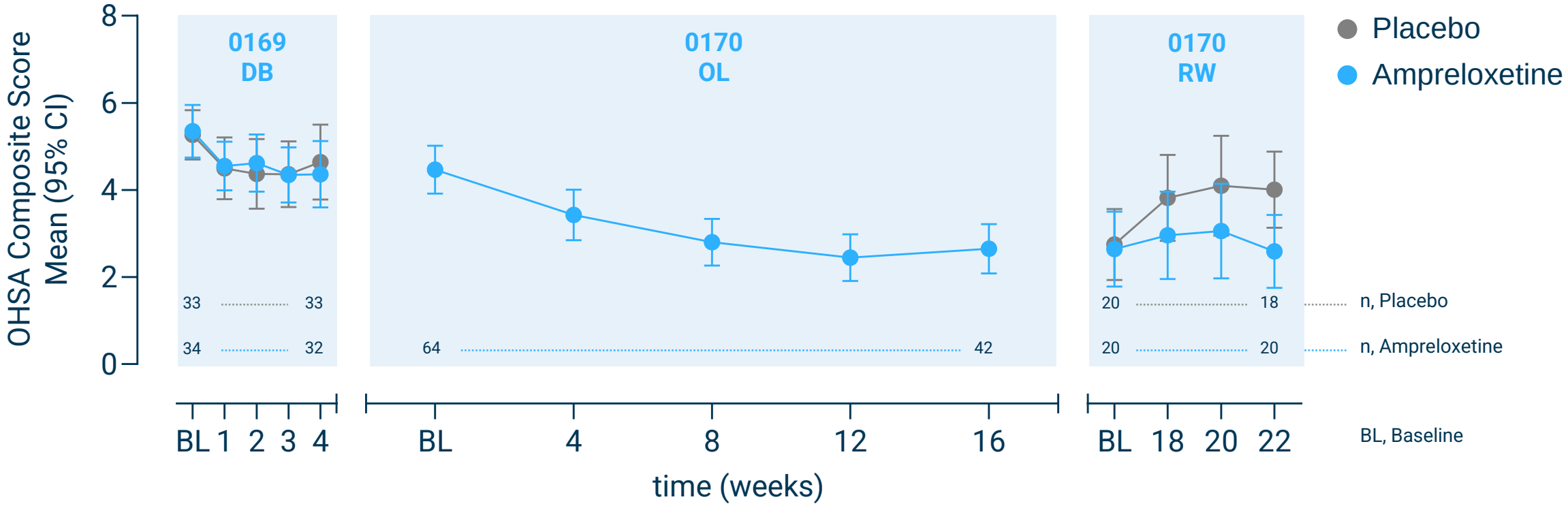
Durable, clinically-significant symptom improvements in MSA demonstrated in initial Phase 3 program



CI, confidence interval; DB, double-blind; MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; OL, open label; RW, randomized withdrawal.

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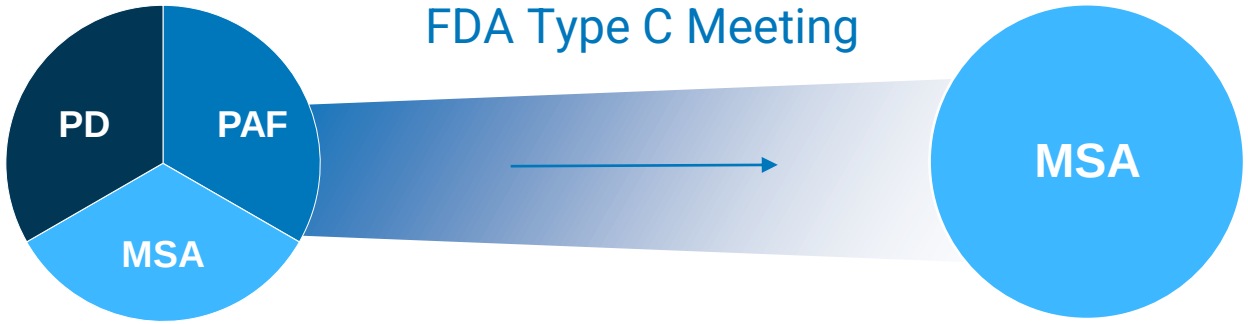
MSA results in Study 0170 Inform pivotal Phase 3

