# Theravance MK Biopharma MK.

Medicines That Make a Difference®

First Quarter 2023 Financial Results and Business Update

May 8, 2023

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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, 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 repurchase of its ordinary shares by way of an open market share repurchase program, the impact of recent headcount reductions in connection with focusing investments in research, the Company's governance policies and plans, the Company's expectations regarding its allocation of resources and maintenance of expenditures, the Company's goals, designs, strategies, plans and objectives, future YUPELRI sales, the ability to provide value to shareholders, the Company's regulatory strategies and timing of clinical studies, possible safety, efficacy or differentiation of our investigational therapy, and contingent payments due to the Company from the sale of the Company's TRELEGY ELLIPTA royalty interests to Royalty Pharma. These statements are based on the current estimates and assumptions of the management of the Company 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 the Company 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: 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 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, and risks associated with establishing and maintaining sales, marketing and distributi

Other risks affecting the Company are in the Company's Form 10-K filed with the SEC on March 1, 2023, 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.

#### **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 non-GAAP net loss from operations provide meaningful information to assist investors in assessing prospects for future performance and actual performance as they provide better metrics for analyzing the 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 and metrics, such as non-GAAP profitability and non-GAAP net loss from operations, are not standardized, it may not be possible to compare these measures with other companies' non-GAAP targets or measures having the same or a similar name. 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 actual GAAP results and other targets.



# Agenda

Introduction and Overview	Rick E Winningham Chief Executive Officer
Commercial and Davidonment Undata	Rhonda F. Farnum Senior Vice President, Chief Business Officer
Commercial and Development Update	Richard A. Graham Senior Vice President, Research and Development
Financial Update	<b>Aziz Sawaf</b> Senior Vice President, Chief Financial Officer
Closing Remarks	Rick E Winningham Chief Executive Officer



## 2023 Targets



- Continue YUPELRI Net Sales growth by executing on targeted strategies to capture sizeable niche market
- Complete PIFR-2 study and provide top-line results in 2H'23

## **Ampreloxetine**

- Initiate Phase 3 CYPRESS trial in MSA patients with symptomatic nOH in Q1'23
- Submit orphan drug designation request in early 2023

### **Financial**

- Expanded Capital Return Program to \$325M, and expect to complete by end of 2023
- Generate Non-GAAP¹ Profit in 2H'23
- ► \$50M potential milestone for TRELEGY Net Sales of ~\$2.86B<sup>2</sup>



# Progress Against 2023 YUPELRI® Targets

Strong Demand Growth in Both Hospital and Community Settings

## **Target**

- ► Continue YUPELRI Net Sales growth by executing on targeted strategies to capture sizeable niche market
- Complete PIFR-2 study and provide top-line results in 2H'23

## **Progress**

- ► Total YUPELRI reported net sales reach \$47.0M up 8% Y/Y¹
- Retail new patient starts and total prescriptions up 61% and 29% Y/Y, accelerating from Q4
- YUPELRI market shares again reach new highs
- On track to complete PIFR-2 study and provide top-line results in 2H'23



# Progress Against 2023 Ampreloxetine Targets

Milestones Achieved with CYPRESS Study

## **Target**

- Initiate Phase 3 CYPRESS trial in MSA patients with symptomatic nOH in Q1'23
- Submit orphan drug designation request in early 2023

## **Progress**

- Initiated Phase 3 CYPRESS trial in MSA patients with symptomatic nOH in Q1'23
- Submitted orphan drug designation request in early 2023
- Anticipate completing CYPRESS enrollment in 2H'24



## Progress Against 2023 Financial Targets

Substantial Progress Made on Buyback Program

## **Target**

- Expanded Capital Return Program to \$325M, and expect to complete by end of 2023
- Generate Non-GAAP¹ Profit in 2H'23
- ► \$50M potential milestone for TRELEGY Net Sales of ~\$2.86B²

## **Progress**

- On track for 2023 completion; \$87M completed YTD through 4/30/23, with \$110M remaining
- ► Remain on track to generate Non-GAAP¹ Profit in 2H'23
- ► \$567M TRELEGY Net Sales in Q1'23





FDA-approved for maintenance treatment of COPD

First and only once-daily, LAMA (long-acting muscarinic agent) nebulized maintenance medicine for COPD

Co-promotion agreement with VIATRIS™ (35% / 65% Profit Share)

