

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549

**FORM 8-K**

Current Report Pursuant  
to Section 13 or 15(d) of the  
Securities Exchange Act of 1934

Date of Report (Date of earliest event Reported): **January 12, 2026**

**THERAVANCE BIOPHARMA, INC.**

(Exact Name of Registrant as Specified in its Charter)

**Cayman Islands**  
(State or Other Jurisdiction of  
Incorporation)

**001-36033**  
(Commission File Number)

**98-1226628**  
(I.R.S. Employer Identification  
Number)

c/o Theravance Biopharma US, LLC  
901 Gateway Boulevard  
South San Francisco, CA 94080  
(650) 808-6000

(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Share \$0.00001 Par Value	TBPH	NASDAQ Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 7.01. Regulation FD Disclosure.**

*The information in this Current Report (including Exhibit 99.1) is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that Section. The information in this Current Report (including Exhibit 99.1) shall not be incorporated by reference into any registration statement or other document pursuant to the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.*

Members of the Theravance Biopharma management team will be conducting one-on-one meetings with analysts and investors in San Francisco, CA from January 12-15, 2026, using a slide presentation which is being furnished pursuant to Regulation FD as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

[99.1](#) [Slide deck entitled Corporate Presentation – January 2026](#)

104 Cover Page Interactive Data File (cover page XBRL tags embedded within the Inline XBRL document)

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**THERAVANCE BIOPHARMA, INC.**

Date: January 12, 2026

By: /s/ Brett Grimaud  
Brett Grimaud  
General Counsel

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# Theravance Biopharma

## Corporate Presentation

January 2026

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# 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, 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 of the 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 and objectives, future growth of YUPELRI sales, the ability to provide value to shareholders, the Company's regulatory strategies and timing of clinical studies, possible differentiation of our investigational therapy, commercial potential and market opportunity of our investigational therapy, the status of patent infringement litigation initiated by its partner against certain generic companies in federal district courts; contingent Trelegy sales-based milestones payable by Royalty Pharma, and expectations around the use of clinical 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 presentation and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to differ 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 affect profitability, whether the milestone thresholds can be achieved, delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from 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, 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, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with a limited number of experts and supporting infrastructure, the ability of the Company to protect and to enforce its intellectual property rights, volatility and fluctuations in the trading price 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 November 12, 2025, and other periodic reports filed with the SEC. In addition to the risks identified in Theravance Biopharma's filings with the SEC, other known or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statement and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. The Company assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

## Non-GAAP Financial Measures

Theravance Biopharma provides a non-GAAP profitability target and a non-GAAP metric in this presentation. Theravance Biopharma believes that the non-GAAP profitability target and net income (loss) provide meaningful information to assist investors in assessing prospects for future performance and actual performance as they provide better metrics of performance of its business by excluding items that may not be indicative of core operating results and the Company's cash position. Because non-GAAP financial targets, non-GAAP profitability and non-GAAP net income (loss) are not standardized, it may not be possible to compare these measures with other companies' non-GAAP targets or similar names. Thus, Theravance Biopharma's non-GAAP measures should be considered in addition to, not as a substitute for, or in isolation from, the Company's GAAP measures and other targets.

This presentation contains a reconciliation of non-GAAP net income (loss) to its corresponding measure, net income (loss). A reconciliation of non-GAAP net income (loss) to the GAAP measure is not available on a forward-looking basis without unreasonable effort due to the uncertainty regarding, and the potential variability of, expenses and other factors.

# Commercial-Stage Biotech Focused on Respiratory and Neurological Diseases

Strong Financial Position and Cash-Generating YUPELRI® Set the Foundation for Near-Term Ampreloxetine PI



## Strong Financial Position

~\$333M in cash and no debt; breakeven in Q3 2025<sup>1</sup>, expected to remain levels in Q4 2025

\$175M in near-term, high probability TRELEGY<sup>2</sup> and YUPELRI sales-based Commitment to **return excess capital** to shareholders



## YUPELRI® Strong Cash Flow Generation

Launched in the U.S. in 2019; 35% U.S. profit share with Viatriis<sup>3</sup>

**Strong cash flow** from U.S. profit share with **IP protection** in the U.S. into Sizable addressable patient population remains<sup>4</sup>



## Ampreloxetine Upcoming Phase 3 Data

Phase 3 CYPRESS randomized withdrawal complete; **topline data expect** FDA Orphan Drug Designation

Targets ~**40,000 underserved patients** in the U.S. with symptomatic nOH

## Demonstrated Success in Advancing In-House Developed Assets through Approval and Successful Comm

FDA, U.S. Food and Drug Administration; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

1. Cash balance of \$332.7M as of 9/30/25; cash flow guidance excludes potential one-time milestones (and associated taxes). 2. Payments from Royalty Pharma (RP) will be triggered if RP receives certain minimum royalty payments from GSK based on TRELEGY global net sales. 3. In the U.S., Viatriis is leading the commercialization of YUPELRI and Theravance Biopharma co-promotes the product under a profit and loss sharing arrangement (65% to Viatriis; 35% to Theravance Biopharma). Refer to our SEC filings for further information. 4. Addressable patient population quantifies the number of patients within the intended target profile. 5. Palma, Kaufmann. Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension; Kalia DJ et al. Clin Med Insights: Cardiol. 2020 14:1179546820953415. 6. Kaplan et al., Parkinsonism Relat Disord. 2023 Dec;117:105920; UCSD Dept. of Neurosciences : <https://neurosciences.ucsd.edu/centers-programs/movement-disorders/community/disease-overview/msa.html>; Internal claims analyses (IQVIA, Veeva, Real Chemistry), CD-10 Codes: G90.3, G23.2.

## Leadership with Extensive Experience in Biotech



**Rick Winningham**  
Chief Executive Officer

 Bristol Myers Squibb

 Jazz Pharmaceuticals

 Rivus  
PHARMACEUTICALS

 Bio



**Aziz Sawaf, CFA**  
SVP, Chief Financial Officer

 GILEAD

 AMGEN

 CALIFORNIA  
LIFE SCIENCES



**Rhonda Farnum**  
SVP, Chief Business Officer

 AMGEN

 Genentech

 ONYX  
PHARMACEUTICALS

 pharmacyclics



**Aine Mi**  
SVP, Development

 Alkermes

 elan

 Allergan

## AMPRELOXETINE

**The first once-daily, selective norepinephrine reuptake inhibitor in development to treat symptomatic neurogenic orthostatic hypotension (nOH) in patients with multiple system atrophy (MSA)**



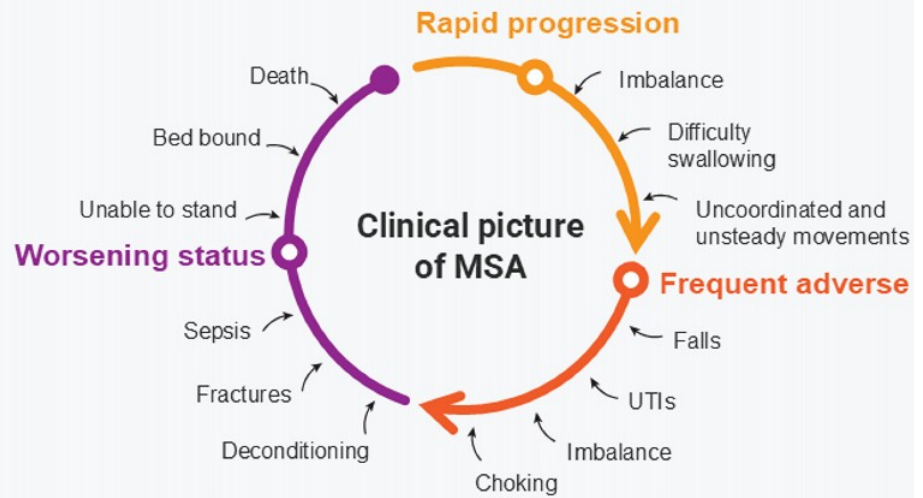
# Multiple System Atrophy (MSA) is a Rare and Severe Neurodegenerative Disease

MSA is characterized by rapid neuronal loss leading to autonomic and motor failure

Age of onset  
**55-60**<sup>1</sup>

Patients in the US  
**~50,000**<sup>2-4</sup>

Median survival  
**8 years**<sup>5</sup>



Autonomic failure in MSA patients causes a drop in blood pressure upon standing this is known as **neurogenic orthostatic hypotension (nOH)**

1. Fanciulli A, Wenning GK. Multiple-system atrophy. N Engl J Med. 2015;372(3):249-263. 2. Kalra DK, et al. Clin Med Insights: Cardiol. 2020 14:1179546820953415. 3. Delveinsight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy, CJ Mathias (1999). 4. The lansis nOH Market Report 2023; Internal claims analyses (IQVIA, Veeva, Real Chemistry); ICD-10 Codes: G90.3, ~90% of patients, and G23.2, ~10%. 5. Goldstein DS, Holmes C, Sharabi Y, Wu T. Survival in synucleinopathies: A prospective cohort study. Neurology. 2015;85(18):1554-1561.

# nOH is One of the Most Debilitating Features of MSA with Severe Consequences

80% of patients with MSA experience nOH symptoms<sup>1</sup>



## Impact

**87%** of patients with nOH report a reduced ability to perform activities<sup>2</sup>

**42%** of patients claim nOH has robbed them of their independence<sup>2</sup>

**Enabling the patient to maintain their ability to perform physical activities by treating nOH symptoms could be lifechanging**

7

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

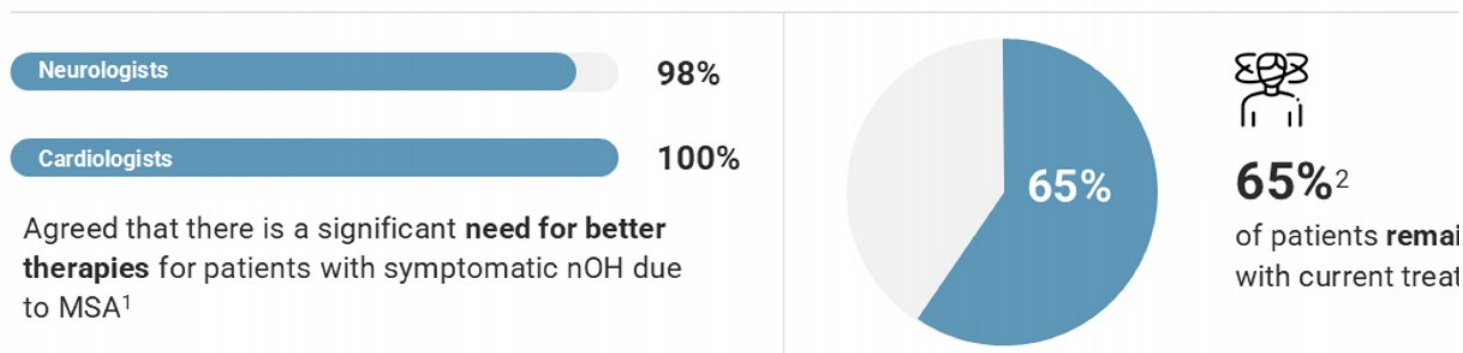
1. Delveinsight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy, CJ Mathias (1999). 2. Claassen D.O., Adler C.H., Hewitt L.A., Gibbons C. (2018), *BMC Neurology*, 18 (1), art. no. 125.

# Patients with nOH due to MSA are Not Optimally Treated

High unmet need for a clinically meaningful treatment option remains

## Limitations of currently available therapies:

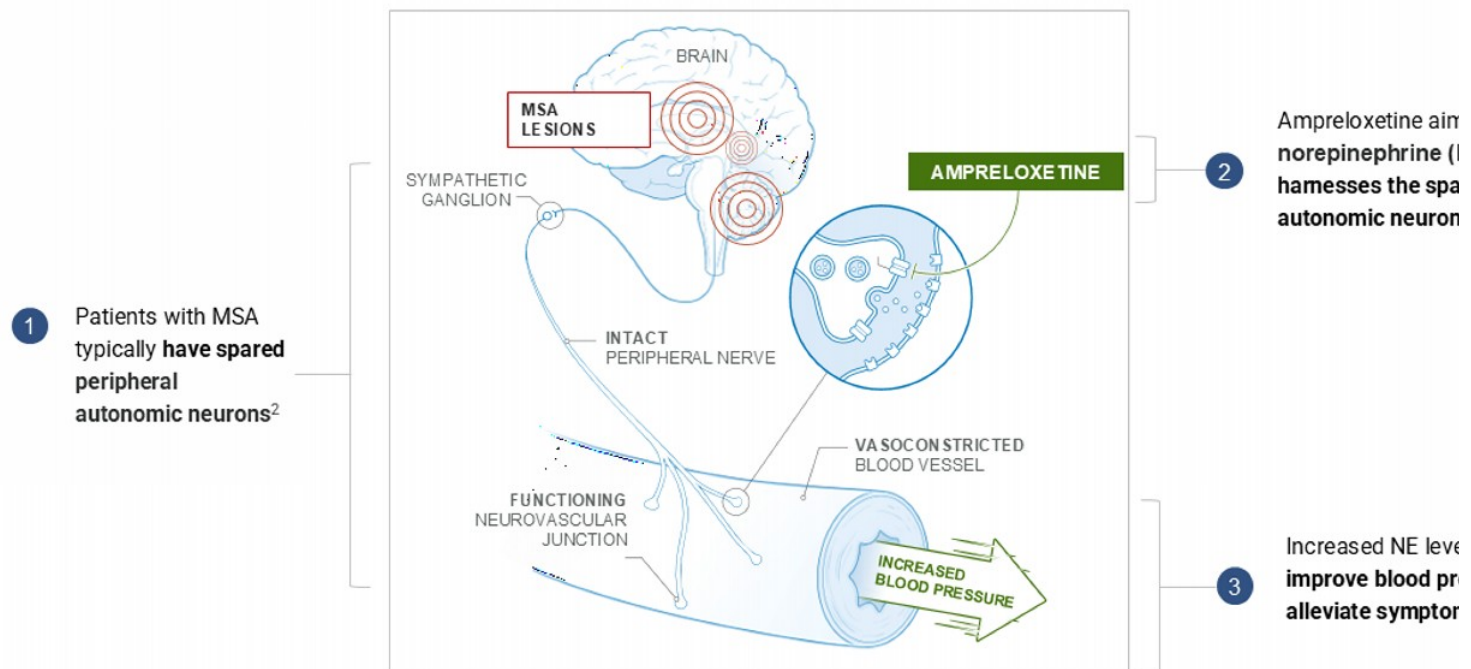
- MOAs are **not tailored** to patients with MSA
- Approved treatments **have not demonstrated durable symptom benefits** in well-controlled studies
- Commonly prescribed therapies carry a boxed warning for **significant risk of worsening supine blood pressure**
- Require **multiple doses a day**, burdening patients that may have difficulty swallowing



MOA, mechanism of action; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.  
1. 150 board certified neurologists and 50 cardiologists were asked "Based on your experience in managing MSA patients with symptomatic nOH, please indicate your level of agreement with the following statements." and were asked to use a 7-point scale where 1=Do not agree at all and 7=Strongly agree. The percentages represent the total percentage of responders that indicated they "strongly agree" or "somewhat agree" in their responses. Survey Date: Dec 2024; 2. MSA Natural History Statistics, NYU September 2019.