Initial Ampreloxetine Program:
Synucleinopathies

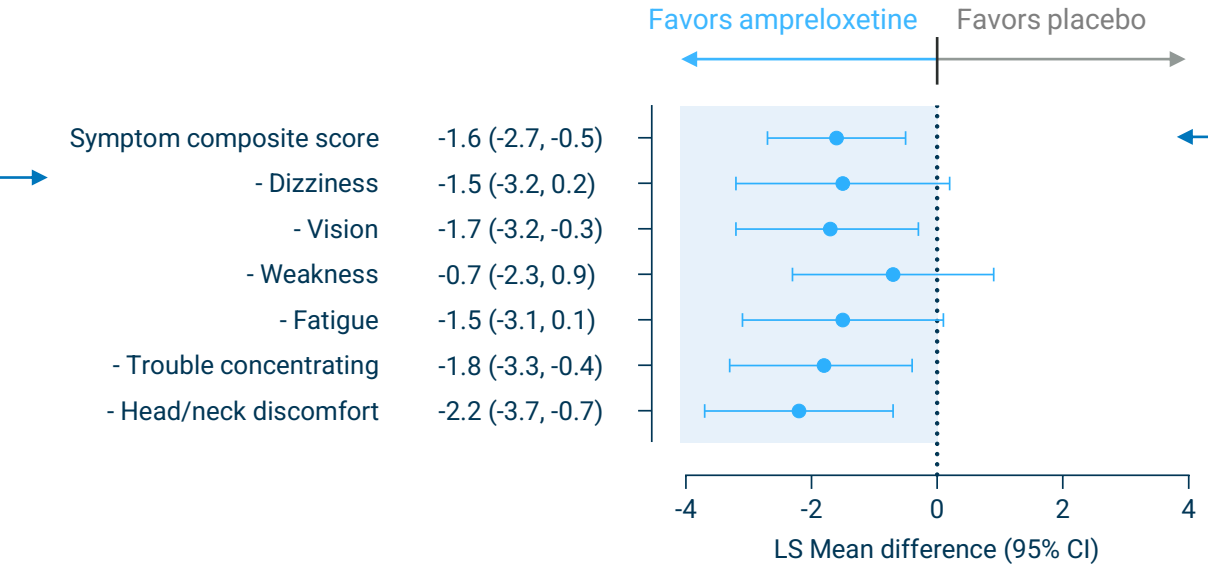


New Ampreloxetine Program:
MSA Focused

CYPRESS
An ampreloxetine study for MSA patients with nOH

Orphan Drug Designation granted by FDA

Focused Endpoint
OHSA #1 "Dizziness"



Broad Endpoint
OHSA Composite

CI, confidence interval; LS, least squares; MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; PAF, pure autonomic failure; PD, Parkinson's disease.

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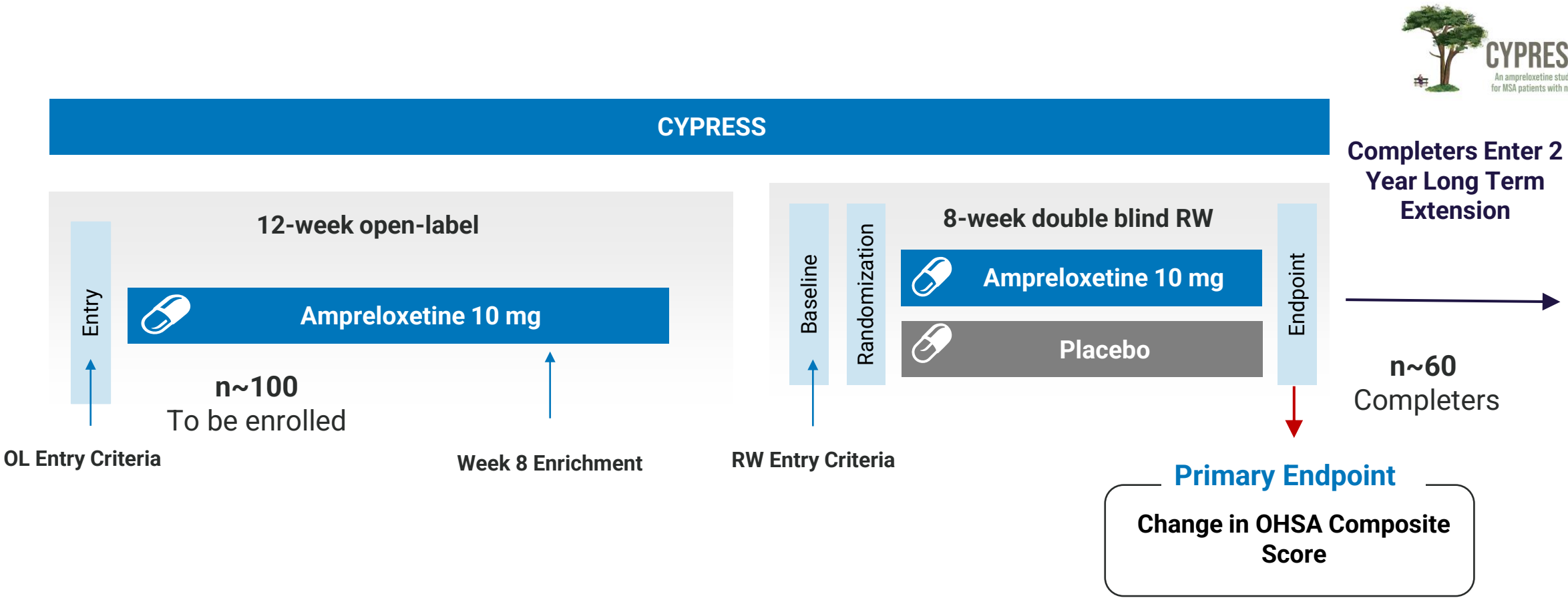
CYPRESS study: randomized withdrawal study design in patients with MSA



MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; OL, open label; RW, randomized withdrawal.

Operational Excellence in CYPRESS

Focus on high-quality study with enrollment completion in open label portion in 2024

CYPRESS EXECUTION

Protocol Design

Infrastructure in place to support remote visits

Reduced site & patient burden

Site Selection

Leading KOLs and many high quality sites from Studies 0169 and 0170

AI effort leverages claims information to enrich our network

Global footprint with sites in Europe, US, Asia/Pac and Latin America

Enrollment

Site & patient engagement

Advocacy & community focus

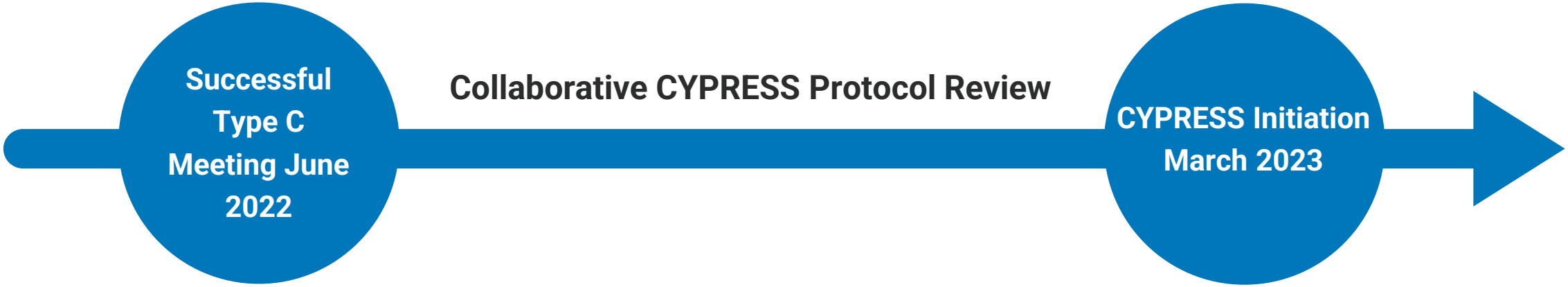
To-date study metrics consistent with expectations

Trial oversight & management

Direct management of study conduct rather than traditional CRO model

KOL, key opinion leader; CRO, contract research organization.

Alignment with FDA on CYPRESS design derisks regulatory path



Aligned with FDA on CYPRESS:

High level RW design including the use of the OHSA composite as primary endpoint

Successful outcome, with Study 170 results as supportive, would fulfill requirement for a full approval

Use of FDA-supported, Anchor-Based Analysis

to establish clinically meaningful thresholds for patient-reported outcomes measures

~1 point change in OHSA Composite identified as clinically meaningful[1]

1. Kaufmann H. (2023, November 15-18). Evaluating clinically meaningful changes in the Orthostatic Hypotension Symptom Assessment domain of the Orthostatic Hypotension Questionnaire. [Poster presentation].

OHSA, orthostatic hypotension symptom assessment; RW, randomized withdrawal.

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Safety profile established in >800 subjects

Phase 1

Phase 1 registration package

- Healthy volunteer studies
- Clinical pharmacology studies

Phase 2

Fibromyalgia

Adult ADHD

Symptomatic nOH

Phase 3

Symptomatic nOH

- 208 patients with MSA, PD & PAF exposed to ampreloxetine in initial P3 program
- 110 patients exposed to ampreloxetine for >6 months and 67 patients >12 months

Safety Profile

Ampreloxetine was generally safe and well-tolerated

No unexpected safety concerns occurred throughout the duration of the studies

Safety profile for the MSA subgroup was also consistent with that of the overall nOH population

No signal for worsening of supine hypertension

ADHD, attention-deficit/hyperactivity disorder; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; PAF, pure autonomic failure; PD, Parkinson's disease.