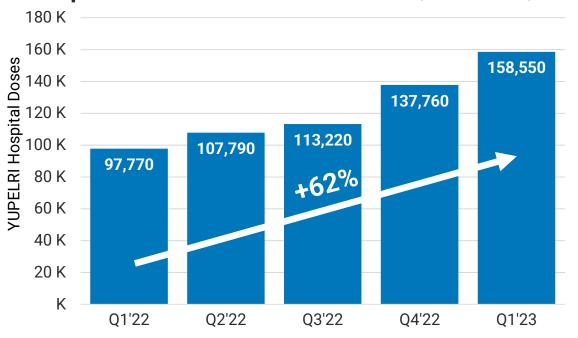


# YUPELRI® | Growing Net Sales and Hospital Volume





### Hospital doses sold increased 62% Q1'23 vs. Q1'22



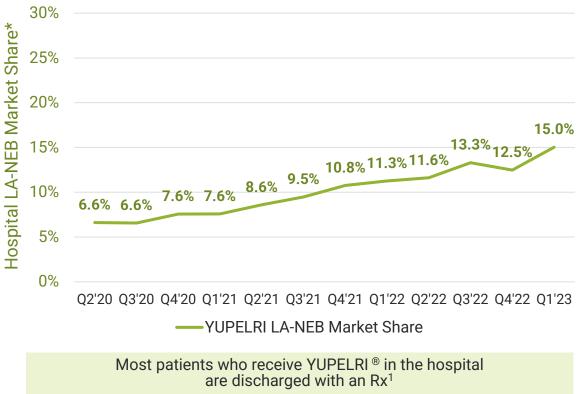
22% rolling 4-quarter growth through Q1'23

52% rolling 4-quarter growth through Q1'23

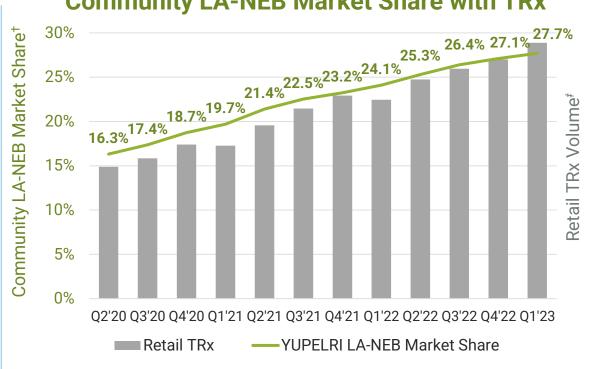


# YUPELRI® Hospital and Community Share Trends

### **Hospital LA-NEB Market Share**



### **Community LA-NEB Market Share with TRx**



TRx volume represents retail only which is typically 33% of Retail + DME Reported DME volume, while lagged, typically follows Retail volume trends

LA-NEB Market: YUPELRI, BROVANA, LONHALA, PERFOROMIST, arformoterol, formoterol

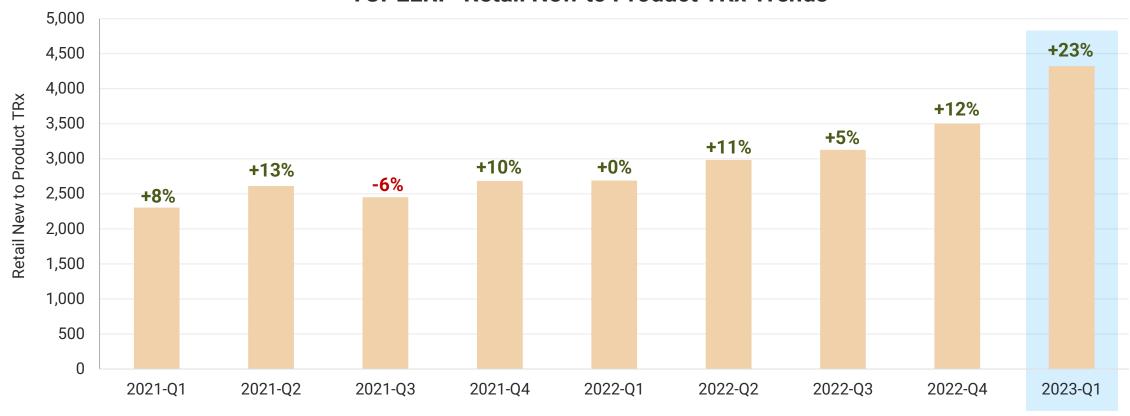


<sup>1.</sup> Joint VTRS/TBPH Market Research.

