# Theravance MK Biopharma MK.

Medicines That Make a Difference®

# Transformed and Focused on Medicines that Make a Difference<sup>®</sup>

September 13, 2022

THERAVANCE BIOPHARMA<sup>®</sup>, THERAVANCE<sup>®</sup>, the Cross/Star logo and MEDICINES THAT MAKE A DIFFERENCE<sup>®</sup> are registered trademarks of the Theravance Biopharma group of companies (in the U.S. and certain other countries). All third party trademarks used herein are the property of their respective owners. © 2022 Theravance Biopharma. All rights reserved.

# **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 1995, as amended, and the Private Securities Litigation Reform Act of 1995.

Examples of such statements include statements relating to: contingent payments due to the Company from the sale of the Company's TRELEGY ELLIPTA royalty interests to Royalty Pharma, the Company's goals, designs, strategies, plans and objectives, including the paydown of the Company's debt, the impact of the Company's restructuring plan, ability to provide value to shareholders, the timing of clinical studies, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations regarding its allocation of resources, potential regulatory actions, product sales or profit share revenue and the Company's expectations for its future financial performance and expectations as to future cash flows. 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 forwardlooking 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 or non-clinical studies indicate the Company's product candidates 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 distribution capabilities with appropriate technical expertise and supporting infrastructure, ability to retain key personnel, the impact of the Company's restructuring actions on its employees, partners and others. In addition, while we expect the effects of COVID-19 to continue to adversely impact our business operations and financial results, the extent of the impact on our ability to generate revenue from YUPELRI® (revefenacin), and the value of and market for our ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time.

Other risks affecting the Company are in the Company's Form 10-Q filed with the SEC on August 8, 2022, 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 or otherwise, except as required by law.



# Theravance Biopharma At-a-Glance



- Commercial product poised for significant near-term growth
- YUPELRI PIFR-2 Phase 4

#### Ampreloxetine

- Phase 3 potential therapy for MSA patients with opportunity to differentiate from existing treatment options
- \$25 million investment from Royalty Pharma to fund majority of Phase 3 costs

Experienced Board and Management team with the right mix of skills and experience to drive value

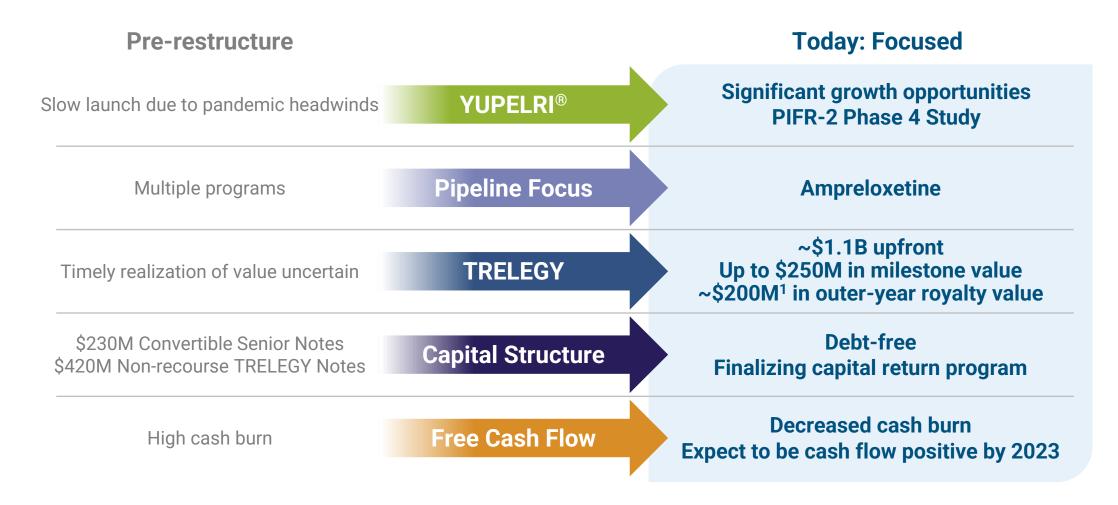
#### **Retained** TRELEGY Value

• Mid- to long-term value from milestone and outer-year royalties

#### **Financials**

- Debt-free balance sheet
- Finalizing capital return program
- On track to be cash flow positive by 2023

# Theravance Biopharma Transformation





1.85% of TRELEGY ELLIPTA royalties return to Theravance Biopharma beginning July 1,2029 for sales ex-U.S., and January 1,2031 for sales within the U.S. Net present value ("NPV") of royalties based on GSK Bloomberg Consensus for TRELEGY ELLIPTA through 2032 for U.S. sales and through 2034 for ex-U.S. sales, discounted at 7%. Ex-U.S. sales for 2033-2034 extrapolated by Management due to limitation of consensus beyond 2032.