Positioned to capitalize rapidly and efficiently upon CYPRESS's potential success

Progress NDA authoring	Alignment with FDA on CMC, non-clinical pharmacology/toxicology, clinical pharmacology programs, work substantially complete, not rate limiting to NDA filing
Cypress Completion	LPI enrolled in open label period in 2H of 2024, remain on track
Top Line Read Out	Data in 2025, 20 weeks to LPV + data cleaning and analysis
File NDA	If positive, incorporate CYPRESS data into NDA and request priority review
Commercial readiness	Plan in place to support successful Launch

CMC, chemistry, manufacturing and controls; LPI, last patient in; LPV, last patient visit; NDA, new drug application.

Opportunity Analysis

Rhonda Farnum
Senior Vice President,
Chief Business Officer

A significant opportunity exists for ampreloxetine

Effective nOH treatment is lacking in MSA

- **High unmet need** due to significant limitations of current therapies
- **Symptoms interfere with daily activities** in 80% of patients with MSA
- **nOH increases risk** of falling and injuries and worsens patients' disability
- **65% of MSA patients remain symptomatic** despite treatment with approved therapies

Smart approach to nOH

- Ampreloxetine is a **selective, high affinity, once-daily** norepinephrine transporter inhibitor
- Uses patients' available NE, should lead to to **sustained** symptomatic benefit over time
- **Unparalleled approach** aims to demonstrate overall improvement in a patient's well-being by addressing a wide range of symptoms

Significant market opportunity

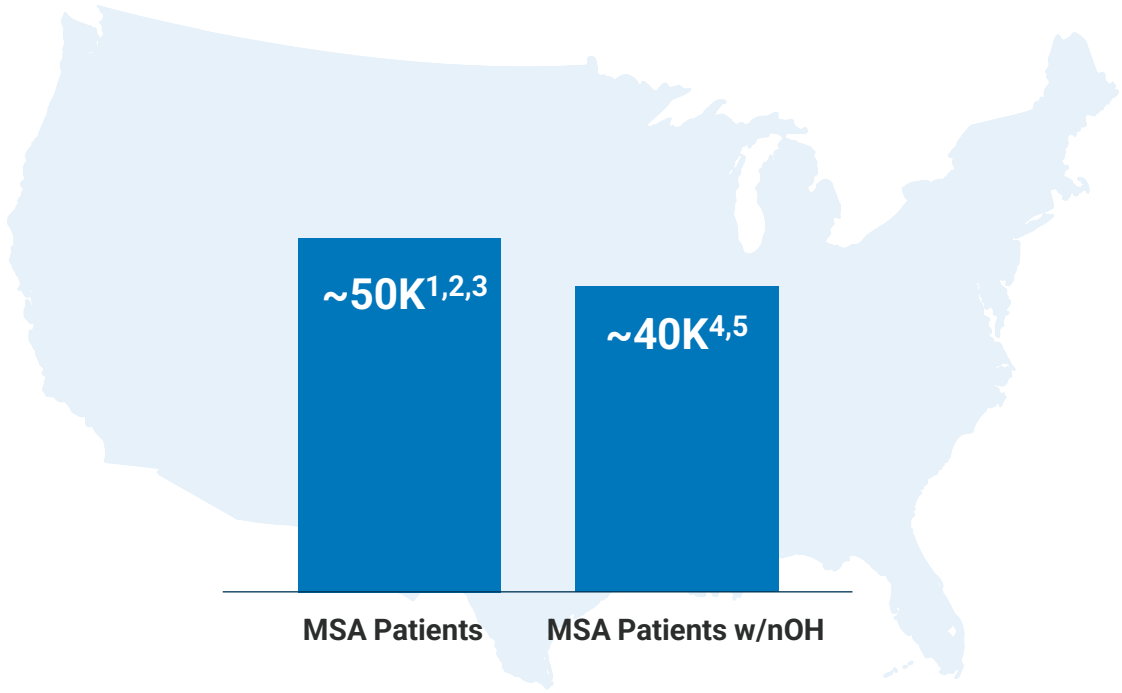
- **NO product in development or on the market** has demonstrated a **durable effect** across a comprehensive set of nOH measures
- nOH in MSA patients is a **rare disease** diagnosed and treated by specialists
- Strong **foundation of experience** in the US with an understanding of the **concentrated MSA market landscape**

MOA, mechanism of action; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; NE, norepinephrine.