<sup>\*</sup> Hospital LA-NEB Market Share - IQVIA DDD through 3/31/2023

# Continued Record-High Retail New Patient Starts 61% Y/Y and 23% Q/Q growth; Key Driver of Future Brand Performance







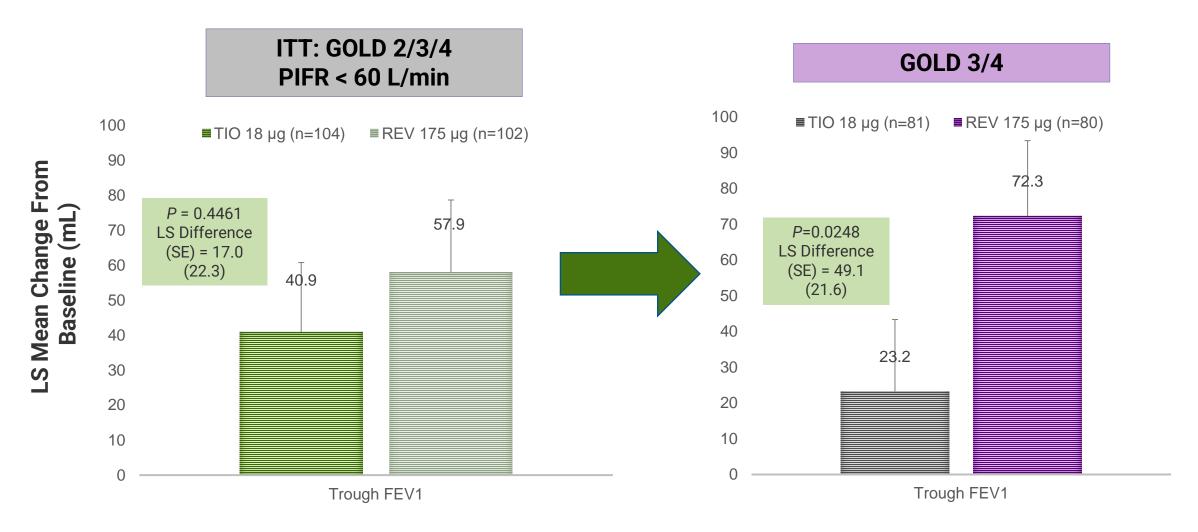
# Development

YUPELRI PIFR-2 Top-line results anticipated H2 '23

CYPRESS (ampreloxetine) Last patient enrolled anticipated H2 '24

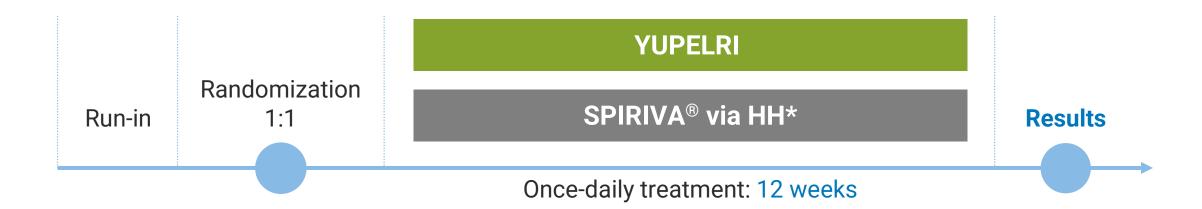


## PIFR-1 Experience Informed PIFR-2 Design



## YUPELRI®:

## Phase 4 Randomized, Double-Blind, Parallel-Group Study (PIFR-2)



### Sample size

- ► N = Up to 488
- Top-line results 2H'23

### **Endpoints**

- Primary: Change from baseline in trough FEV<sub>1</sub> (Day 85)
- Key secondary: Trough overall treatment effect on FEV<sub>1</sub>

# **Ampreloxetine**

Investigational once-daily norepinephrine reuptake inhibitor

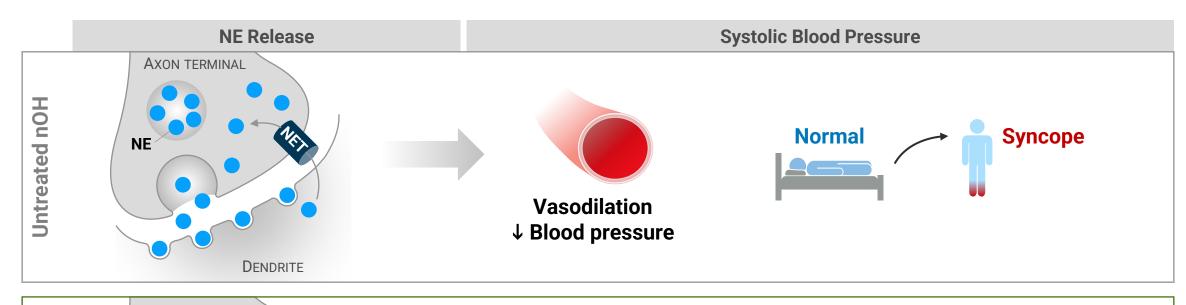
For symptomatic neurogenic orthostatic hypotension (nOH) in multiple system atrophy (MSA) patients

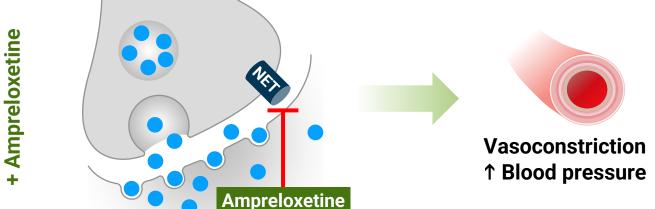


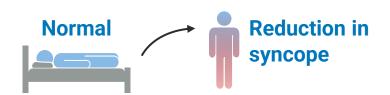
# Our CYPRESS Study is Now Recruiting



# Ampreloxetine: Designed to Reduce Symptoms in MSA







- Potentiates endogenous norepinephrine<sup>1</sup>
- Increases blood pressure<sup>2</sup>
- Leads to durable effectiveness<sup>2</sup>



Palma JA, Kaufmann H. Mov Disord Clin Pract 2017;4:298-308.

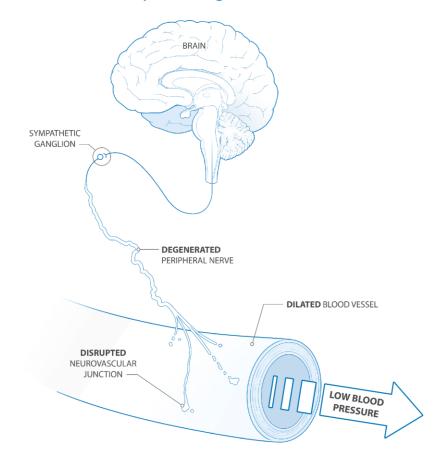
- 1. Data from MSA patients reported after 4 weeks of ampreloxetine administration in study 0169.
- 2. Data from MSA patients at week 6 of the randomized withdrawal period of study 0170.