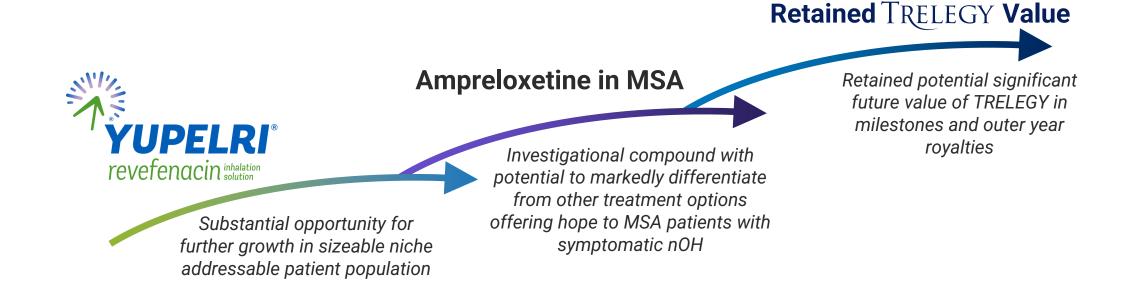
### Investment Highlights

- Transformed and focused therapeutics company
- Attractive pipeline and programs with YUPELRI<sup>®</sup>, ampreloxetine and retained potential significant TRELEGY value
- Strong, debt-free balance sheet
- Finalizing capital return program
- Sustainable, annual cash flow generation 2023
- Experienced Board and Management team with the right mix of skills and experience to drive value



# Theravance Biopharma: Key Pillars of Value

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



# Theravance is well positioned to maximize the value of its assets from a position of financial strength



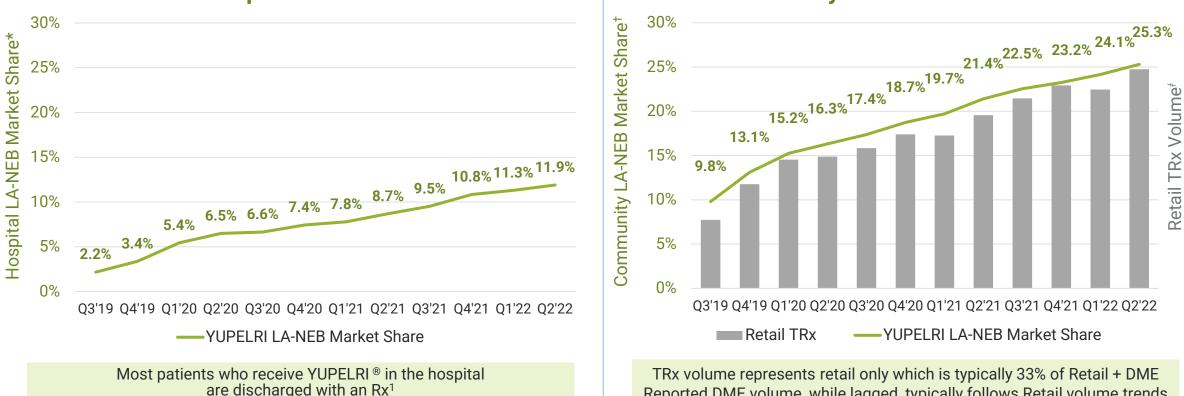


### FDA-approved for maintenance treatment of COPD First and only once-daily, LAMA (long-acting muscarinic agent) nebulized maintenance medicine for COPD