An innovative, durable, and convenient treatment for nOH patients is needed

nOH prevalence in the US

~40K MSA Patients with nOH



An opportunity for Theravance Biopharma

Established nOH treatment paradigm

- ~80% of MSA patients suffer from nOH
- nOH is included in treatment guidelines

Specialist networks in place, concentrated market

- Autonomic and movement disorder specialists treat patients with MSA
- Patients with nOH are identified and managed by specialty institutions

Patients have few options

- Midodrine and droxidopa have a short-term effect, require multiple daily doses and increased risk of supine hypertension

1. *"Estimating the prevalence and incidence of multiple system atrophy in the USA: Insights from a national claims database"*, Parkinsonism and Related Disorders 11/4/2023. 2. UCSD Dept. of Neurosciences (25K-75K): https://neurosciences.ucsd.edu/centers-programs/movement-disorders/community/disease-overview/msa.html; 3. Thelansis nOH Market Report 2023; Internal claims analyses (IQVIA, Veeva, Real Chemistry). nOH graphics reflect the mid-point of the provided ranges.4. Kalra DK, et al. Clin Med Insights: Cardiol. 2020 (70%-90%);14:1179546820953415. 5. Delveinsight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy, CJ Mathias (1999). MSA, multiple system atrophy; nOH neurogenic orthostatic hypotension.

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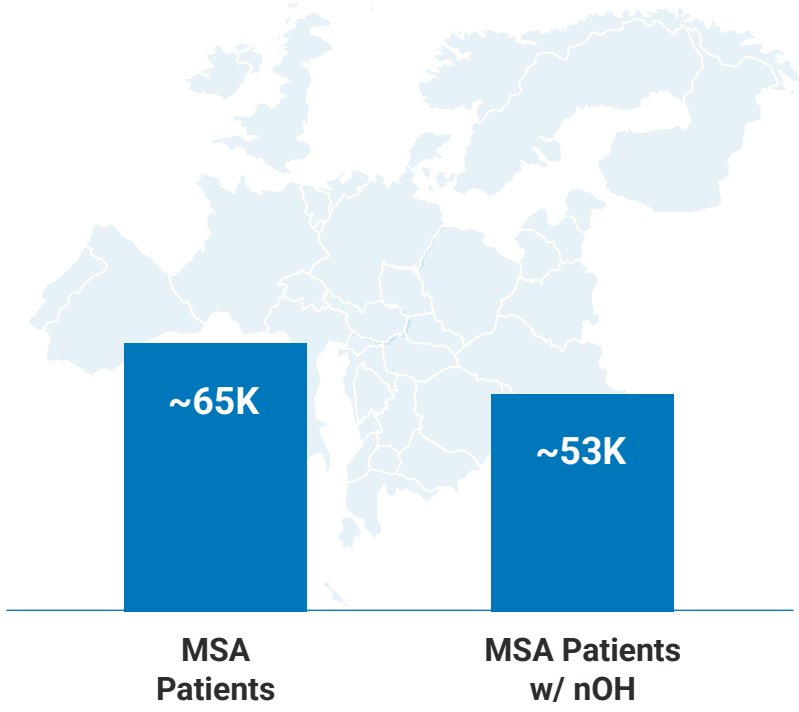
Ampreloxetine ex-U.S. opportunity

Significant unmet needs in leading therapeutics markets

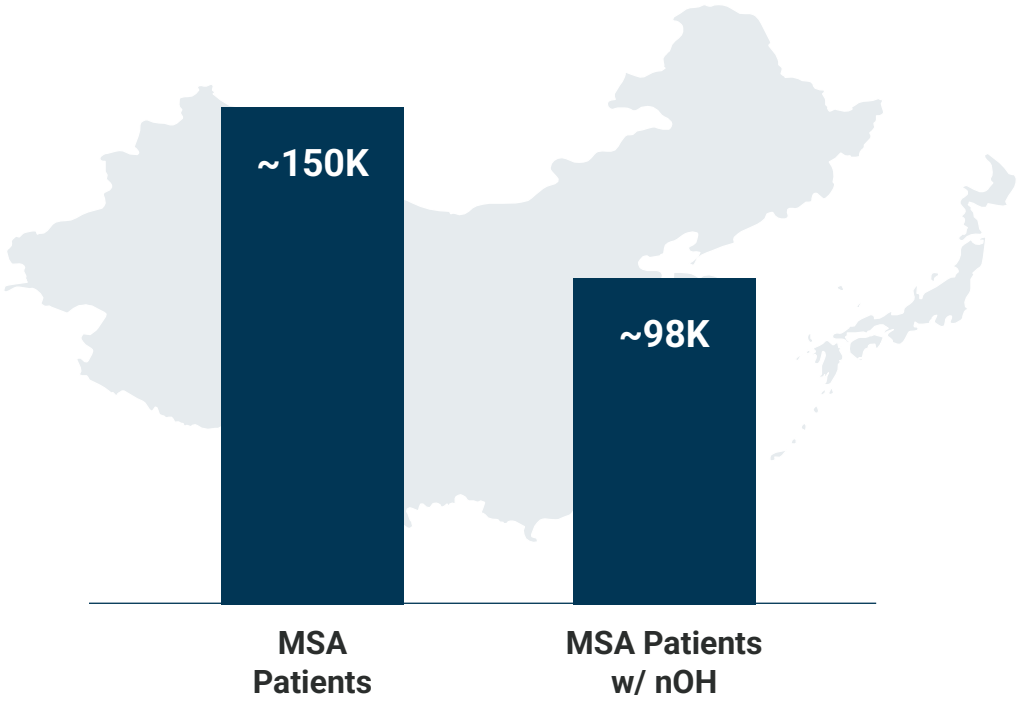
Prevalence in Europe[1,2]