# Amprexetine Intended to Target the Underlying Physiology of nOH in Patients with MSA

Investigational, first-in-class<sup>1</sup> highly selective long-acting norepinephrine reuptake inhibitor (NETi)



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

1. Reflects Theravance Biopharma's expectations for amprexetine based on data collected to date. Amprexetine is in development and not approved for any indication. No conclusion can be drawn regarding its safety or efficacy. Date on file.

2. Norcliffe-Kaufmann L, Kaufmann H, Palma JA, et al. *Ann Neurol* 2018;83:522-531.

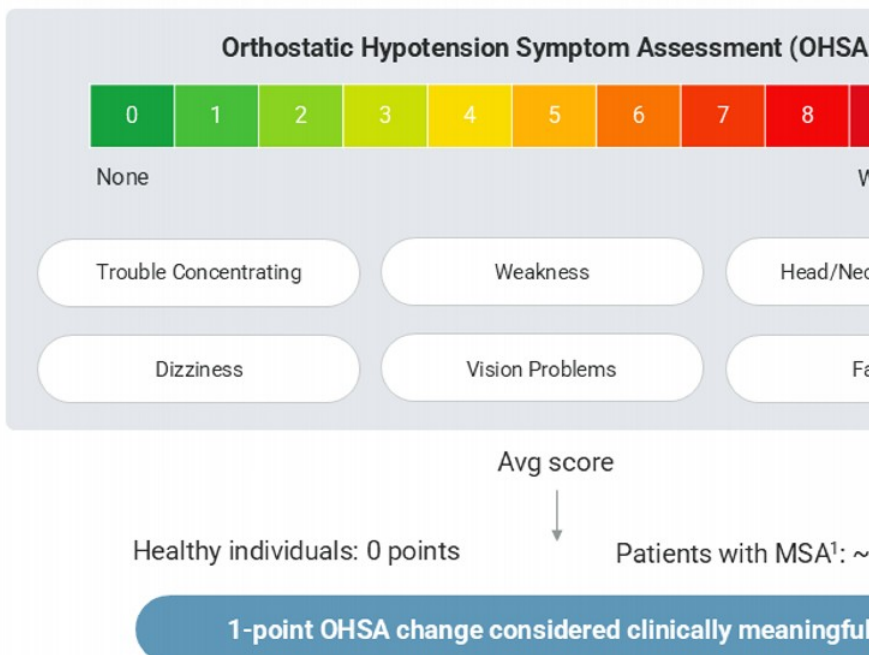
# The Orthostatic Hypotension Symptom Assessment (OHSA) is an FDA-Accepted for Regulatory Approval

A 1-point change in OHSA composite score is considered clinically meaningful<sup>1</sup>

## Orthostatic Hypotension Symptom Assessment (OHSA):

- Patient reported measure of nOH symptom burden, addressing 6 key symptoms
- Questionnaire developed by autonomic system experts
- Accepted by the FDA as an outcome measure for drug approval<sup>2</sup>

Symptom intensity can be measured by the **OHSA**



FDA, U.S. Food and Drug Administration; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

1. Kaufmann, H., Palma, J.A., Vickery, R. et al. Establishing minimally clinically important differences for the orthostatic hypotension questionnaire (OHQ). *Clin. Auton. Res.* (2025). <https://doi.org/10.1007/s10286-025-01168-y>.





2. 2032020RIG1S000 - FDA, [www.accessdata.fda.gov/drugsatfda\\_docs/nda/2014/2032020Orig1s000SumR.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/2032020Orig1s000SumR.pdf). Accessed 8 Sept. 2024.

AMPRELOXETINE

**Clinical Development**



# Amprelosetine Development Program Overview

Pre-clinical	Phase 2 PoC	Initial Phase 3 <sup>1</sup>	Current Study Phase 3 CYPRESS
<p><b>Novel</b> chemical entity, discovered and developed at Theravance Biopharma</p> <p><b>Potent and high-affinity NET inhibitor</b></p> <p>Orally bioavailable with half life that supports <b>QD dosing</b></p> <p>Mechanism of action consistent with <b>durability of effect</b></p>	<p>Demonstrated <b>sustained, clinically meaningful symptom improvement</b> for up to 5 months in nOH</p> <p>nOH symptom improvements associated with increases in standing SBP</p>	<p>Proposed indication of symptomatic <b>nOH in patients with MSA</b></p> <p><b>Expanded</b> to broader population based on unmet need</p> <p>MSA patients showed <b>sustained symptom improvement<sup>2</sup></b></p> <div style="display: flex; justify-content: space-around; align-items: center;">    </div>	<p>Refocused to <b>MSA</b></p> <p>Designed to <b>be seen in MSA</b></p> <p>Phase 3 program</p> <p><b>Clear FDA re</b> forward with CYPRESS data</p> 

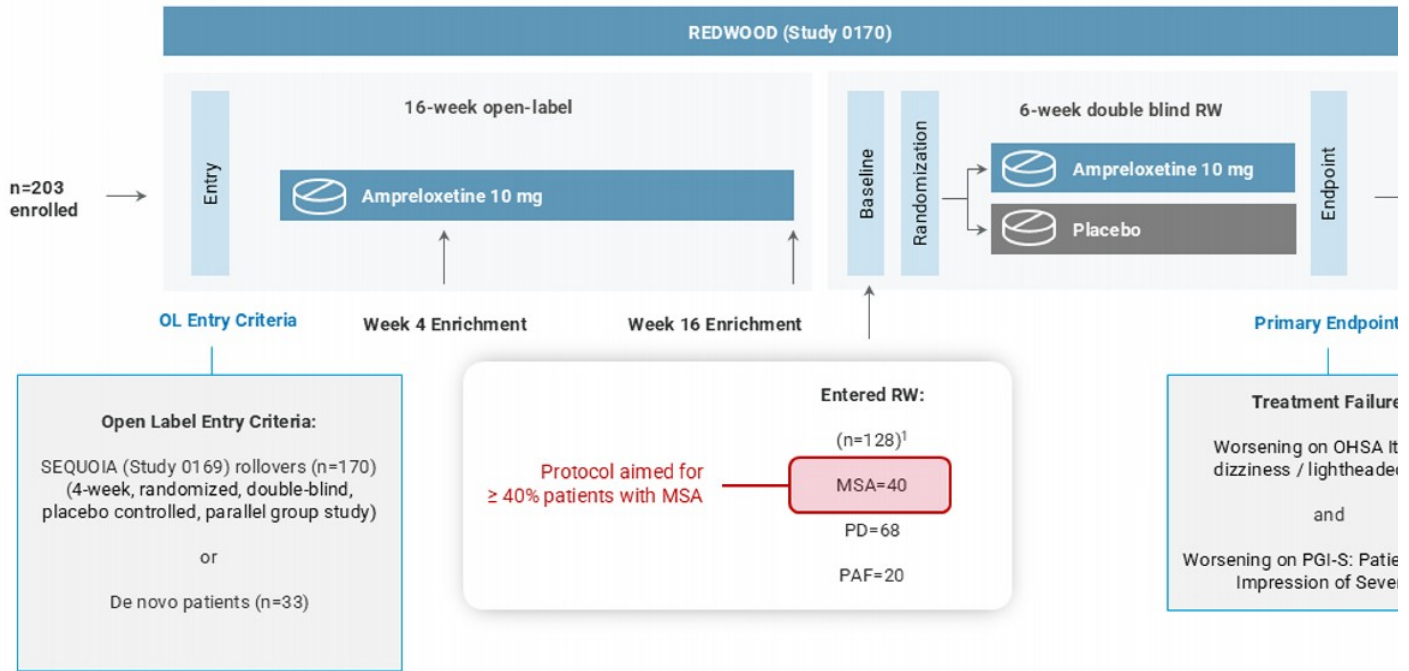
FDA, U.S. Food and Drug Administration; MSA, multiple system atrophy; NE, norepinephrine; NET, norepinephrine transporter; nOH, neurogenic orthostatic hypotension; QD, once a day; SBP, systolic blood pressure

1. The initial Phase 3 program included the SEQUOIA (Study 0169), REDWOOD (Study 0170), and the long-term extension OAK study.

2. Confirmatory study ongoing. Amprelosetine is in development and not approved for any indication. No conclusion can be drawn regarding its safety or efficacy. Date on file.

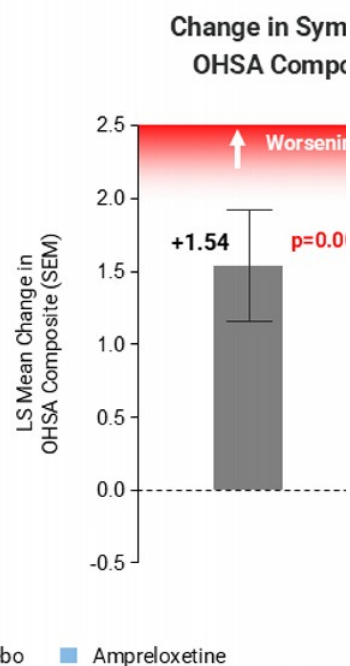
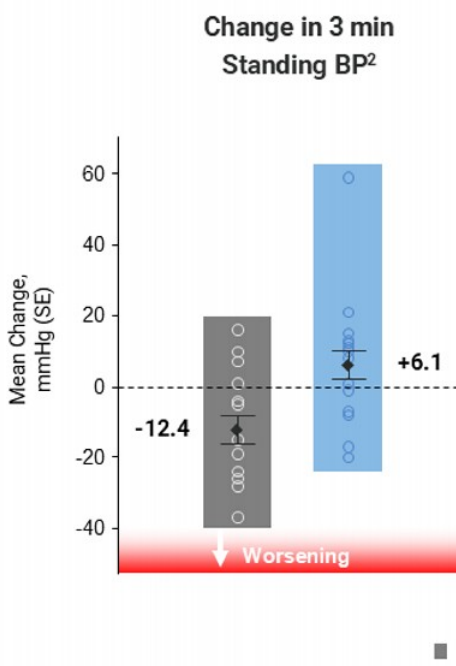
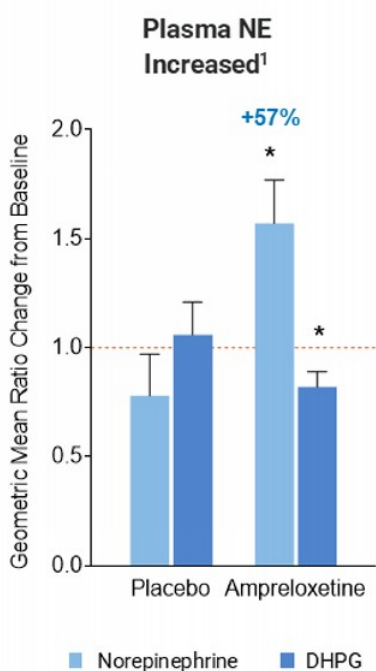
# Initial Phase 3 Studies Enrolled Patients with MSA, Parkinson's and PAF

Purposefully enrolled higher percentage of patients MSA in REDWOOD (Study 0170)



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.  
 1. Study 0170 was terminated early because of negative results from Study 0169 (n=128 vs. 154 anticipated).