# YUPELRI<sup>®</sup> Hospital Sales and Community TRx Trends

Continued market share growth across both the hospital and retail channels



**Hospital Market Share** 

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

1. Joint VTRS/TBPH Market Research

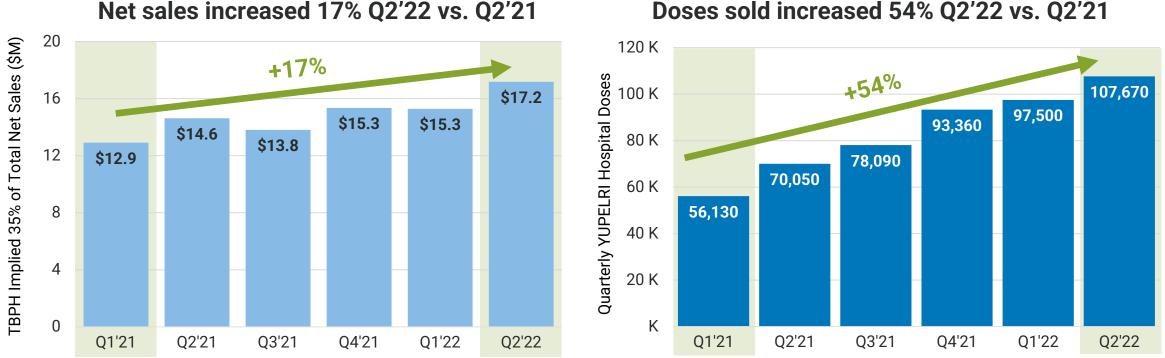
Theravance <u>XX</u> Biopharma 🔼

**Community Market Share with TRx** 

Reported DME volume, while lagged, typically follows Retail volume trends

8

### YUPELRI<sup>®</sup> | Gaining Momentum in Sales and Hospital Volume



Doses sold increased 54% Q2'22 vs. Q2'21



Source: IQVIA DDD, HDS, VA and Non-Reporting Hospital through 6/30/2022. See TBPH 10K filed February 28, 2022 for greater detail re TBPH implied 35%.

# Substantial opportunity for further YUPELRI<sup>®</sup> 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 Therapy<sup>3</sup> ~80% of Drug Treated

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

#### COPD is under-diagnosed<sup>1</sup>

- 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:

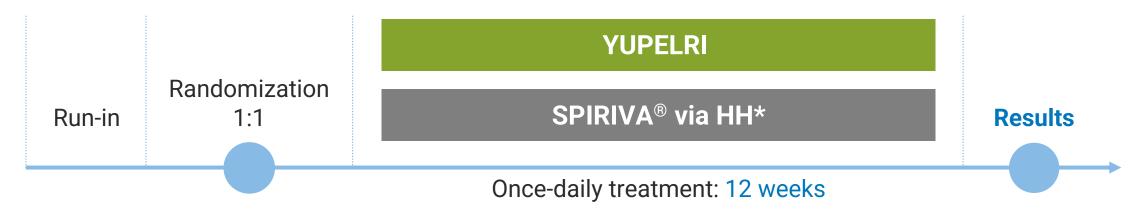
- Moderate-to-very-severe COPD (73-92%<sup>4</sup>); once-daily LAMAs are first-line therapy for moderate-to-very severe COPD patients
- Patients with suboptimal PIFR (19–78% of COPD patients<sup>5</sup>)
- Patients with cognitive or dexterity challenges
  - ~36% of COPD patients present episodes of 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.

### YUPELRI<sup>®</sup>: Phase 4 Randomized, Double-blind, Parallel-group Study (PIFR-2)



#### Sample size

Potential to increase from n=366 to n=488 resulting from a pre-specified per-protocol blinded sample size reestimation; top-line results in 2H '23

#### Endpoints

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



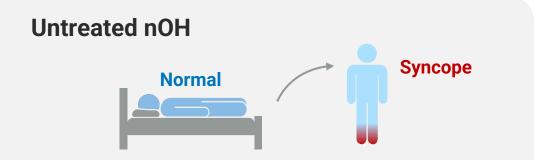
Phase 4, Randomized, Double-Blind, Parallel-Group Study in Adults With Severe-to-Very-Severe COPD and Suboptimal Inspiratory Flow Rate. \*Dry powder inhaler (Spiriva® HandiHaler®). FEV<sub>1</sub>, forced expiratory volume in 1 second; PIFR, peak inspiratory flow rate.