45-60K MSA Patients with nOH



Prevalence in China & Japan[1]

90-105K MSA Patients with nOH



1. Thelansis nOH Market Report 2023; TBPH Internal Analysis. nOH graphics reflect the mid-point of the provided ranges.
2. Prevalence estimate for Germany, France, UK, Italy and Spain.
MSA, multiple system atrophy; nOH neurogenic orthostatic hypotension.

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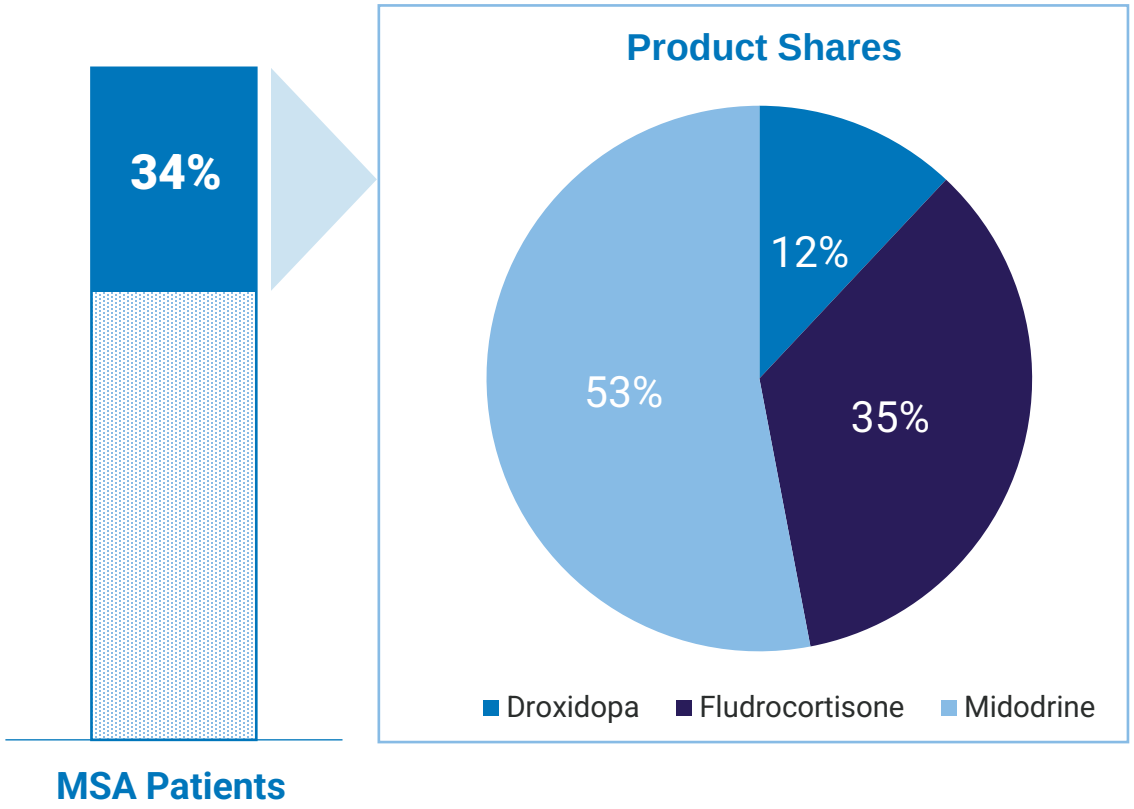
MSA patients with nOH are not optimally treated

Only ~34% of patients are treated, current therapies have not worked in this patient population[1]



A high unmet need remains, clinically meaningful options are needed

Advocacy groups, patients and caregivers are actively engaged and seeking new therapies to better manage nOH

Physicians report an urgency to treat patients with nOH due to the impact on quality of life, high risk of injury from falls, and caregiver burden

1. Veeva Compass patient-level claims data, MSA patients (G90.3) with at least 1 Rx from 2020-2023. Product share defined as total "days supplied" in this patient population.
MSA, multiple system atrophy; nOH neurogenic orthostatic hypotension.