## Effective Treatment Requires Intact Peripheral Nerves

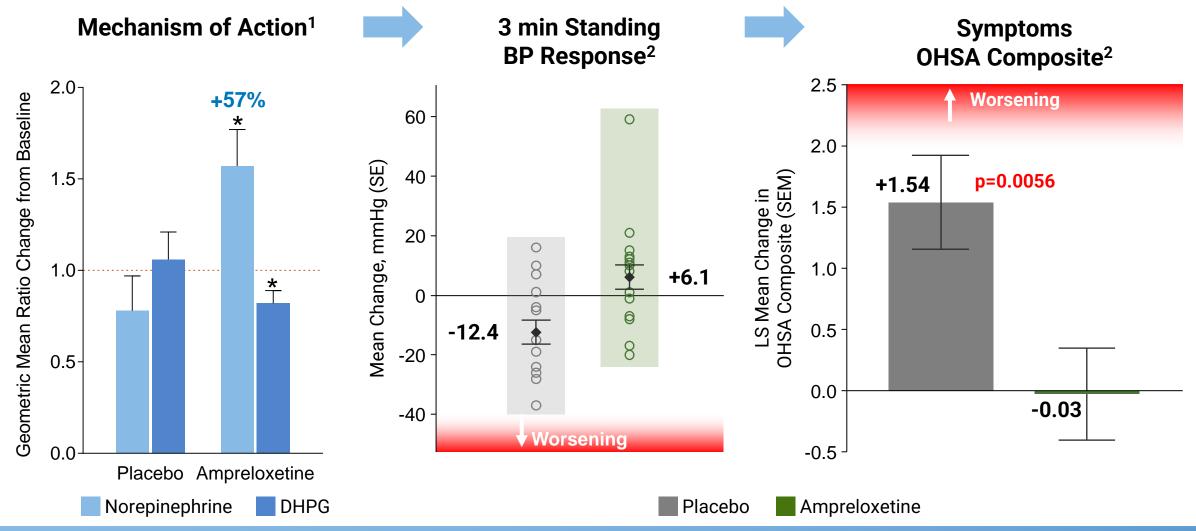
## **Multiple System Atrophy Central Degeneration** BRAIN AMPRELOXETINE SYMPATHETIC GANGLION PERIPHERAL NERVE **VASOCONSTRICTED BLOOD VESSEL FUNCTIONING NEUROVASCULAR** JUNCTION INCREASED BLOOD PRESSURE

### **Parkinson's Disease/Pure Autonomic Failure**

**Peripheral Degeneration** 



# Increased Norepinephrine, Prevented Blood Pressure Drop and Symptoms Worsening in MSA<sup>1, 2</sup>





1. Data from MSA patients. Error bars represent SE. \* p < 0.05 comparison to baseline reported after 4 weeks of ampreloxetine administration in study 0169.

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

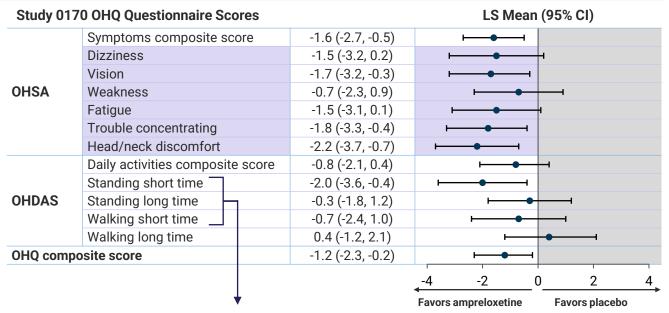
BP, blood pressure; DHPG, dyhydroxyphenylglycol; LS, least-squares; MSA, multiple system atrophy; OHSA, orthostatic hypotension symptom assessment; SE, standard error; SEM, standard error of mean.

## The Unique Benefits of Ampreloxetine Treatment



## **Unique efficacy and durability**

First-in-class therapy effective in treating a **constellation of cardinal symptoms in MSA patients:** 



Improvement in **activities of daily living** that require walking and standing for a short time<sup>1</sup> which could favorably impact caregiver burden

Clinically meaningful and durable effectiveness well beyond 2 weeks



### **Patient-friendly dosing**

MSA patients may have difficulty swallowing:

- Once-daily dosing, single 10mg tablet
- Low dosing frequency improves compliance
- Decreases caregiver burden