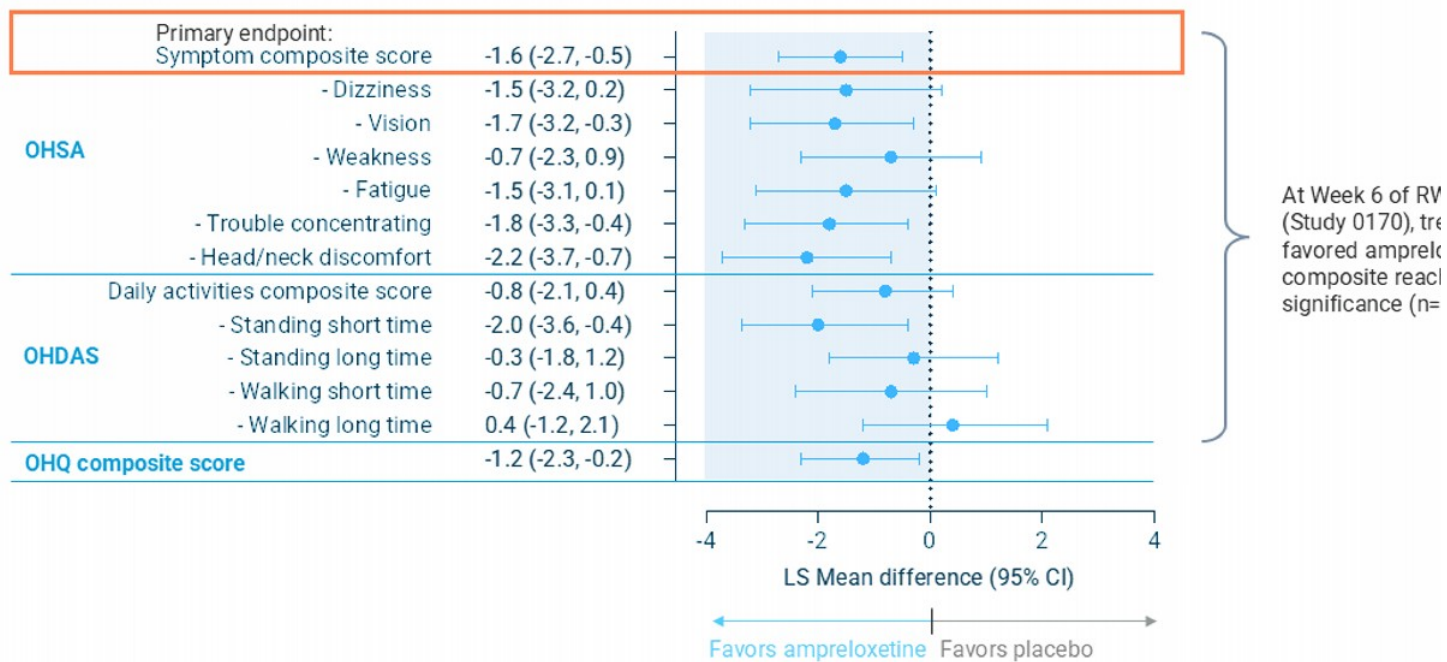
# Mechanism of Action in MSA Patients Supported by Initial Phase 3 Studies



BP, blood pressure; DHPG, dihydroxyphenylglycol; LS, least-squares; MSA, multiple system atrophy; NE, norepinephrine; OHSA, orthostatic hypotension symptom assessment; SE, standard error; SEM, standard error of mean.

1. Data from MSA patients. Error bars represent SE. \* p < 0.05 comparison to baseline reported after 4 weeks of ampreloxetine administration in SEQUOIA (study 0169). 2. Data from MSA patients at Week the randomized withdrawal period of REDWOOD (study 0170). Ampreloxetine is in development and not approved for any indication.

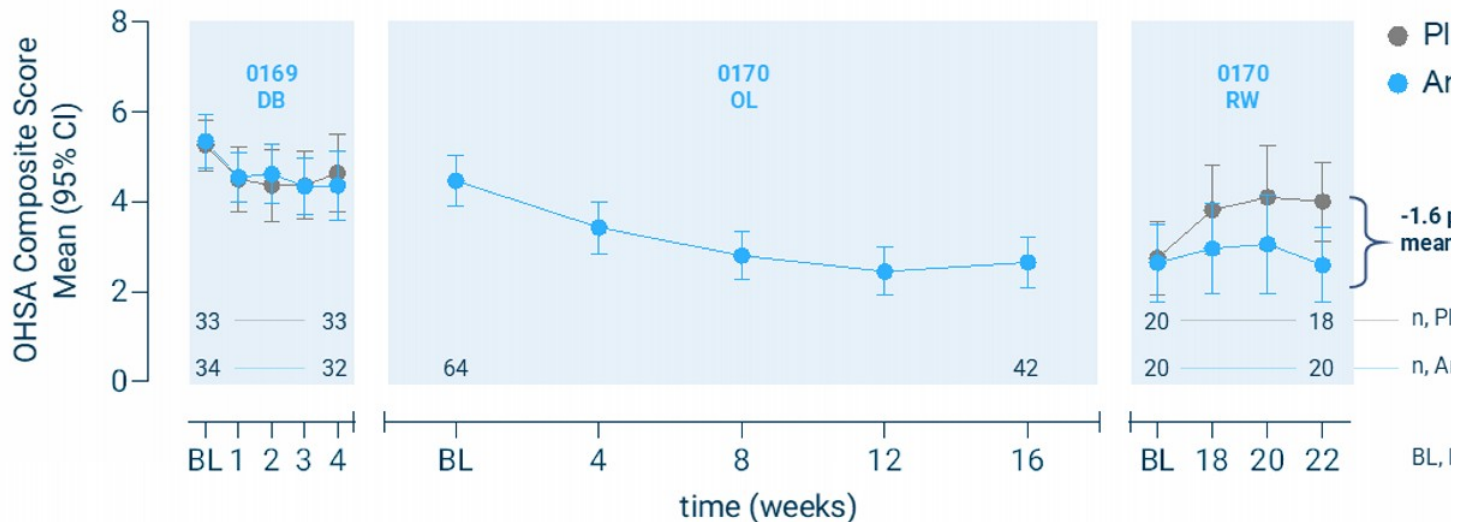
# Consistent Symptom Benefits Observed Across Individual OHSA Items in Patients with MSA in the Phase 3 REDWOOD Study<sup>1</sup>



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; RW, randomized withdrawal.  
 \*Data from MSA patients at Week 6 of the randomized withdrawal period of REDWOOD (study 0170); individual item score analyses are post-hoc except for dizziness.  
 1. Freeman R, et al. Precision therapy with amprelosetine for neurogenic orthostatic hypotension in multiple system atrophy. MedRxiv. <https://doi.org/10.1101/2025.08.12.25332833>.

# Amprelosetine Demonstrated a Durable, Clinically-Significant Symptom Benefit in Patients with MSA in the Phase 3 REDWOOD Study<sup>1</sup>

Pre-specified subgroup analysis of patients with MSA:

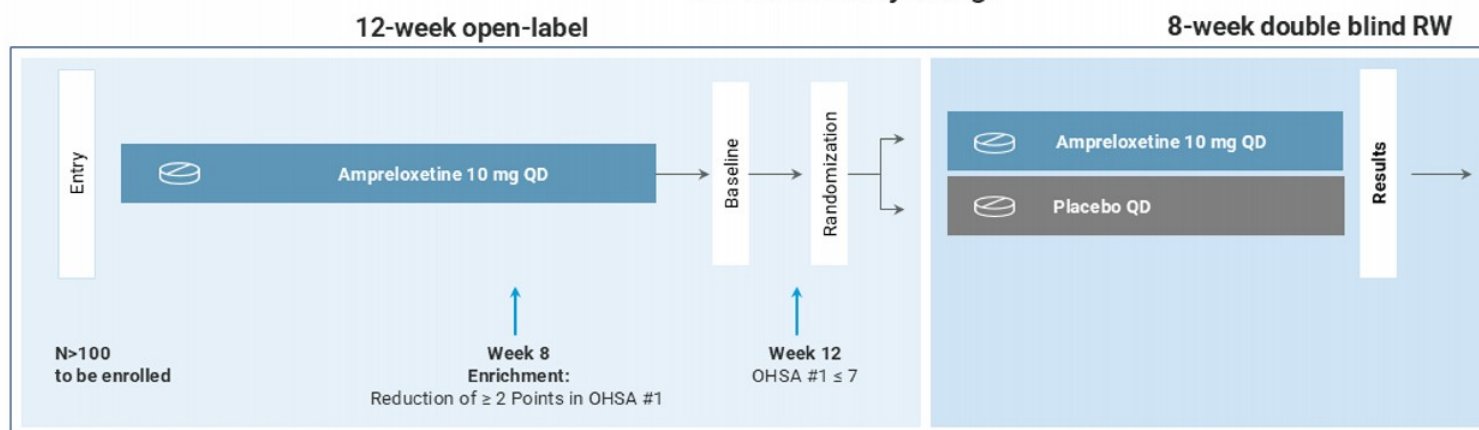


Patients with nOH due to MSA saw a clinically-meaningful 1.6 point benefit in the OHSA composite score at Week 6 of the RW period (n=40)\*

16 CI, confidence interval; DB, double-blind; MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; OL, open label; RW, randomized withdrawal, LS mean: Least Squares Mean  
 1. Data in MSA patients on file. Further validation is underway in CYPRESS.  
 \*all 40 randomized MSA participants were included in the primary analysis model.

# Pivotal Phase 3 CYPRESS Trial was Informed by REDWOOD Study Results in P with nOH due to MSA

## CYPRESS Study Design



**Primary endpoint:** OHS composite score

**Secondary endpoints:**

- OHDAS composite score
- Standing: Change from baseline in ability to stand for a short time (item 1)
- OHDAS Walking: Change from baseline in ability to walk for a short time (item 3)

**Exploratory Endpoints:**

- Standing blood pressure
- OHQ composite score
- OHQ items score
- Hospital Anxiety and Depression Scale (HADS)
- PGI-S and PGI-C
- PK/PD

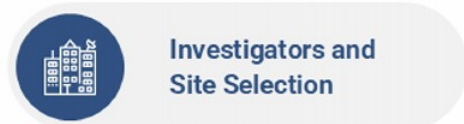
# CYPRESS Design and Execution Optimizes Probability of Success

Replicating the elements that led to the observed benefits in patients with MSA in the REDWOOD study



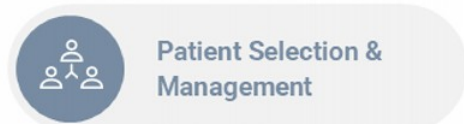
## Protocol Design

CYPRESS protocol **leverages learnings** from REDWOOD (Study 0170) to **enhance likelihood of reproducing benefits** observed in MSA patients through using the co-OHSA primary endpoint, the randomized withdrawal design, and the same enrichment



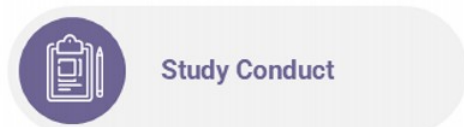
## Investigators and Site Selection

Engagement with **leading KOLs, MSA centers of excellence, and top academic sites** in REDWOOD.



## Patient Selection & Management

Using the **same external enrollment committee** as REDWOOD **ensures study integrity and patient quality** through consistent enrollment criteria and independent review of MSA diagnosis.



## Study Conduct

**Direct study management** enables real-time oversight and agile execution, support training focused on study conduct, retention and **minimizing variability**.

## CYPRESS Topline Readout will Provide an Extensive Data Set



### Population

- Patient disposition: status during OL and RW
- Baseline characteristics: demography, clinical characteristics and OHQ score



### Efficacy

- Primary endpoint: OHSA composite score
- Secondary endpoints: OHDAS Composite Score, OHDAS1, OHDAS3
- Exploratory endpoint: blood pressure (seated, supine and standing)
- Forest plot of OHQ compositions score and individual items (e.g., dizziness, etc.), longit



### Safety

Adverse events and serious adverse events

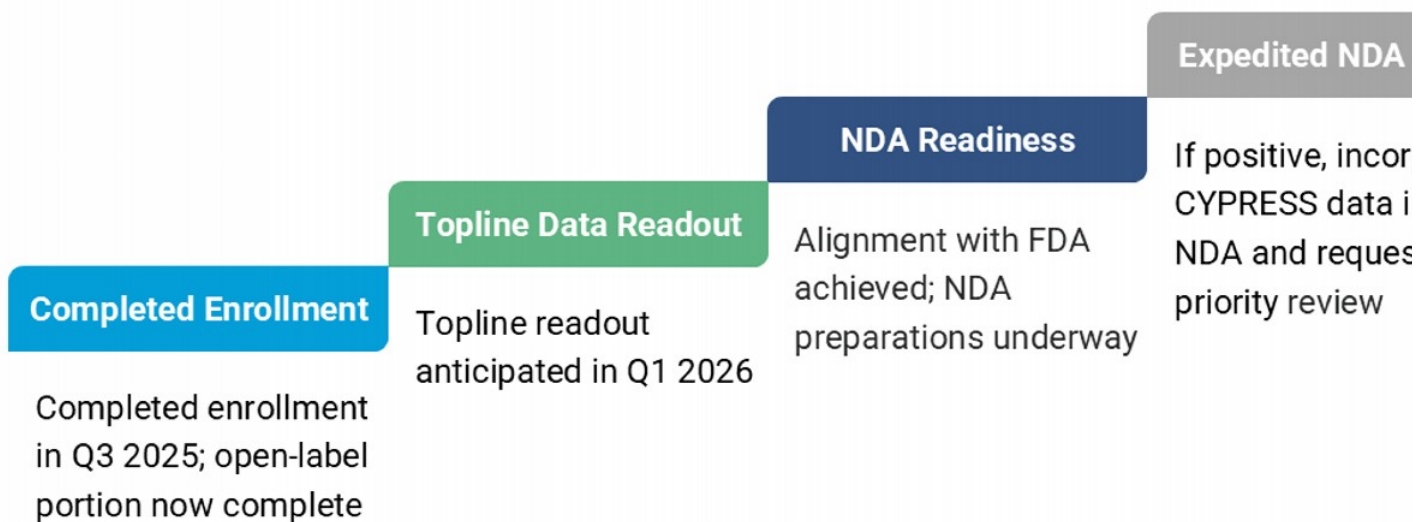


### Clinical meaningfulness

Meaningful change thresholds for OHSA composite score

CYPRESS study replicated the elements that led to the observed benefits in patients with MSA in the REDWOOD study