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Treatment landscape is concentrated, commercial efforts will focus on MSA, nOH specialists

Targeted Approach

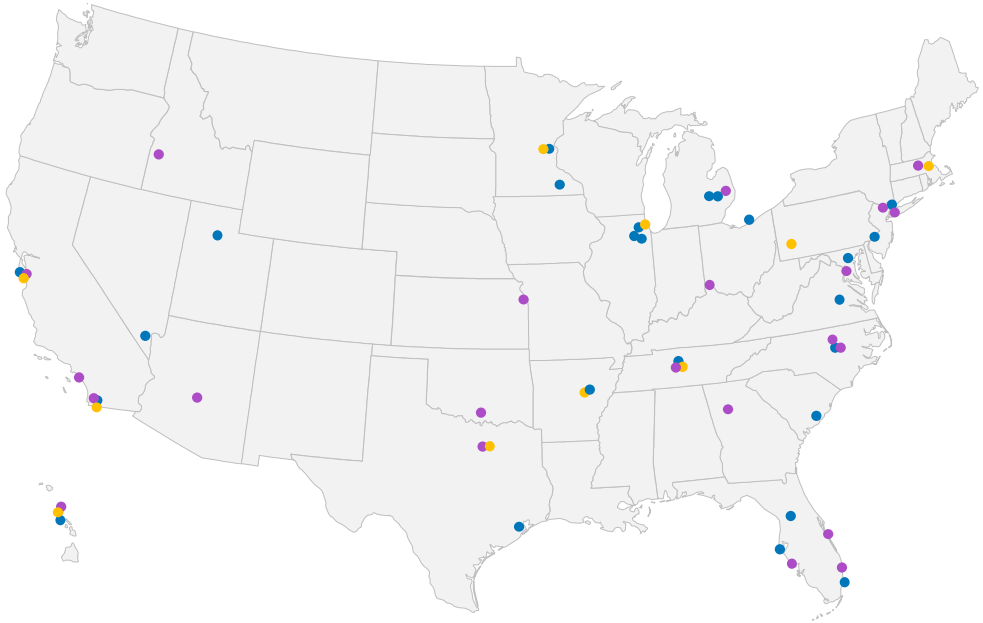
31
MSA Centers of Excellence

29
CYPRESS Trial Sites (US)

~90
High Volume MSA **Specialists**[2]

~250
High Volume MSA **Accounts**[2]

MSA Centers of Excellence[1] and CYPRESS Sites



1. Centers of Excellence: https://missionmsa.org/resource-library/centers-of-excellence-overview/, https://www.psp.org/centers-of-care
2. Veeva Compass patient-level claims data, MSA patients (G90.3), 1/1/2023-12/31/2023.
MSA, multiple system atrophy; nOH neurogenic orthostatic hypotension.

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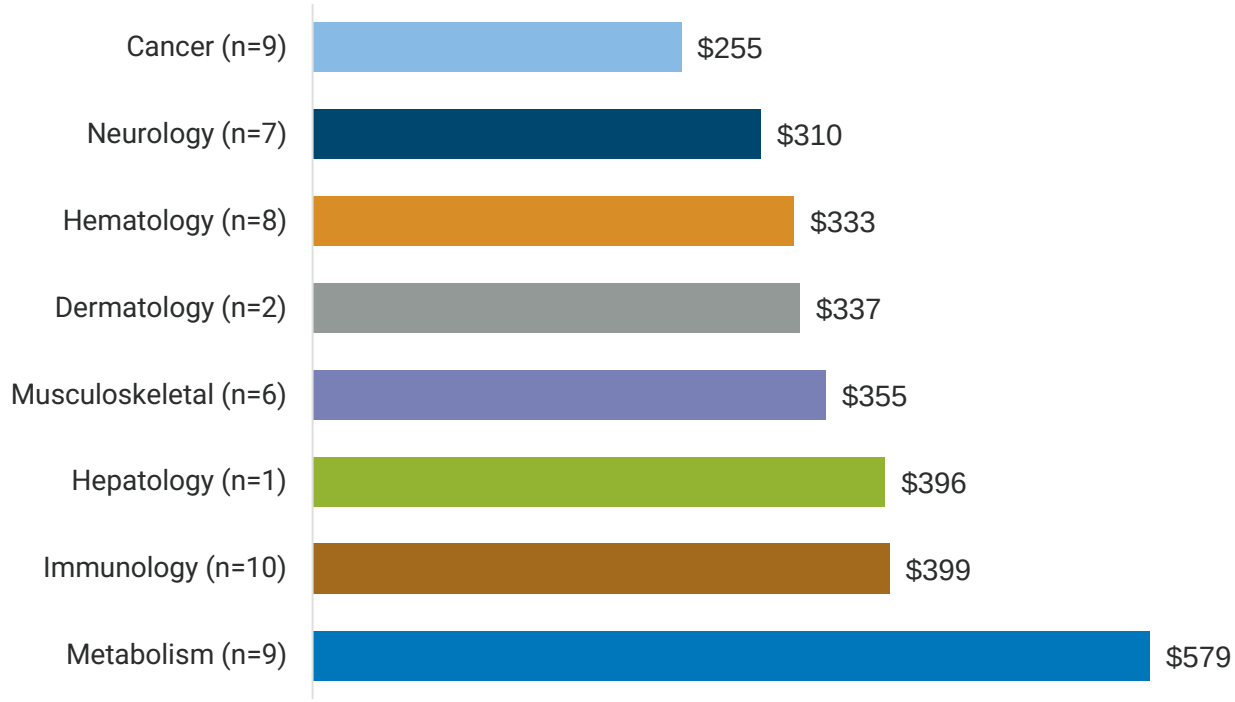
Planning a rare disease launch in the current market