### **Differentiated safety profile**

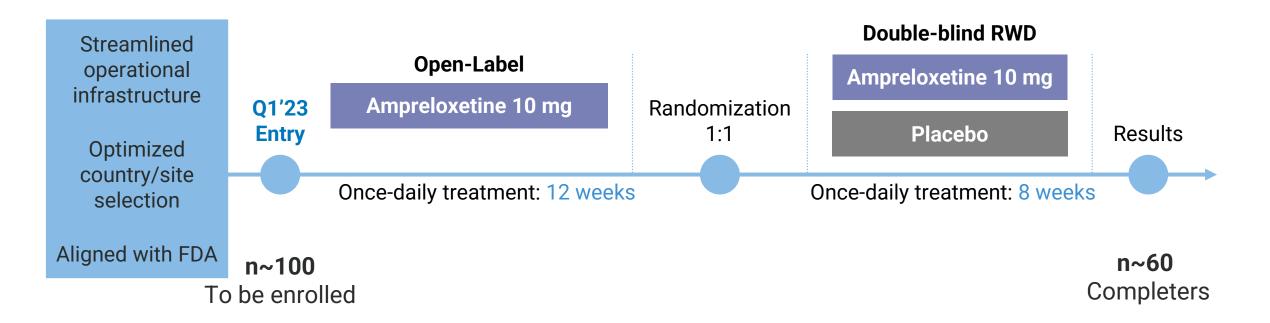
**Supine hypertension** with droxidopa and midodrine<sup>2,3</sup> **Absence** of a signal would be a differentiator:

- Available to patients with supine hypertension
- Can be taken anytime of day/night
- Potential to be combined with other drugs



# Offering Hope to MSA Patients with Symptomatic nOH

Study 0197 (CYPRESS): Phase 3 randomized withdrawal study in patients with MSA Primary endpoint: change in OHSA composite score





# New Era in Treating MSA Symptoms: Product Positioning

**MSA Prevalence** 

**Prevalence of nOH in MSA Patients** 

**Addressable Patient Population** 

~50K MSA patients in U.S.<sup>1</sup> (considered orphan disease)

**70%-90%** of MSA patients experience **nOH** symptoms<sup>2</sup>

**35K – 45K** MSA patients with nOH symptoms

### **Current Treatment Landscape**

**Unique Treatment Profile** 

Indication	dication	
Efficacy / Durability	urability	Efficacy
Dosing	Dosing	
Safety	Safety	

Droxidopa <sup>3</sup>	Midodrine <sup>4</sup>
Symptomatic nOH	ОН
OHSA#1; clinical effectiveness >2 weeks not established	Increase in systolic blood pressure 1 min after standing
3x daily, titration to effect	3x daily

**Black box warning** for supine hypertension

Ampreloxetine
Symptomatic nOH associated with MSA
OHSA composite; clinically meaningful and durable response >20 weeks
Once-daily
No signal for supine hypertension

# **Financial Update**



## First Quarter 2023 Financials

	Three Months Ended March 31,			
(\$, in thousands)		2023 2022		2022
	(Unaudited)		_	
Revenue:				
Viatris collaboration agreement	\$	10,411	\$	10,687
Collaboration revenue		6		9
Licensing revenue		-		2,500
Total revenue		10,417		13,196
Costs and expenses:				
Research and development (1)		14,572		23,253
Selling, general and administrative (1)		19,183		17,842
Restructuring and related expenses (1)		1,574		9,324
Total costs and expenses		35,329		50,419
Loss from continuing operations (before tax and other income & expense)		(24,912)		(37,223)
Income from discontinued operations (before tax)		-		14,313
Share-based compensation expense:				
Research and development		2,441		4,530
Selling, general and administrative		4,223		5,498
Restructuring and related expenses		357		4,517
Total share-based compensation expense		7,021		14,545
Operating expense excl. share-based compensation and one-time expenses:				
R&D operating expense (excl. share-based comp and restructuring exp.)		12,131		18,723
SG&A operating expense (excl. share-based comp and restructuring exp.)		14,960		12,344
Total operating expenses excl. share-based compensation and one-time expenses		27,092		31,067
Non-GAAP net loss from continuing operations (2)		(14,912)		(25,190)

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<sup>1.</sup> Amounts include share-based compensation.

<sup>2.</sup> Non-GAAP net loss from continuing operations consists of GAAP net loss before taxes excluding share-based compensation expense and non-cash interest expense; see reconciliation on Slide 25 and the section titled "Non-GAAP Financial Measure" on Slide 2 for more information.

# First Quarter 2023 Financials (Cont'd)

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

	•	Three Months Ended March 31,		
		2023 2022		2022
		(Unau	dited)	
GAAP Net Loss from Continuing Operations	\$	(22,088)	\$	(40,259)
Adjustments:				
Share-based compensation expense		7,021		14,545
Non-cash interest expense		550		-
Income tax expense (benefit)		(395)		524
Non-GAAP Net Loss from Continuing Operations	\$	(14,912)	\$	(25,190)
Non-GAAP Net Loss per Share from Continuing Operations				
Net loss - basic and diluted	\$	(0.24)	\$	(0.33)
Shares used to compute per share calculations - basic and diluted		62,934		75,247

## Q1 2023 Financial Highlights

## Significant Capital Returns from a Position of Strength

Metric	Q1 '23 (M)	Q1 '22 (M)	Note
VIATRIS Collaboration Revenue	\$10.4	\$10.7	
SG&A and R&D Expense, ex-SBC & One-time Items	\$27.1	\$31.1	
Share-Based Compensation	\$6.7	\$10.0	Excluding restructuring expenses
Non-GAAP Loss from Continuing Operations <sup>1</sup>	(\$14.9)	(\$25.2)	
Cash and Cash Equivalents <sup>2</sup> (as of quarter-end)	\$260.0	\$147.5	• \$55M of share buybacks in Q1'23
Debt (as of quarter-end)	\$0.0	\$621.5	
Shares Outstanding (as of quarter-end)	60.5	76.1	• ~5.2M shares repurchased in Q1'23



<sup>1.</sup> Non-GAAP loss from continuing operations consists of GAAP loss before taxes excluding share-based compensation expense and non-cash interest expense; see reconciliation on Slide 25 and the section titled "Non-GAAP Financial Measure" on Slide 2 for more information.