# **Ampreloxetine (TD-9855)**

Investigational once-daily norepinephrine reuptake inhibitor for symptomatic neurogenic orthostatic hypotension in multiple system atrophy patients

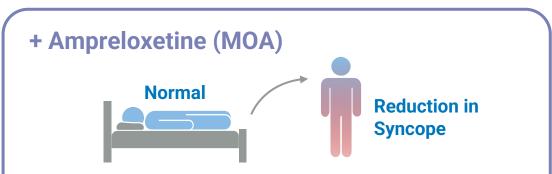


# Offering Hope to MSA Patients with Symptomatic nOH



#### **nOH Prevalence in MSA Patients**

- ~50K MSA patients in US<sup>1</sup> (meets orphan disease criteria)
- 70–90% of MSA patients experience nOH symptoms<sup>2</sup>
- Despite available therapies, many MSA patients remain symptomatic with nOH



# Prevents blood pressure drop and symptoms worsening in MSA<sup>3</sup>

- ✓ Increased standing blood pressure
- ✓ Increased brain perfusion
- $\checkmark~{\rm Reduce~symptoms~of~symptomatic~nOH^4}$

Theravance Biopharma Medicines That Make a Difference

1. 2019 IQVIA Claims Analysis; NIH; 2. Mathias CJ, et al. J Neurol 1999 Oct;246(10):893-8; 3. Data from MSA patients at week 6 of the randomized withdrawal period of study 0170. 4. Palma JA, Kaufmann H. Mov Disord Clin Pract 2017;4:298-308. MOA, mechanism of action; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension.

### Offering Hope to MSA Patients with Symptomatic nOH Potential for ampreloxetine to differentiate from approved therapies

	Droxidopa	Midodrine	Ampreloxetine <sup>1</sup>
Indication	Symptomatic nOH	ОН	Symptomatic nOH associated with MSA
МОА	Norepinephrine prodrug; vasoconstrictor	Desglymidodrine prodrug; alpha <sub>1</sub> - receptor agonist; vasoconstrictor	Norepinephrine transporter reuptake inhibitor
Dosing	3x daily, titration to effect	3x daily	Once-daily
Clinical Efficacy/ Durability	OHSA#1, clinical effectiveness >2 weeks not established	Increase in systolic blood pressure 1 min after standing	OHSA composite; clinically meaningful and durable response <b>over 22 weeks</b>
Clinical Safety	<b>Black box warning</b> fo	r supine hypertension	No signal for supine hypertension in safety database of >800 patients and healthy subjects



1. Reflects Theravance Biopharma's expectations for ampreloxetine based on clinical trial data to date. Ampreloxetine is in development and not approved for any indication. Data on file. MOA, mechanism of action; MSA, multiple system atrophy; nOH, neurogenic orthostatic hypotension; OH, orthostatic hypotension; OHSA, orthostatic hypotension symptom assessment.

# Offering Hope to MSA Patients with Symptomatic nOH



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

#### **Platform Presentations**

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

#### 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

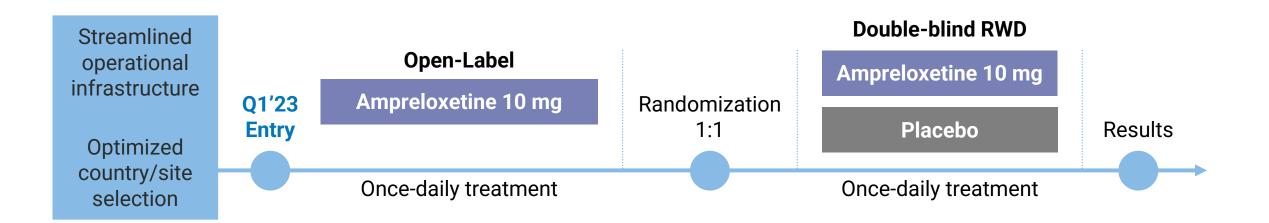
#### Biaggioni I, et al. Abstract 34 / Virtual Poster 106

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



# Offering Hope to MSA Patients with Symptomatic nOH

Phase 3 randomized withdrawal study in patients with MSA Primary endpoint: change in OHSA composite score