Factors impacting US launch opportunity

- **Therapeutic Area**
- **Disease Prevalence**
- **Dosing** [One-time, chronic]
- **Efficacy, Safety**
- **Competitive Landscape**

Recent orphan drug launches

Average launch price ($K) for chronic therapies by therapeutic area (n=52)



Source: Cantor Fitzgerald, Biotechnology Equity Research, April 11, 2024.
Includes 63 drugs approved in the US between 1/22/2021-3/21/2024; average launch price based on WAC (wholesale acquisition cost).

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Commercial imperatives for launch excellence

DESIGN

Create a targeted, optimized US launch plan, leveraging TBPH expertise and infrastructure

Capitalize on unique understanding of nOH in MSA patients

BUILD

Leverage fundamental capabilities while investing in a targeted and innovative approach for a rare disease launch

Capitalize on proven success in the US hospital market

Implement ROW partnering strategy

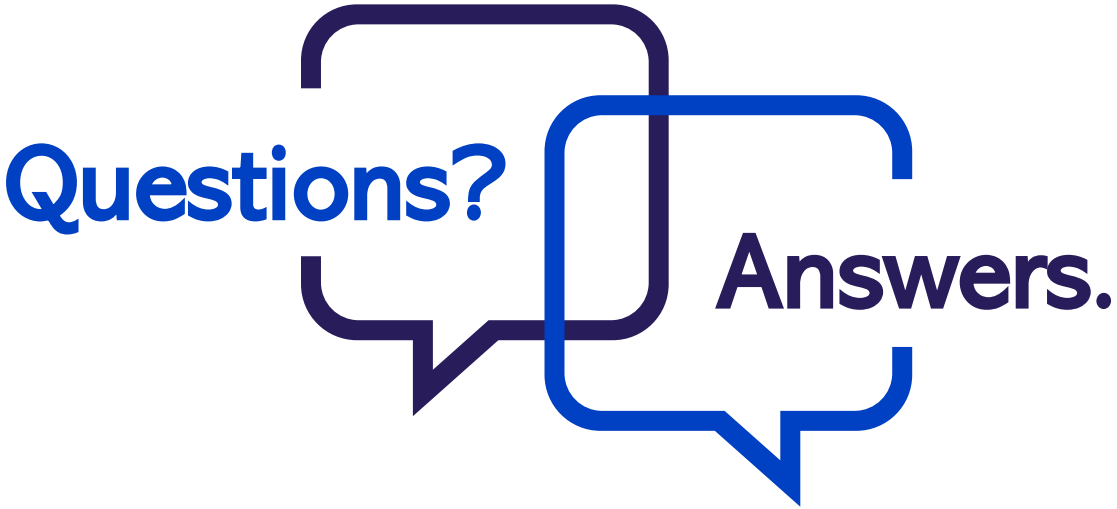
TRANSFORM

Potential to deliver a clinically meaningful treatment and impact the lives of MSA patients suffering from symptoms of nOH

Ampreloxetine approval would propel Theravance into a new era – transforming a rare neurological condition

Theravance is moving forward with great momentum in anticipation of launching ampreloxetine in the US

MSA: multiple system atrophy; nOH: neurogenic orthostatic hypotension; ROW: rest of world; TBPH: Theravance Biopharma; US: United States.


Questions?
Answers.