<sup>2.</sup> Cash, cash equivalents and marketable securities. SBC, Share-Based Compensation.

# \$325 Million Capital Return Program

On Track to Complete Program by Year-End

Complete (\$95M)

√ ~\$95M: Purchased GSK's equity stake in Theravance (Sep'22) and completed Dutch auction tender offer (Nov'22)

Open Market Share Buybacks Complete (\$120M)

- √ ~\$33M completed in Dec'22
- √ ~\$55M completed in 2023, through 3/31/23
- √ ~\$87M completed in 2023, through 4/30/23

As of 3/31/23: \$183M complete; \$142M remaining

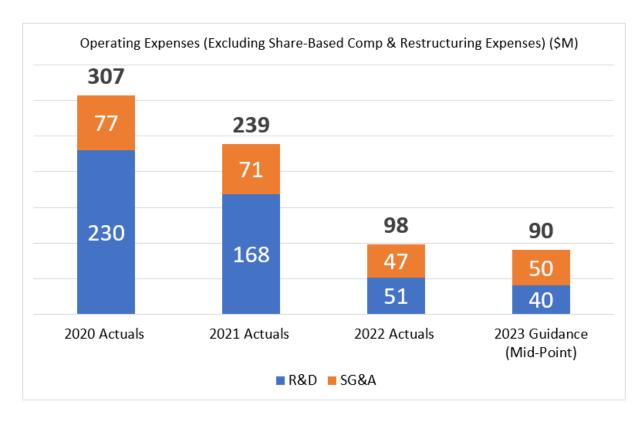
As of 4/30/23: \$215M complete; \$110M remaining



## 2023 Financial Guidance

## Expected to Generate Non-GAAP<sup>1</sup> Profit in 2H 2023

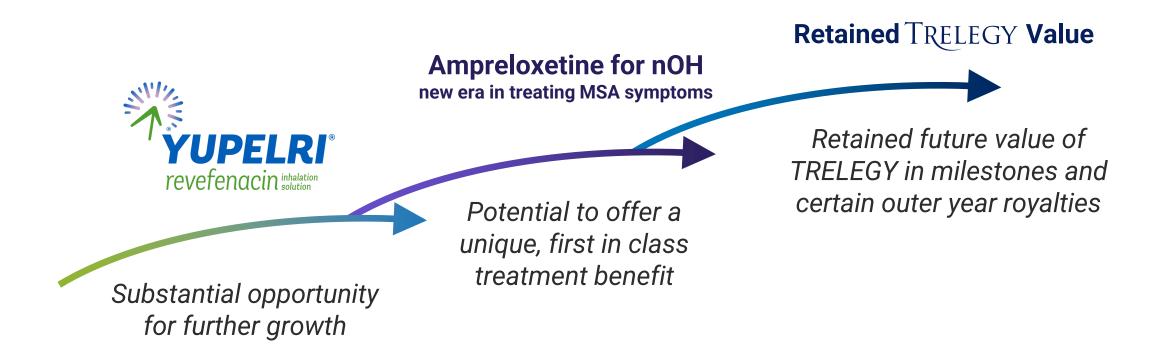
- 2023 OPEX Guidance Range:
  - R&D: \$35M \$45M
  - SG&A: \$45M \$55M
- Guidance Excludes:
  - Non-cash share-based compensation
  - One-time severance and termination costs associated with 2023 headcount reduction:
    - Incurred \$1.6M in Q1'23
    - No further severance and termination costs expected
- Share-Based Compensation:
  - Expected to decline materially in 2023 vs. 2022
  - Q1'23 down 34% year-over-year, excluding restructuring costs, and 52%, including restructuring





## Theravance Biopharma: Positioned for Value Creation

Three distinct drivers of value over the near, mid, and long-term



Positioned to create value from a foundation of financial strength



## **Q&A Session**

Rick E Winningham
Chairman and Chief Executive Officer



Aziz Sawaf, CFA
Senior Vice President,
Chief Financial Officer



Rhonda F. Farnum Senior Vice President, Chief Business Officer



Richard A. Graham Senior Vice President, Research and Development





# 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 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.

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 consult 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 colored 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 instruct patients to 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 at once and alternative 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 higher than placebo, 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 ongoing maintenance therapy. LAMAs are a cornerstone of maintenance therapy for COPD and YUPELRI® is positioned as the first once-daily single-agent bronchodilator product for COPD patients who require, or prefer, nebulized therapy. YUPELRI®'s stability in both metered dose inhaler and dry powder device formulations suggest that this LAMA could also serve as a foundation for novel handheld combination products.