## Positioned to Capitalize Rapidly Upon Potential Positive Readout from Pivotal Phase 3 CYF

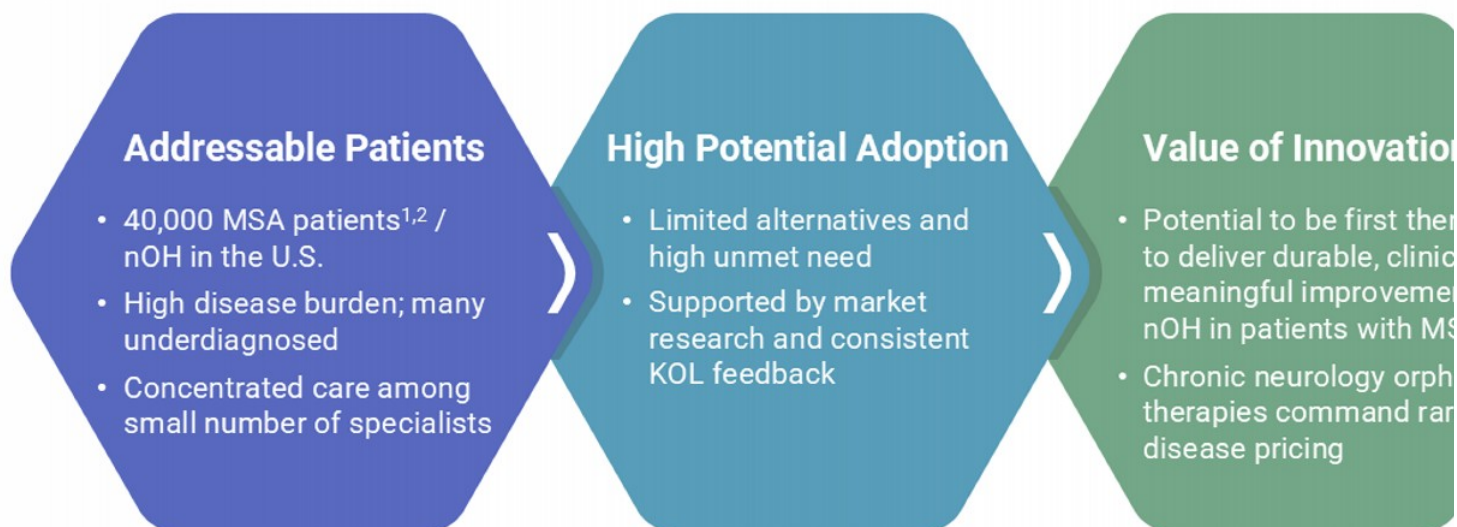


AMPRELOXETINE

## Market Opportunity



# Concentrated, Rare Neurology Market with Potential Therapeutic Breakthrough



Concentrated rare neuro market + high unmet need globally + rare disease economics

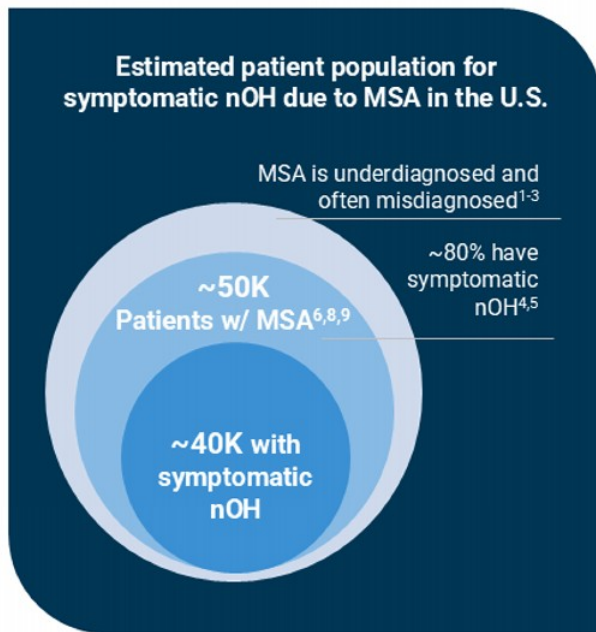
## Blockbuster Potential

KOL, key opinion leader, MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

1. Palma, Kaufmann. Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension; Kalra DK, et al. Clin Med Insights: Cardiol. 2020 14:1179546820953415. 2. Kaplan et al., Parkinsonism Relat Disord. 2023 Dec;117:105920; UCSD Dept. of Neurosciences : <https://neurosciences.ucsd.edu/centers-programs/movement-disorders/community/disease-overview/msa.html>; Internal claims analyses (IQVIA, Veeva, Real Chemistry), ICD-10 Codes: G90.3, G23.2.

# ~40,000 Patients with MSA Suffer from Symptomatic nOH in the U.S.

Epidemiology supported by detailed claims analysis, substantiated by several leading institutions



## Claims level analysis supports epidemiology assumption

- U.S. patient-level claims data using ICD-10 codes most commonly associated with MSA<sup>6</sup>
- Coding practices validated through external experts<sup>7</sup>
- Similar claims-based analysis published in 2023<sup>8</sup>
- Leading institutions support estimated epidemiology (e.g., I

## Linking patients to treating specialists:

- Initial targeting efforts suggest treating physicians are highly concentrated within **autonomic and movement disorder centers, large neurology practices, and select academic institutions**
- Approach enables efficient deployment of commercial and resources across a **small, specialized physician universe**

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

1. Krismer F, et al. *Lancet Neurol*. nOH 2024;23(12):1252-1266. 2. DeRignt J. Multiple System Atrophy. In: *Essential Neuropsychology: A Concise Handbook for Adult Practitioners*. Springer; 2021. 3. Goolla M, et al. *Frontiers in Neurology*. 2023;14:1210220. 4. Palma, Kaufmann. *Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension*. 5. Kalra DK, et al. *Clin Med Insights: Cardiol*. 2020 14:1179546820953415. 6. Internal claims analyses (IQVIA, Veeva, R Chemistry). ICD-10 Codes: G90.3, ~90% of patients, and G23.2, ~10%. 7. Medical coding consultant, as well as primary market research with EHR specialists, billing & coding specialists, neurologists, and movement disorder specialists. 8. 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. 9. UCSD Dept. of Neurosciences (25K-75K). <https://neurosciences.ucsd.edu/centers-programs/movement-disorders/community/disease-overview/msa.html>.

# Significant Commercial Opportunity for Amprexetine Given Available Treatm

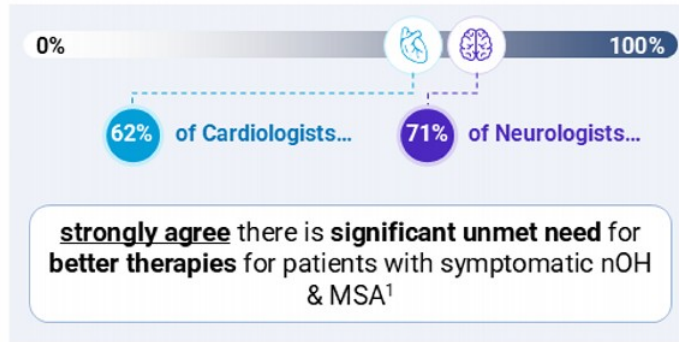
Only ~34% of patients are treated,<sup>1</sup> current therapies limited in this patient population

	Amprexetine (investigational) <sup>2</sup>	Current Treatment Landscape <sup>3</sup>	
		Midodrine	Droxidopa
Indication	Symptomatic nOH in patients with MSA	Symptomatic OH	Symptomatic nOH
Efficacy- Primary Endpoint	OHSA Composite Score	Increase in systolic blood pressure	OHSA Item #1
Durability of Response	20 weeks (CYPRESS Study Design)	Effectiveness not studied beyond 3-4 weeks	Effectiveness beyond 2 weeks has not been established
Dosing	1x/day <i>No titration or dose adjustment</i>	3x/day	3x/day <i>Requires titration</i>
Supine Hypertension	No worsening of supine hypertension observed in clinical studies to date	Boxed warning for increased risk of supine hypertension	
<p><b>Fludocortisone</b> is used off-label as volume expander, despite limited evidence, with 1x/day dosing (requires titration). Adverse events include hypertension, edema and congestive heart failure; requires strict monitoring of blood pressure and potassium</p>			

MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; OHSA, orthostatic hypotension symptom assessment.  
 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. 2. Reflects Theravance Biopharma's expectations for amprexetine. Amprexetine is in development and not approved for any indication. No conclusion can be drawn regarding its safety or efficacy. Data on file. 3. The information in the table presents factual information gathered from approved product prescribing information and are not intended to make comparisons of available therapies and investigational drug as there are no head-to-head comparative studies or data supporting any such comparisons.

# Ampreloxetine has an Opportunity to Address the Significant Unmet Need In n Treatment with its Unique Target Product Attributes

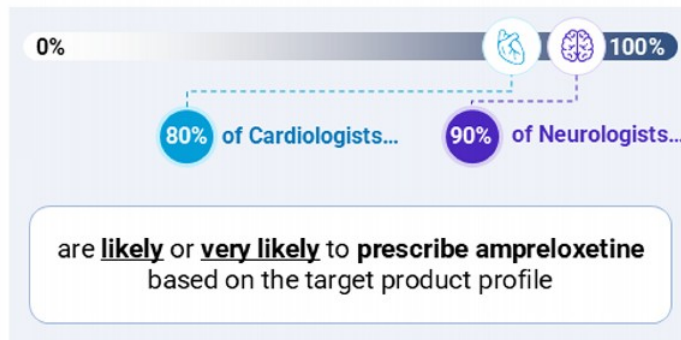
Majority of HCPs acknowledge significant unmet need for better nOH treatments in MSA



“Options are generally limited to begin with. But given the efficacy, lack of supine hypertension and convenience of dosing, it would be a no-brainer.”

Neurologist

Majority of HCPs have favorable reactions to ampreloxetine's target product profile



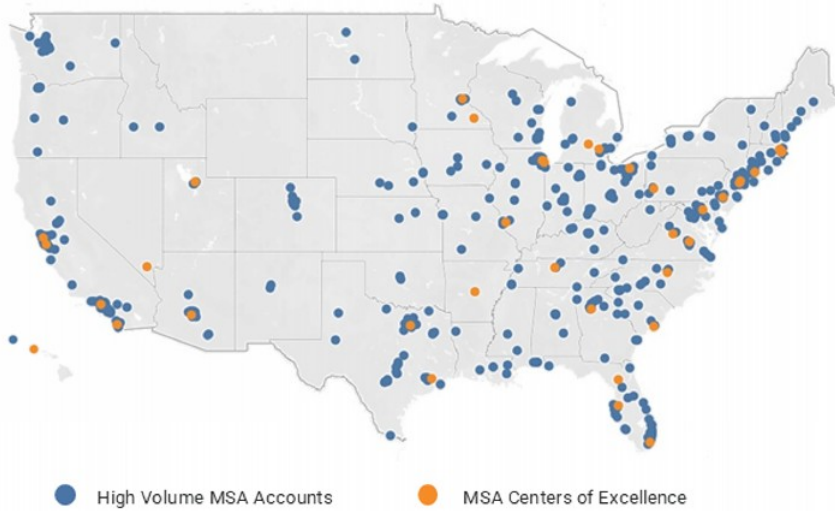
“Easier to use with l effects. Once daily, attractive. Also, no adjustments need multiple medical co is attractive.”

Ca

# Targeted Launch Plan Leverages Concentrated MSA Treatment Landscape

Lean commercial infrastructure required for focused execution

## High Volume MSA Accounts<sup>1</sup> and Centers of Excellence<sup>2</sup>



**~550**

High Volume MSA Accounts<sup>1</sup>

**~90**

MSA Specialists with 10+ Patients<sup>1</sup>

**40**

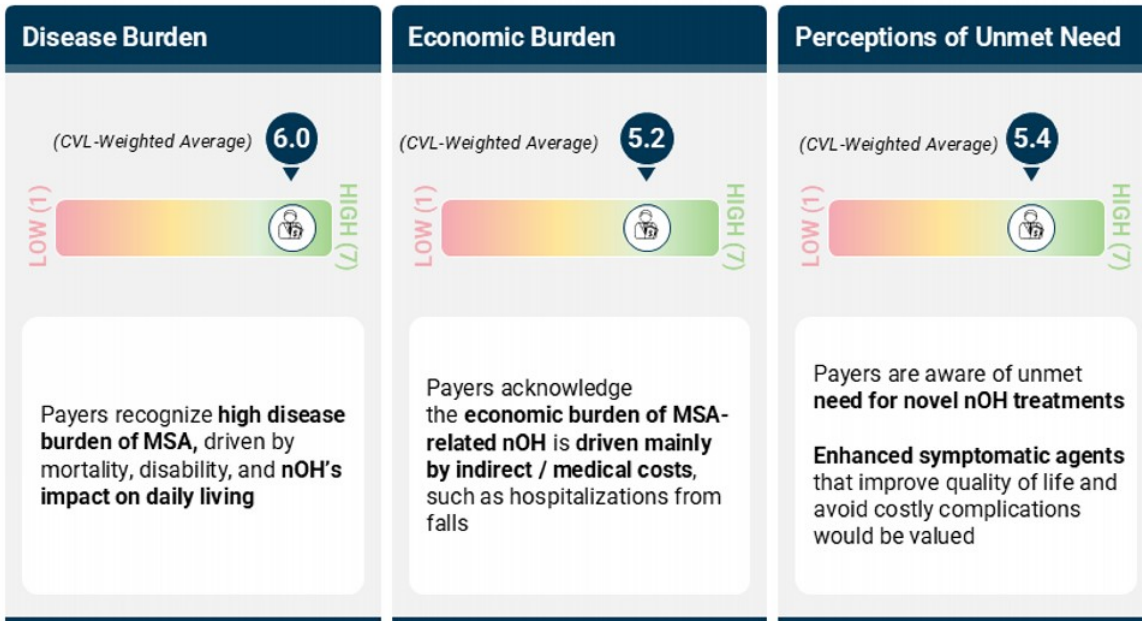
MSA Centers of Excellence

**26**

CYPRESS Trial Sites (U.S.)

**Investment plans aligned with lean, rare-disease industry benchmarked spend**

# Payers Acknowledge its High Burden and Large Unmet Need for Novel Treatment



“ I think [nOH] is a consideration b that immediatel activities of dai functionality, et completely debil. certain extent.

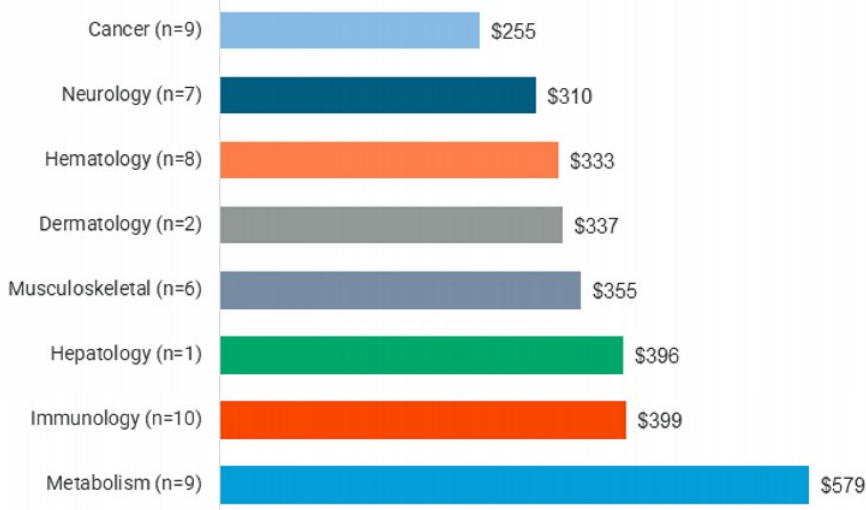
“ ...the syncope r nOH is a proble because this is a population and f patients at this the hospital.

# Premium Value Opportunity Driven by Unmet Need and Clinical Impact

Pricing Expectations Consistent with Recent Rare Disease Approvals

## Rare Disease Launches ('21-'24)<sup>1</sup>

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



## Amprelosetine is well positioned to meet pricing expectations for patients with nOH



**Serious disorder with negative impact on quality of life**  
For ~80% of patients with MSA, nOH, there is a significant impact on quality of life, including morbidity, mortality, and health care costs.



**Value for patients and caregivers**  
Treating nOH equates to functional improvement, reducing dependency and the burden of a constellation of symptoms patients experience.

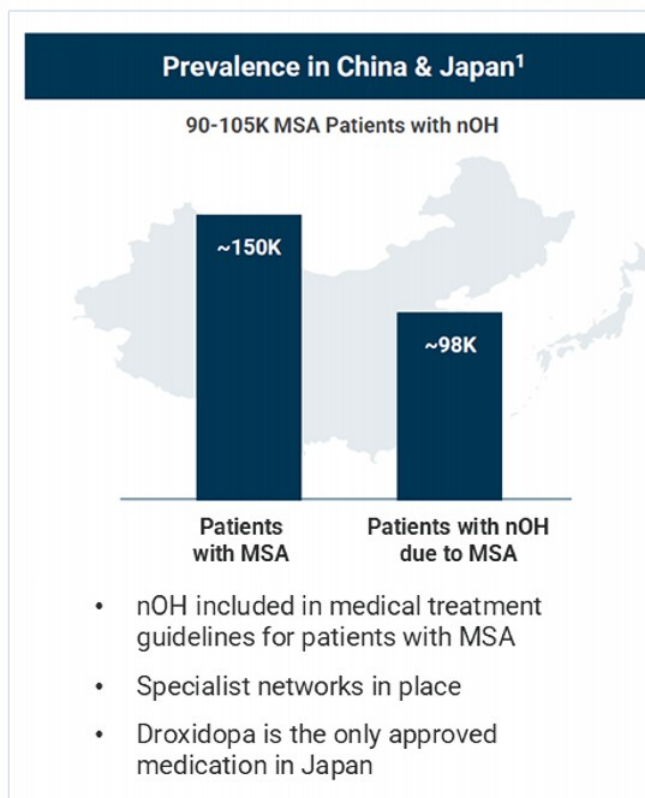
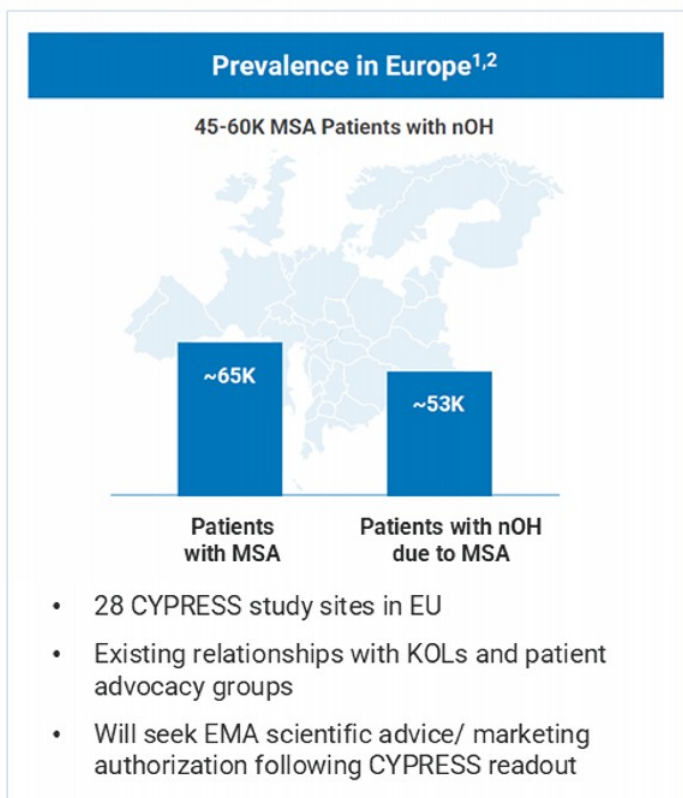


**Targeted, Orphan Drug Opportunity**  
Overall low total budget impact; high value for patients in the U.S.<sup>2,3</sup>

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

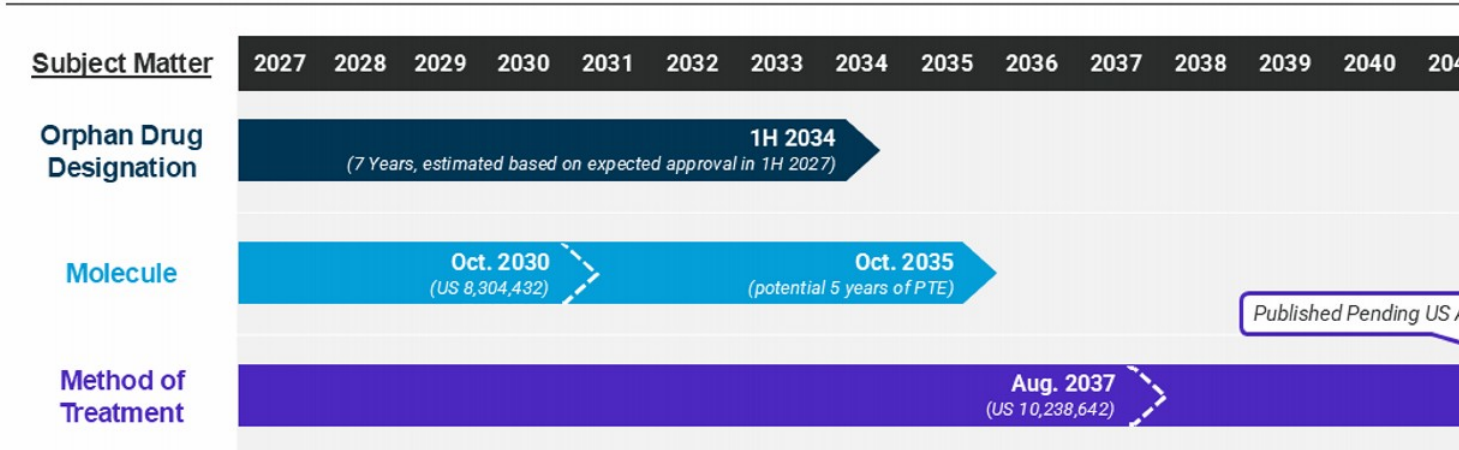
1. Cantor Fitzgerald, Biotechnology Equity Research, April 11, 2024. Includes 63 drugs approved in the US between 1/22/2021-3/21/2024; average launch price based on WAC (wholesale acquisition cost).  
2. Palma, Kaufmann. Epidemiology, Diagnosis, and Management of Neurogenic Orthostatic Hypotension; Kalra DK, et al. Clin Med Insights: Cardiol. 2020 14:1179546820953415. 3. Kaplan et al., Parkinsonism Relat Disord. 2023 Dec;117:105920; UCSD Dept. of Neurosciences : <https://neurosciences.ucsd.edu/centers-programs/movement-disorders/community/disease-overview/msa.htm>; Internal claims analyses (IQVIA, Veeva, Real Chemistry), ICD-10 Codes: G90.3, G23.2.

# Meaningful Market Opportunity for Amprelosetine Exists in Europe and Asia



# Amprexetine US Intellectual Property Summary

## Potential Duration of US LOE



# Amprexetine: Potential to Transform Care in a Rare and Debilitating Disease



Addresses rare neurological disorder with **high unmet need**



**De-risked Phase 3 program** designed with FDA alignment; Orphan Drug Designation



**Near-term catalyst:** Phase 3 data expected Q1 2026



**Potential to become standard of care** for symptomatic nOH in MSA



**Substantial commercial opportunity** in U.S. and ex-U.S. markets



**High profit potential** based on low cost of goods and lean commercial model



## The Only Once-Daily, Nebulized LAMA Maintenance Medicine for COPD

COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist.



# Nebulized Maintenance Therapy: A Critical Treatment Option in COPD

- Nebulized therapy is an important alternative for many COPD patients
- Nebulization addresses dexterity, strength, inspiratory flow, and complex hand-breath coordination limitations<sup>1</sup>
- 28% of Medicare FFS COPD patients have filled a prescription for a nebulizer<sup>2</sup>



**YUPELRI** is the only once-daily **nebulized LAMA** medication for COPD approved in the



**14-16M**

patients with diagnosed COPD in the U.S.<sup>4</sup>



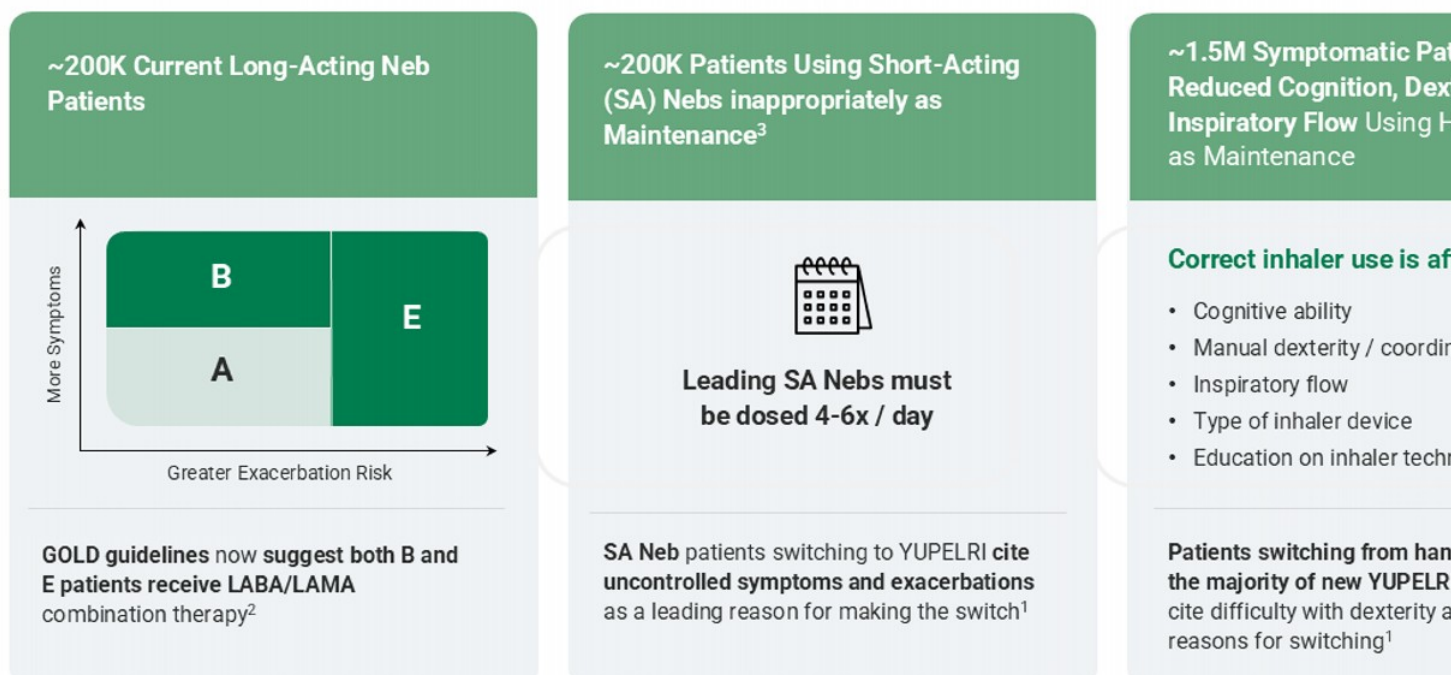
**~1.9M**

can benefit from YUPELRI<sup>5</sup>

COPD, chronic obstructive pulmonary disease; FFS, Fee For Service; LAMA, long-acting muscarinic antagonist.