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# Appendix

## Patent Protection Into Late 2030s

Compound	Invention	Granted / Pending Application	Estimated Patent Expiry
YUPELRI® / revefenacin	Composition of Matter	Granted US	2028 (once PTE awarded)
	Polymorph	Granted US	2030-2031
	Method for the maintenance treatment of COPD patients	Granted US	2039
Ampreloxetine	Composition of Matter	Granted US	2030 (plus PTE of up to 5 years)
	Method of Treating nOH	Granted US	2037



## Viatris Collaboration Agreement Revenue

Theravance Entitled to Share of US profits (65% to Viatris; 35% to Theravance)

35% of YUPELRI® Net Sales



Reimbursement of shared Theravance expenses (65%)



Payment of shared Viatris expenses (35%)



Viatris Collaboration Agreement Revenue

Cash amount receivable from Viatris<sup>1,2</sup>

Collaboration Revenue, in any given period can fluctuate by the absolute and relative expenses incurred by Viatris and Theravance, in addition to the Net Sales generated in the period



<sup>2.</sup> Amount included as a receivable on the balance sheet as "Receivables from collaborative arrangements".

## TRELEGY ELLIPTA Milestones and Royalties

GSK's TRELEGY ELLIPTA (FF/UMEC/VI): First and only once-daily single inhaler triple therapy

### Mid-Term Value

Up to \$250M of Sales-based milestones<sup>1,2</sup> between 2023–2026:

Year	Royalties <sub>2</sub>	Global Net Sales Equivalent	Milestone
2023	\$240M	\$2,863M	\$50M
2024	\$240M	\$2,863M	\$25M
20241	\$275M	\$3,213M	\$50M
2025	\$260M	\$3,063M	\$25M
20251	\$295M	\$3,413M	\$50M
2025	\$270M	\$3,163M	\$50M
20261	\$305M	\$3,513M	\$100M

Long-Term Value

Outer-Year Royalties<sup>3</sup> return in 2029:

- Ex-US royalties return Jul. 1, 2029
- US royalties return after Jan. 1, 2031
- · Paid directly from Royalty Pharma

Q1'23 Net Sales of \$567M | FY 2022 Net Sales of \$2.1B4

GSK remains exclusively responsible for commercialization of TRELEGY ELLIPTA



## Theravance Biopharma and Royalty Pharma Deal Summary

### TRELEGY ELLIPTA

Upfront: \$1.1B (Received)

Milestones: Up to \$250M

Year	Royalties <sub>2</sub>	Global Net Sales Equivalent	Milestone
2023	\$240M	\$2,863M	\$50M
2024	\$240M	\$2,863M	\$25M
2024 <sub>1</sub>	\$275M	\$3,213M	\$50M
2025	\$260M	\$3,063M	\$25M
20251	\$295M	\$3,413M	\$50M
2025	\$270M	\$3,163M	\$50M
20261	\$305M	\$3,513M	\$100M

- Outer Year Royalty ("OYR"): 85% of royalties for TRELEGY ELLIPTA return to Theravance Biopharma:
  - On and after January 1, 2031 for U.S. sales<sup>3</sup>
  - On and after July 1, 2029 for ex-U.S. sales<sup>3</sup>

## **Ampreloxetine**

(Unsecured Royalty)

- Upfront payment: \$25M (Received)
- 1st Regulatory approval milestone: \$15M
  - Approval by either FDA or first of the EMA or all four Germany, France, Italy and Spain
- Future royalties paid to Royalty Pharma:
  - 2.5% on annual global net sales up to \$500M
  - 4.5% on annual global net sales > \$500M



<sup>1.</sup> If both milestones are achieved in a given year, Theravance Biopharma will only earn the higher milestone.

<sup>2.</sup> Based on 100% of TRELEGY ELLIPTA royalties.

<sup>3.</sup> U.S. royalties expected to end late 2032; ex-U.S. royalties expected to end mid-2030s and are country specific.

# Substantial Opportunity for Further YUPELRI® Growth

Once-Daily Nebulized LAMA COPD treatment represents a sizeable niche market

### Estimated 2021 **YUPELRI Patient Funnel (US)**

~16M COPD Diagnosed<sup>1</sup> 2% Annual Growth Rate<sup>2</sup>

~13M Drug Treated<sup>2</sup> ~81% of COPD Diagnosed (up to 83% by 2029)

~10M on Maintenance Therapy3 ~80% of Drug Treated

~50-70K Patients on YUPELRI < 1% of Maintenance Therapy

Patent No 11,484,531, methods of treating COPD, expiring in 2039, is now listed in the Approved Drug Products with Therapeutic Equivalence Evaluations

- COPD is under-diagnosed1
- COPD patients with or without symptoms may be treated with rescue and/or maintenance therapies
- Estimated patient counts from volume using average 'days of therapy' assumptions vary considerably across DME and retail channels