1. Donahue, 2019. 2. Avalere, 2024. YUPELRI is contraindicated in patients with hypersensitivity to revefenacin or any component of this product. 3. YUPELRI should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD, or for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled short-acting beta2-agonist. 4. CDC, 2023, NIH. 5. Addressable patient population quantifies the number of patients within the intended target profile. Sources: Citeline Pharma Custor Intelligence Primary Research April 2023, Symphony Health METYS Prescription Dashboard, SolutionsRx Med B FFS.

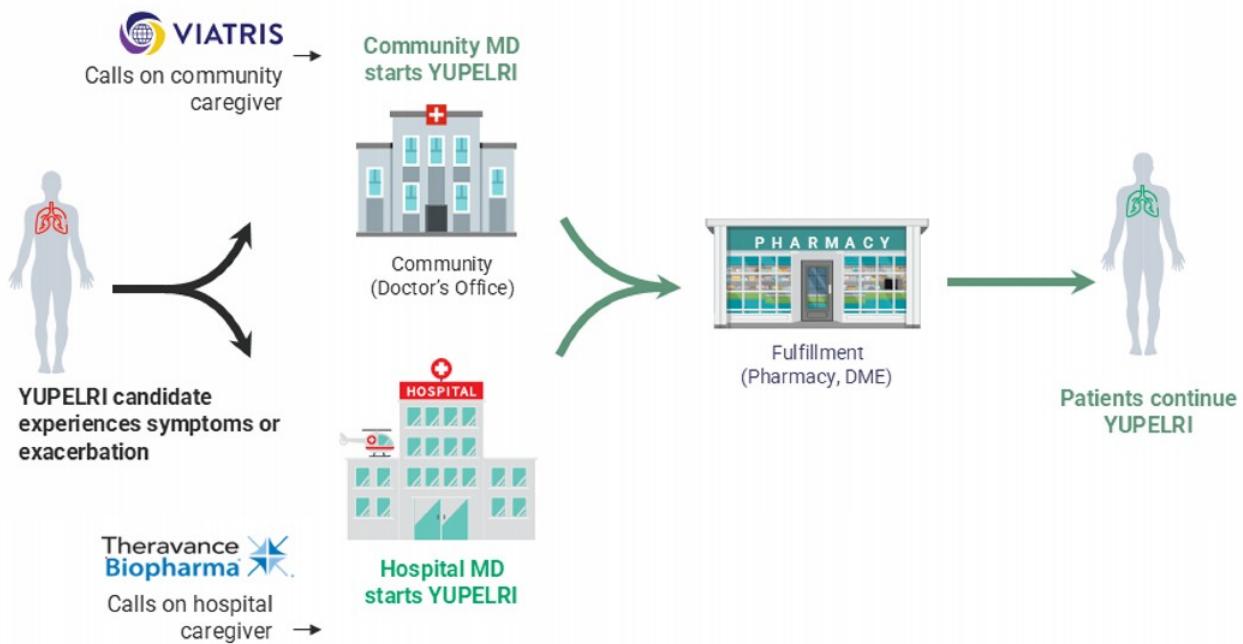
# YUPELRI® Opportunity: Expand Use of Neb LAMA in ~1.9M Patients with COPD



34  
 COPD, chronic obstructive pulmonary disease; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist; Neb, nebulized therapy.  
 1. Addressable patient population quantifies the number of patients within the intended target profile. Source: Joint VTRS/TBPH Market Research (Jun'24). 2. Global Initiative for Chronic Obstructive Lung Disease 2024 Report. 3. Medications indicated to address bronchospasm per US package insert. COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

# Theravance / Viatris Partnership Drives YUPELRI® Prescription Growth

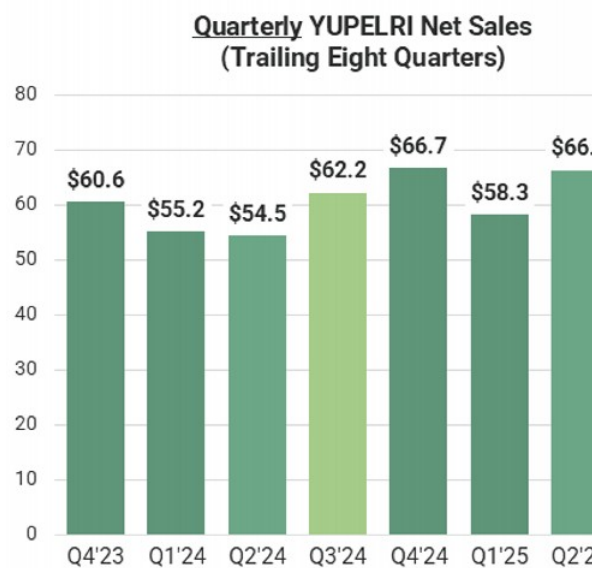
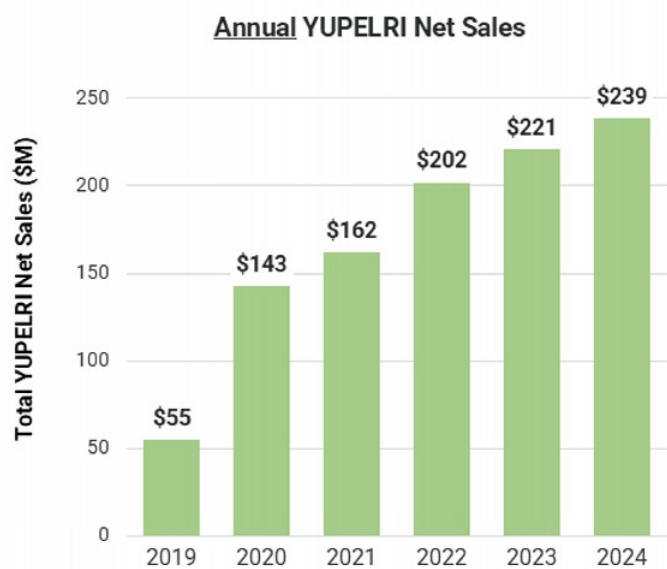
U.S. Co-Promotion Agreement (35% / 65% Profit Share)



Hospital sta  
sizeable con  
the business

- >80% of pat  
YUPELRI in  
leave with a  
continue th
- Theravance  
coordinate  
to ensure st  
Transition o

## Continued Year-over-Year YUPELRI® Net Sales Growth in the U.S.



**Net sales increased 15% Q3 '25 / Q3 '24**

# Strong Q3 Performance and Expanding YUPELRI® Profitability

## Growth in Q3 2025

- Q3 2025 U.S. net sales of \$71.4M up 15% vs. Q3 2024
- Hospital doses growth of 29% vs Q3 2024; new hospital market share high of 21%
  - Hospital setting serves as key point of initiation; majority of patients receive script at c

## Continued Opportunity

- Sizable addressable patient population remains<sup>2</sup>
- Increasing adoption of concomitant use with LAMA/LABA and switches from handheld-on
- Success in further diversification of product fulfillment
- New analyses presented at CHEST 2025 further strengthen evidence supporting YUPELRI
- Eligible to receive tiered royalties ranging from 14% to 20% on net sales in China

## Profitable Brand, Expanding Margins and Strong IP

- Theravance receives 35% of U.S. profits<sup>3</sup>
- \$25M milestone for 1st year in which U.S. net sales > \$250M<sup>4</sup>
  - ~\$54 million required in Q4 2025 to trigger \$25 million milestone in 2025
- IP protection in the U.S. into 2039

LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonist.

1. Joint VTRS/TBPH Market Research. 2. Addressable patient population quantifies the number of patients within the intended target profile. Source: Joint VTRS/TBPH Market Research. 3. In the US, Viatriis leading the commercialization of YUPELRI, and Theravance Biopharma co-promotes the product under a profit and loss sharing arrangement (65% to Viatriis; 35% to Theravance Biopharma). 4. As of 9/30/25, Theravance Biopharma is eligible to receive from Viatriis potential global development, regulatory and sales milestone payments (excluding China and adjacent territories) totaling up to \$205.0 million in the aggregate; refer to our SEC filings for further information.

## Granted Patent Protection into Late 2030s

Compound	Invention	Patent Expiry
YUPELRI® / revefenacin	Composition of Matter	2028
	Polymorph	2030-2031
	Method for the maintenance treatment of COPD patients	2039

- Total of 7 generics filed ANDAs in November 2022, with 1 subsequent filer
- Litigation settled with 7 out of the 8 generics, all with licensed entry dates of April 2039 to major versions of YUPELRI®, subject to certain exceptions as is customary in these type of agreements
- Only party still involved in litigation is Mankind Pharma, Ltd., which has stipulated it will not sell product prior to August 2031
  - Litigation continues over patents expiring in 2039

GSK's TRELEGY

**The First and Only Once-Daily Triple Therapy in a Single Inhaler for Adult Patients with COPD or Asthma**

Milestones from Royalty Pharma

COPD, chronic obstructive pulmonary disease



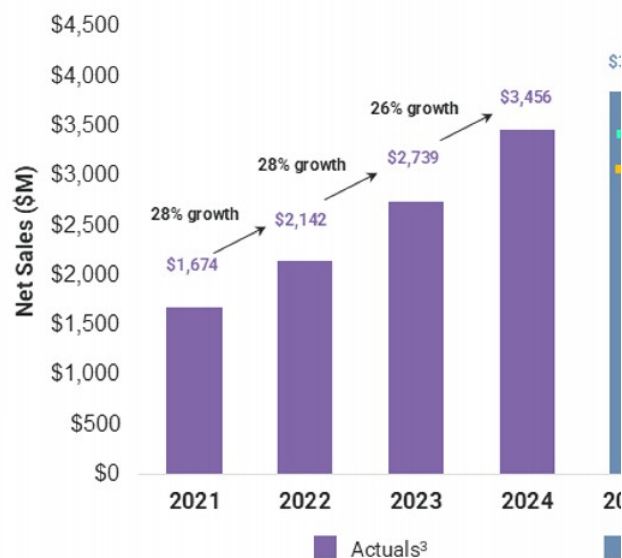
# On Pace to Achieve \$150M in TRELEGY Sales Milestones in 2025 and 2026

Q3'25 Net Sales of \$1.0B and YTD Net Sales of \$2.9B, up 13% YoY

## 2025 and 2026 Sales Milestones<sup>1</sup>

Year	Global Net Sales Equivalent	Royalty Threshold <sup>2</sup>	Milestone to Theravance
2025 <sup>1</sup>	\$3,063M	\$260M	\$25M
	\$3,413M	\$295M	\$50M
2026 <sup>1</sup>	\$3,163M	\$270M	\$50M
	\$3,513M	\$305M	\$100M

## Strong TRELEGY Global Net Sales Growth



40 1. If both milestones are achieved in a given year, Theravance Biopharma will only earn the higher milestone, payable by Royalty Pharma (RP) pursuant to the Equity Purchase and Funding Agreement, dated as of July 13, 2022, by and between Theravance Biopharma, Inc. and Royalty Pharma Investments 2019 ICAV. 2. Based on 100% of TRELEGY ELLIPTA royalties. 3. GSK-reported Net Sales in USD. 4. Bloomberg Consensus as of 11/6/25.

## Financials and Capital Management



## Third Quarter 2025 Financial Highlights

Metric	Q3 '25 (M)	Q3 '24 (M)	Note
VIATRIS Collaboration Revenue	\$20.0	\$16.9	19% growth YoY driving improved p
SG&A and R&D Expense, ex-SBC	\$21.9	\$21.2	
Share-Based Compensation	\$4.6	\$5.0	Down 8% YoY due to continued cos
GAAP Net Income (Loss)	\$3.6	(\$12.7)	
Non-GAAP Net Income (Loss) <sup>1</sup>	\$2.3	(\$2.9)	
Cash and Cash Equivalents <sup>2</sup> (as of quarter-end)	\$332.7	\$91.4	Increase driven by TRELEGY royalty p second quarter of 2025
Debt (as of quarter-end)	\$0.0	\$0.0	
Shares Outstanding (as of quarter-end)	50.7	49.2	

SBC, Share-Based Compensation.

1. Non-GAAP net income (loss) consists of GAAP net income (loss) before taxes less (i) share-based compensation expense; (ii) non-cash interest expense; (iii) non-cash impairment expense; and (iv) non-recurring revenue and income items; see reconciliation on Slide 16 and the section titled "Non-GAAP Financial Measures" on Slide 2 for more information. 2. Cash, cash equivalents and marketable securities

# Reaffirmed Operating Expense Guidance with Improved Margin Outlook

## 2025 OPEX Guidance:

- R&D (excluding share-based comp): \$32M - \$38M
- SG&A (excluding share-based comp): \$50M - \$60M
- Share-Based Compensation: \$18M - \$20M

## 2025 Non-GAAP Profit/(Loss) Guidance<sup>1</sup>:

- Achieved non-GAAP breakeven in Q3 2025
- Expect to remain at similar levels in Q4 2025
- Guidance excludes potential milestones for TRELEGY & YUPELRI

## Milestone Accounting:

- TRELEGY: If \$50M milestone achieved in Q4, \$50M recognized as Other Income in Q4'25
- YUPELRI: If \$25M milestone achieved in Q4, \$25M recognized as License Revenue in Q4'25



# Commercial-Stage Biotech Focused on Respiratory and Neurological Diseases

Strong financial position and cash-generating YUPELRI® set the foundation for near-term Phase 3 catalyst

<b>Ampreloxetine</b> Phase 3 Data in Q1 2026	Potential first-in-class; designed to treat patients with symptomatic nOH in MSA	<ul style="list-style-type: none"><li>Phase 3 CYPRESS randomized withdrawal complete; data expected in Q1</li><li>Targeting 40,000<sup>1,2</sup> patients with nOH due to MSA in the U.S.</li><li>FDA Orphan Drug Designation</li><li>Significant ex-U.S. opportunity with ~53K patients in EU<sup>3,4</sup> and ~98K patients in Japan</li></ul>
<b>YUPELRI®</b> Strong Cash Flow Generation	First-in-class nebulized LAMA for COPD developed in-house	<ul style="list-style-type: none"><li>35% US profit share with Viatriis<sup>5</sup></li><li>Strong growth potential remains<sup>6</sup></li><li>Eligible to receive tiered royalties ranging from 14% to 20% on net sales in Japan</li></ul>
<b>Financial Profile</b> Robust Cash Position and Milestones	Cash of \$333M <sup>7</sup> + \$175M of highly probable near-term milestones <sup>5,9</sup>	<ul style="list-style-type: none"><li>\$333M in cash   no debt; breakeven in Q3 2025<sup>8</sup>, expected to remain at similar level</li><li>Highly probable near-term milestones: \$150M from TRELEGY<sup>9</sup>   \$25M from Japan</li><li>Commitment to return excess capital to shareholders</li></ul>

FDA, U.S. Food and Drug Administration; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

1. Kalra DK, et al. Clin Med Insights: Cardiol. 2020 (70%-90%);14:1179546820953415. 2. Delve Insight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy. 3. The lansis nOH Market Report 2023; TBPH Internal Analysis. 4. Prevalence estimate for Germany, France, UK, Italy and Spain. 5. In the US, Viatriis is leading the commercialization of YUPELRI and Theravance Biopharma co-promotes the product under a profit and loss sharing arrangement (65% to Viatriis; 35% to Theravance Biopharma). Refer to our SEC filings for further information. 6. Sources: Citeline Pharma Custom Intelligence Primary Research April 2023, Symphony Health METYS Prescription Dashboard, SolutionsRx Med B FFS. 7. As of September 30, 2025. 8. Cash flow guidance excludes potential one-time milestones (and associated taxes). 9. Payments from Royalty Pharma (RP) will be triggered if RP receives certain minimum royalty payments from GSK based on TRELEGY global net sales.

# Appendix



## Third Quarter 2025 Financials (Unaudited)

(\$, in thousands)	Three Months Ended September 30,		Nine Months Ended Se	
	2025	2024	2025	(Unaudited)
	(Unaudited)		(Unaudited)	
<b>Revenue:</b>				
Viatri collaboration agreement	\$ 19,990	\$ 16,868	\$ 54,073	\$
Licensing revenue	-	-	7,500	
Total revenue	19,990	16,868	61,573	
<b>Costs and expenses:</b>				
Research and development (1)	8,112	9,268	30,054	
Selling, general and administrative (1)	18,333	16,875	55,132	
Impairment of long-lived assets (non-cash)	-	1,562	-	
Total costs and expenses	26,445	27,705	85,186	
<b>Loss from operations (before tax and other income &amp; expense)</b>	<b>\$ (6,455)</b>	<b>\$ (10,837)</b>	<b>\$ (23,613)</b>	<b>\$</b>
<b>Share-based compensation expense:</b>				
Research and development	1,080	1,111	3,137	
Selling, general and administrative	3,496	3,852	10,859	
Total share-based compensation expense	4,576	4,963	13,996	
<b>Operating expense excl. share-based compensation:</b>				
R&D operating expense (excl. share-based compensation)	7,032	8,157	26,917	
SG&A operating expense (excl. share-based compensation)	14,837	13,023	44,273	
<b>Total operating expenses excl. share-based compensation</b>	<b>\$ 21,869</b>	<b>\$ 21,180</b>	<b>\$ 71,190</b>	<b>\$</b>
<b>Non-GAAP net income (loss) (2)</b>	<b>\$ 2,260</b>	<b>\$ (2,897)</b>	<b>\$ (10,583)</b>	<b>\$</b>

1. Amounts include share-based compensation. 2. Non-GAAP net income (loss) consists of GAAP net income (loss) before taxes excluding (i) share-based compensation expense; (ii) non-cash interest expense; (iii) non-cash impairment expense; and (iv) non-recurring revenue and income items; see reconciliation on Slide 16 and the section titled "Non-GAAP Financial Measures" on Slide 2 for more information.

# Third Quarter 2025 Financials (Unaudited)

## (Cont'd)


### Reconciliation of GAAP Net Income (Loss) to Non-GAAP Net Income (Loss) (In thousands, except per share data)

	Three Months Ended September 30,		Nine Months Ended Septe	
	2025	2024	2025	2024
	(Unaudited)		(Unaudited)	
<b>GAAP Net Income (Loss)</b>	\$ 3,615	\$ (12,698)	\$ 44,871	\$
<u>Adjustments:</u>				
Licensing revenue (1)	-	-	(7,500)	
Net gain on realized contingent milestone and royalty assets (1)	-	-	(75,137)	
Non-cash impairment expense of long-lived assets (1)	-	1,562	-	
Share-based compensation expense	4,576	4,963	13,996	
Non-cash interest expense	573	630	1,879	
Income tax (benefit) expense	(6,504)	2,646	11,308	
<b>Non-GAAP Net Income (Loss)</b>	<b>\$ 2,260</b>	<b>\$ (2,897)</b>	<b>\$ (10,583)</b>	<b>\$</b>
<b>Non-GAAP Net Income (Loss) per Share</b>				
Non-GAAP net income (loss) per share - basic	\$ 0.04	\$ (0.06)	\$ (0.21)	\$
Non-GAAP net income (loss) per share - diluted	\$ 0.04	\$ (0.06)	\$ (0.21)	\$
Shares used to compute non-GAAP net income (loss) per share - basic	50,520	49,038	50,137	
Shares used to compute non-GAAP net income (loss) per share - diluted	51,908	49,038	50,976	

(1) Non-recurring item

# Appendix

COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist.



# YUPELRI® (revefenacin) Inhalation Solution

YUPELRI® inhalation solution is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

## Important Safety Information (US)

YUPELRI is contraindicated in patients with hypersensitivity to revefenacin or any component of this product.

YUPELRI should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD, or for symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled beta2-agonist.

As with other inhaled medicines, YUPELRI can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs following dosing with YUPELRI, it should be treated immediately with an inhaled, short-acting bronchodilator. YUPELRI should be discontinued immediately and alternative therapy should be instituted.

YUPELRI should be used with caution in patients with narrow-angle glaucoma. Patients should be instructed to immediately contact their healthcare provider if they develop any signs and symptoms of acute narrow-angle glaucoma, including eye pain or discomfort, blurred vision, visual halos or images in association with red eyes from conjunctival congestion and corneal edema.

Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and contact a healthcare provider immediately if symptoms occur.

Immediate hypersensitivity reactions may occur after administration of YUPELRI. If a reaction occurs, YUPELRI should be stopped and appropriate treatments considered.

The most common adverse reactions occurring in clinical trials at an incidence greater than or equal to 2% in the YUPELRI group, and not seen in the placebo group, included cough, nasopharyngitis, upper respiratory infection, headache and back pain.

Coadministration of anticholinergic medicines or OATP1B1 and OATP1B3 inhibitors with YUPELRI is not recommended.

YUPELRI is not recommended in patients with any degree of hepatic impairment.

## About YUPELRI® (revefenacin) Inhalation Solution

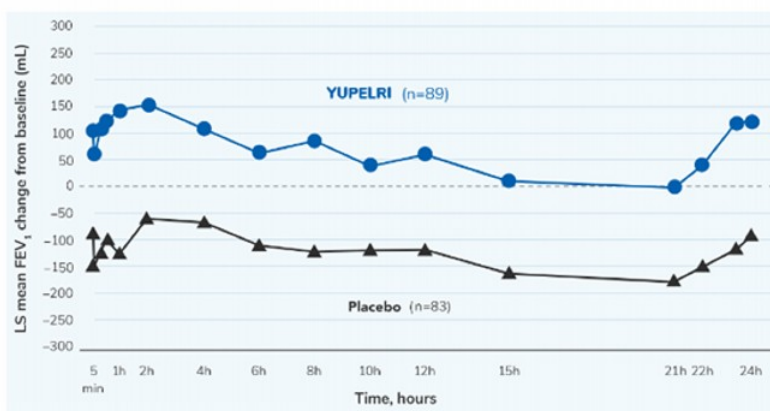
YUPELRI® (revefenacin) inhalation solution is a once-daily nebulized LAMA approved for the maintenance treatment of COPD in the US.

Market research by Theravance Biopharma indicates approximately 9% of the treated COPD patients in the US use nebulizers for on therapy.<sup>1</sup> LAMAs are a cornerstone of maintenance therapy for COPD and YUPELRI® is positioned as the first once-daily single-agent product for COPD patients who require, or prefer, nebulized therapy. YUPELRI®'s stability in both metered dose inhaler and dry powder formulations suggest that this LAMA could also serve as a foundation for novel handheld combination products.

# YUPELRI® Delivers a Full 24 Hours of Efficacy in a Single, Nebulized Daily Dose

## 24-Hour Lung Function at 12 Weeks

Consistent Improvement in FEV<sub>1</sub> vs placebo over 24 hours on days 84/85<sup>1,2</sup>



## Safety Demonstrated in 3 Clinical Studies

Adverse reactions from two 12-week placebo-controlled effi

### Adverse reactions ≥ 2% incidence and higher than placebo<sup>1</sup>

Adverse Reactions	YUPELRI (n=395)
Cough	17 (4%)
Nasopharyngitis	15 (4%)
Upper respiratory tract infection	11 (3%)
Headache	16 (4%)
Back pain	9 (2%)

Fewer patients discontinued treatment with YUPELRI (13%) than with placebo

**Safety results from a 52-week, long-term trial consistent with observed in previous studies (n=1,055)<sup>1</sup>**

FEV<sub>1</sub>, forced expiratory volume in one second; LS, least squared.

1. YUPELRI [package insert]. Morgantown, WV: Mylan Specialty LP; 2. YUPELRI was studied in two 12-week, randomized, double-blind, placebo-controlled, parallel-group confirmatory studies (Studies 1 and 2) to evaluate the efficacy of once-daily YUPELRI vs placebo in patients with moderate to very severe COPD. In Studies 1 and 2, serial spirometry was performed on a sub-study population. Pooled results are shown. Primary efficacy endpoint was change from baseline in trough (pre-dose) FEV<sub>1</sub> at day 85 vs placebo. In Studies 1 and 2, a prespecified exploratory analysis was performed. In Study 1, LS mean changes from baseline in FEV<sub>1</sub> ranged from 55.8 mL to 240.4 mL in the YUPELRI group, and from -113.6 mL to 59.6 mL in the placebo group. In Study 2, LS mean changes from baseline in FEV<sub>1</sub> ranged from 19.8 mL to 148.5 mL in the YUPELRI group, and from -176.4 mL to -13.0 mL in the placebo group. Data on file.

## Comparison of Yupelri, Dupixent, and Ohtuvayre in COPD Treatment

Criteria	Yupelri (revefenacin)	Dupixent (dupilumab)	Ohtuvayre (ensifentrine)
<b>Mechanism/Class</b>	Long-acting muscarinic antagonist (LAMA)	IL-4R $\alpha$ antagonist	Dual PDE3/PDE4 inhibitor
<b>FDA Approved Use</b>	Maintenance treatment of COPD in adults	Add-on maintenance treatment of COPD in adults with eosinophilic phenotype	Maintenance treatment of COPD in adults
<b>GOLD 2025 Recommended Use</b>	First-line bronchodilator for GOLD B/E; backbone of LAMA $\pm$ LABA therapy	<b>Add-on to triple therapy</b> to reduce exacerbations in eosin $\geq$ 300/ $\mu$ L	<b>Add-on/alternative to LAMA</b> if dyspnea persists
<b>Delivery Method</b>	Once-daily nebulization	Subcutaneous injection every 2 weeks	Twice-daily nebulization

AMPRELOXETINE

## Appendix



# Recent Publications and Presentations Highlight Durable Symptom Benefit Observed in Previous REDWOOD/0170 Study in MSA Patients<sup>1</sup>

## Publications

**"Precision therapy with ampreloxetine for neurogenic orthostatic hypotension in multiple system atrophy"** manuscript submitted, under review and pre-print posted on medRxiv

- Highlights **durable symptom and daily function improvement** in MSA subgroup from the REDWOOD study<sup>1</sup>

**"Establishing Minimally Clinically Important Differences for the Orthostatic Hypotension Questionnaire (OHQ)"** Kaufmann H, et al. manuscript published in *Clinical Autonomic Research*