### **Growth opportunities within numerous patient segments**

**YUPELRI** may be appropriate for COPD patients, including but not limited to:

- Moderate-to-very-severe COPD (73–92%4); once-daily LAMAs are first-line therapy for moderate-to-very severe COPD patients
- Patients with **suboptimal PIFR** (19–78% of COPD patients<sup>5</sup>)
- Patients with cognitive or dexterity challenges
  - ~36% of COPD patients present episodes of cognitive impairment; ~33% of elderly patients have inadequate hand strength for inhalers<sup>6</sup>
- Patients inappropriately using short-acting nebulized treatment as maintenance therapy
- Patients transitioning from hospital to home care after being stabilized on nebulized treatment during hospitalization



- 1. American Lung Association.
- 2. Clarivate COPD Disease Landscape & Forecast US 2021.
- 3. Revefenacin COPD Joint Venture Research 2016.
- 4. Safka KA, et al. Chronic Obstr Pulm Dis 2017.
- 5. Mahler DA. et al. Chronic Obstr Pulm Dis 2019
- 6. Armitage JM, Williams SJ Inhaler technique in the elderly. Age Ageing 1988 17:275-278. COPD, chronic obstructive pulmonary disease; DME, durable medical equipment; LAMA, long-acting muscarinic antagonist; PIFR, peak inspiratory flow rate.

# Offering Hope to MSA Patients with Symptomatic nOH



33rd International Symposium on the Autonomic Nervous System November 2-5, 2022: Sheraton Maui, Hawaii

### Platform Presentations, Session 1, November 2, 2022

### Biaggioni I, et al. Abstract 34 / Virtual Poster 106

A phase 3, 22-week, multi-center, randomized withdrawal study of ampreloxetine in treating symptomatic nOH

### Kaufmann H, et al. Abstract 33 / Virtual Poster 117

Blood pressure and pharmacodynamic response of ampreloxetine, a norepinephrine reuptake inhibitor, in patients with symptomatic nOH

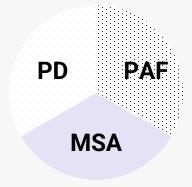
### Freeman R, et al. Abstract 30 / Virtual Poster 4

Longitudinal analysis of ampreloxetine for the treatment of symptomatic nOH in subset of patients with MSA

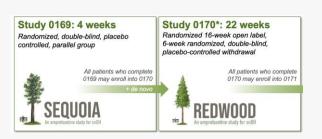


## Shift Toward Broad Symptomatic Improvement for MSA Patients

### "Old" Ampreloxetine Program



"Dizziness" based indication for short-term effectiveness



### "New" MSA-focused Ampreloxetine Program



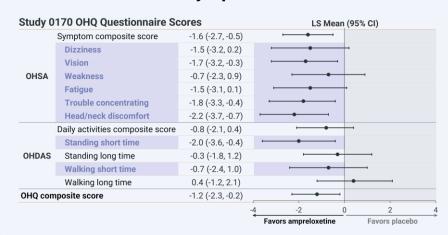


In study 0170, ampreloxetine **prevented blood pressure drop and symptoms worsening in MSA**<sub>1</sub>

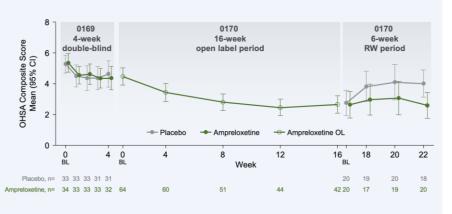
Support from the scientific and medical community with 3 scientific presentations presented at the American Autonomic Society meeting<sub>2</sub>

Aligned with FDA on new Phase 3 study for approval with OHSA composite as primary endpoint

#### **Constellation of symptoms-based indication**



#### **Durable effectiveness**





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

2. Biaggioni I, et al. Abstract 34 / Virtual Poster 106; Kaufmann H, et al. Abstract 33 / Virtual Poster 117; Freeman R, et al. Abstract 30 / Virtual Poster 4.

MSA, Multiple System Atrophy; nOH, neurogenic orthostatic hypotension; OHDAS, orthostatic hypotension daily activity scale; OHQ, orthostatic hypotension questionnaire; OHSA, Orthostatic Hypotension Symptom Assessment; PAF, Pure Autonomic Failure; PD, Parkinson's Disease.

## 2022: A Year of Transformation



- Three consecutive quarters of alltime high Net Sales and Profit in Q2-Q4
- Continued community market share growth every quarter since launch
- 53% Y/Y growth in hospital volume, a key driver of overall brand performance<sup>1</sup>
- Initiated PIFR-2 study

## **Ampreloxetine**

- In study 0170, prevented blood pressure drop and symptoms worsening in MSA<sup>2</sup>
- Aligned with FDA on new Phase 3 study for NDA filing with OHSA composite score as primary endpoint
- Three scientific platform presentations at American Autonomic Society meeting<sup>3</sup>
- Secured up to \$40 million from Royalty Pharma for funding ampreloxetine development; \$25M to fund majority of new P3 study

## **Financial**

- Sold TRELEGY ELLIPTA royalty interests for \$1.1B upfront, while retaining value through milestones and certain outer-year royalties
- ► Eliminated all debt, ~\$650 million
- Completed financial restructuring
- ► Initiated \$250 million capital return program, of which ~62% was completed as of February 27, 2023