- Defines meaningful change thresholds, enhancing clinical interpretation

## AAS Presentations

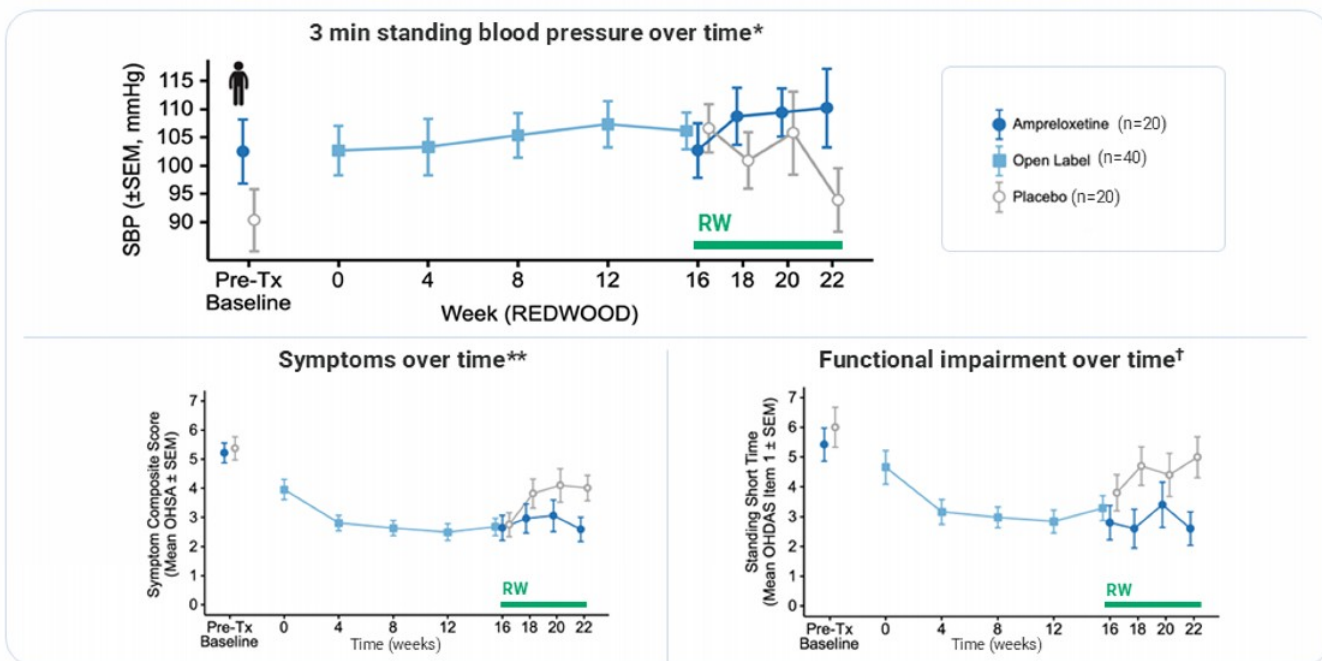


**36<sup>TH</sup> INTERNATIONAL SYMPOSIUM ON THE AUTONOMIC NERVOUS SYSTEM**

One platform presentation and three poster presentations highlighting:

- Results from the REDWOOD study in MSA subgroup
- Rigorous methodologies to support enrollment and retention in the ongoing Phase 3 CYPRESS study

# Amprelosetine Increase in Standing Blood Pressure Correlated with Improvement in Symptoms and Daily Activities in Patients with MSA in the REDWOOD/0170 Study



## No signal for worsening of supine hypertension<sup>1</sup>

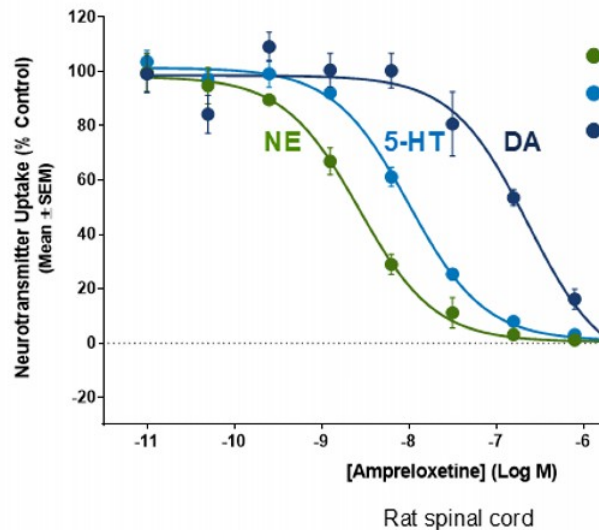
MSA, multiple system atrophy; OHDAS, orthostatic hypotension daily activity scale; OHSA, orthostatic hypotension symptom assessment; RW, randomized withdrawal. Freeman R, et al. Precision therapy with amprelosetine for neurogenic orthostatic hypotension in multiple system atrophy. MedRxiv. <https://doi.org/10.1101/2025.08.12.25332833>. \*Longitudinal analysis of blood pressure at 3 minutes of standing at entry (Pre-treatment baseline), throughout the 16-week open-label period, and in the randomized withdrawal in the analysis population set of REDWOOD. \*\*Longitudinal analysis of mean OHQ symptom assessment composite scores, after censorship for early withdrawal, in the subgroup of randomized MSA patients. †Shows OHDAS item 1 scores capturing severity of interference of symptoms of nOH on standing for a short time. 1. Amprelosetine is in development and not approved for any indication. No conclusion can be drawn regarding its safety or efficacy.

# Ampreloxetine is a Potent and Selective Norepinephrine Reuptake Inhibitor (NRI)

Ampreloxetine is intended to target and correct the norepinephrine imbalance

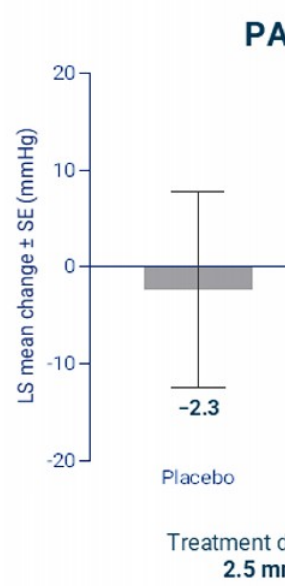
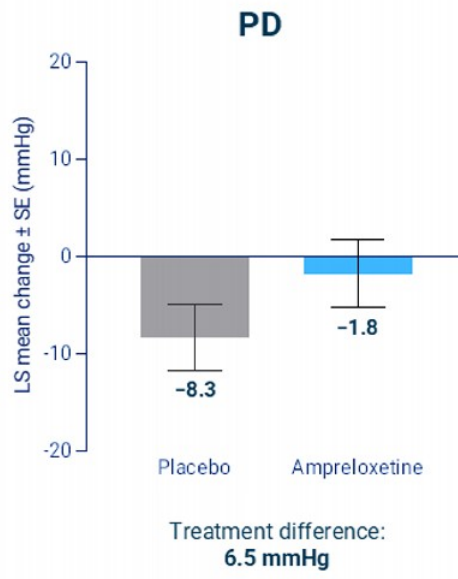
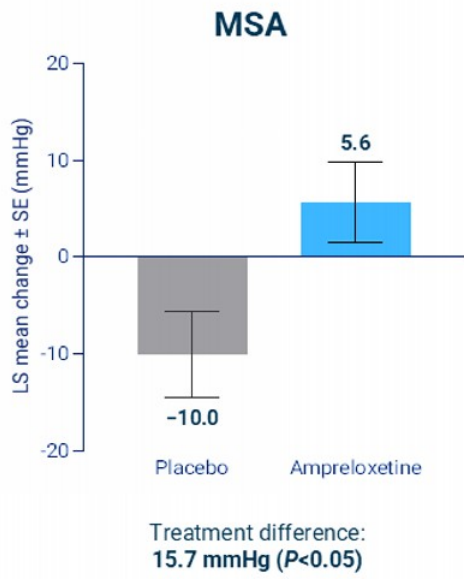
- Novel chemical entity, discovered and developed at Theravance Biopharma
- Potent and high-affinity NRI
- Orally bioavailable with half life that supports QD dosing
- Mechanism of action consistent with durability of effect
- At 10mg QD: >90% Projected Mean NET Occupancy, <50% Projected SERT Occupancy

Pre-clinical studies confirmed ampreloxetine selective and potent NRI



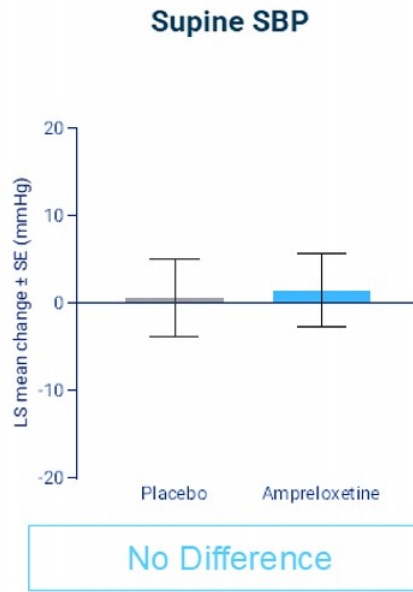
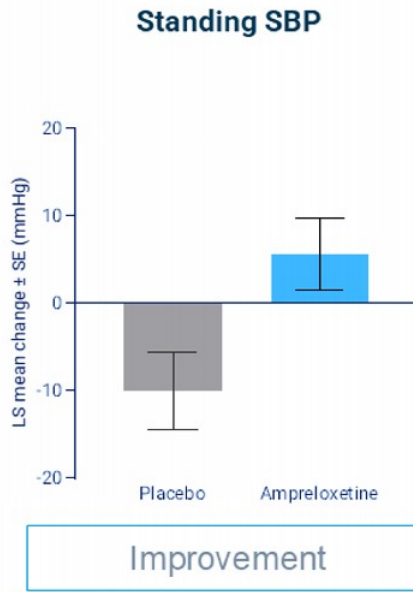
# Ampreloxetine Preferentially Improved Standing Systolic Blood Pressure in MSA

Data from randomized withdrawal period in Study 0170



# Ampreloxetine Improved Upright Blood Pressure “Physiologically”

Data from MSA patients at week 6 of the randomized withdrawal period of study 0170



Standing blood pressure without evidence of increase in supine blood pressure

Approved therapies increase supine > standing blood pressure

# Study 0170 Randomized Withdrawal Period: Overall Disposition

## Low frequency of discontinuations overall

- Only two discontinuations for adverse events – one each in placebo and ampreloxetine groups

	Placebo (n = 64)	Ampreloxetine (n = 64)	Total (n = 128)
<b>Completed treatment</b>	61 (95.3)	58 (90.6)	119 (93.0)
<b>Discontinued treatment</b>	3 (4.7)	6 (9.4)	9 (7.0)
Adverse event	1 (1.6)	1 (1.6)	2 (1.6)
Study terminated by sponsor	2 (3.1)	3 (4.7)	5 (3.9)
Withdrawal by patient	0	1 (1.6)	1 (0.8)
Other	0	1 (1.6)	1 (0.8)

All data are presented as n (%).

# Study 0170 Randomized Withdrawal Period: AE Summary

## Randomized withdrawal period

- TEAEs were similar between placebo and amprelosetine group
- No adverse events of supine hypertension were observed
- No clinically significant differences for laboratory parameters, ECG changes, ambulatory BP monitoring, an
- Two deaths: 1 respiratory tract infection (unrelated) and 1 unknown cause

	Placebo (n = 64)	Amprelosetine (n = 64)
Any TEAEs	16 (25.0)	17 (26.6)
TEAEs related to study drug	2 (3.1)	5 (7.8)
SAEs	2 (3.1)	4 (6.3)
SAEs related to study drug	1 (1.6)	2 (3.1)
TEAEs leading to permanent study drug discontinuation	1 (1.6)	1 (1.6)
Deaths during study	0	2 (3.1)

All data are presented as n (%). Amprelosetine was administered at 10mg once daily.

# AEs in MSA Subgroup: Randomized Controlled Phases of Studies 0169 and 0170

## Ampreloxetine appears safe and well-tolerated in MSA patients

- Overall, the AE profile was similar between placebo and ampreloxetine groups during the randomized controlled phases
- Only 2 SAEs considered related to study drug – 1 each in placebo and ampreloxetine groups

	Study 0169		Study 0170 RW period	
	Placebo (n = 33)	Ampreloxetine (n = 35)	Placebo (n = 20)	Ampreloxetine (n = 20)
Any TEAEs	19 (57.6)	19 (54.3)	7 (35.0)	4 (20.0)
TEAEs related to study drug	5 (15.2)	5 (14.3)	1 (5.0)	1 (5.0)
SAEs	2 (6.1)	4 (11.4)	1 (5.0)	2 (10.0)
SAEs related to study drug	0	0	1 (5.0)	1 (5.0)
TEAEs leading to permanent study drug discontinuation	0	1 (2.9)	0	0
Deaths during study	0	0	0	0

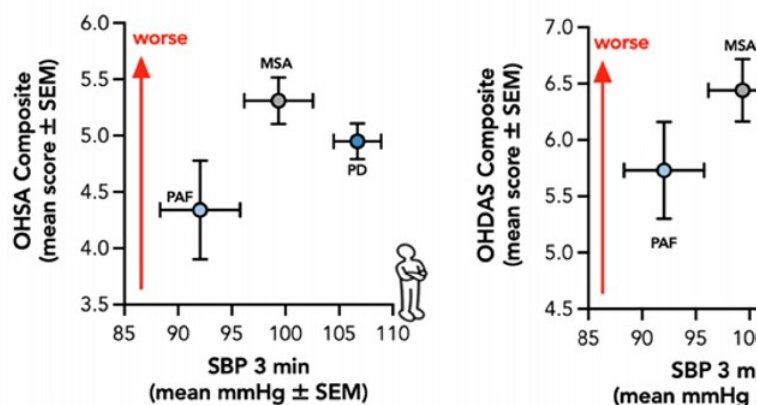
All data are presented as n (%). Ampreloxetine was administered at 10mg once daily. Patients are only counted once in each row.

# MSA Patients with nOH Suffer Worse Symptom Burden and Daily Functioning

## Study 0169 Analysis Presented at AAS

- Amongst patients with  $\alpha$ -synucleinopathies, **MSA patients reported the highest symptom burden, most severe impact to activities of daily living and worst quality of life**, despite treatment with available anti-hypotensive medications
- **There remains a significant unmet need** for better nOH treatments, especially for MSA patients

## Baseline Symptom and Daily Activity Impact vs Systolic



AAS, American Autonomic Society; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; OHDAS, orthostatic hypotension daily activity scale; OHS, orthostatic hypotension symptom assessment; SBP, systolic blood pressure; SEM, standard error of the mean.  
Impact of symptomatic neurogenic orthostatic hypotension (nOH) on symptom burden and daily functioning in patients with alpha synucleinopathies. V Iodice, T Guerin, S Johnstone, L Norcliffe-Kaufmann, Miller, R Vickery. Presented at International Symposium on the Autonomic Nervous System, Nov 6-9, 2024, Santa Barbara, CA.