### **Sale of Economic Interest** GSK's TRELEGY ELLIPTA (FF/UMEC/VI): Once-daily single inhaler triple therapy



### Retained Value of Theravance Biopharma's 85% TRELEGY ELLIPTA Interest<sup>1</sup>

### Over \$1.5 Billion in potential total value to Company shareholders



GSK remains exclusively responsible for commercialization of TRELEGY ELLIPTA



1. All of its units in Theravance Respiratory Company, LLC. 2. The first milestone payment, of \$50.0 million, will be triggered if Royalty Pharma receives \$240.0 million or more in royalty payments from GSK with respect to 2023 TRELEGY global net sales, which we would expect to occur in the event TRELEGY global net sales reach approximately \$2.863 billion. *3.* 85% of TRELEGY ELLIPTA royalties return to Theravance Biopharma beginning July 1, 2029 for sales ex-U.S., and January 1, 2031 for sales within the U.S. Net present value ("NPV") of royalties based on GSK Bloomberg Consensus for TRELEGY ELLIPTA through 2032 for U.S. sales and through 2034 for ex-U.S. sales, discounted at 7%. Ex-U.S. sales for 2033-2034 extrapolated by Management due to limitation of consensus beyond 2032.

# Theravance Biopharma and Royalty Pharma Deal Summary

#### **TRELEGY ELLIPTA**

- Upfront: \$1.1B
- Milestones: Up to \$250M

Year	Royalties <sub>2</sub>	Global Net Sales Equivalent	Milestone
2023	\$240M	\$2,863M	\$50M
	\$240M	\$2,863M	\$25M
2024 <sub>1</sub>	\$275M	\$3,213M	\$50M
2025	\$260M	\$3,063M	\$25M
2025 <sub>1</sub>	\$295M	\$3,413M	\$50M
0005	\$270M	\$3,163M	\$50M
2026 <sub>1</sub>	\$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>
  - NPV estimated at  ${\sim}\$200 M^4$

#### Ampreloxetine (Unsecured Royalty)

- Upfront payment: \$25M
- 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



. If both milestones are achieved in a given year, Theravance Biopharma will only earn the higher milestone. . Based on 100% of TRELEGY ELLIPTA royalties.

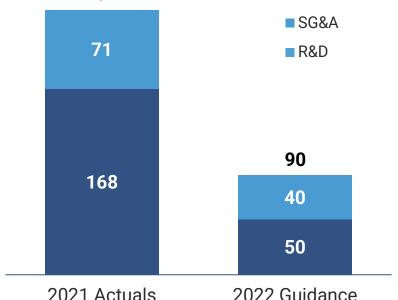
3. U.S. royalties expected to end late 2032; ex-U.S. royalties expected to end mid-2030s and are country specific.

4. Net present value ("NPV") of royalties based on GSK Bloomberg Consensus for ELLIPTA through 2032 for U.S. sales and through 2034 for ex-U.S. sales, discounted at 7%. Ex-U.S. sales for 2033-2034 extrapolated by Management due to limitation of consensus beyond 2032.

# **Financial Guidance**

- **<u>Reiterating</u>** 2022 OPEX guidance:
  - R&D: range of \$45–55M
  - SG&A: range of \$35-45M
- 2022 guidance includes ~\$10M in <u>non-recurring</u> spend:
  - Majority in Q1 to support completion of late-stage programs
  - OPEX Q3 and onward will reflect recurring spend only
- Guidance excludes:
  - Non-cash share-based compensation (SBC)
  - One-time restructuring, severance & termination costs
    - ~ 11.7M in 2022 ( $3M_2$  Q1 /  $1.6M_3$  Q2 /  $0.8M_4$  Q3 /  $M_4$  Q4)
  - One-time transaction related costs of \$5.1M YTD





#### Theravance Biopharma expects to approach breakeven cash flow from operations in 2H 2022 and become sustainably cash flow positive going forward on an annual basis



Excludes non-cash share-based compensation (SBC), one-time restructuring, severance and termination costs, and one-time transaction related legal expenses.
\$4.8M of cash related expenses and \$4.5M of non-cash expenses.
\$1.2M of cash related expenses and \$0.4M of non-cash expenses.

4.) Q3 / Q4 are estimates and subject to change; primarily comprised of non-cash expenses.

### An Experienced Leadership Team

#### **Rick E Winningham Chairman and Chief Executive Officer**

Former CEO, Theravance, Inc. (now INVA) Former President (Oncology/Immunology/Oncology Therapeutics Network), Bristol Myers Squibb



#### Andrew A. Hindman Senior Vice President, **Chief Financial Officer**

Former Chief Business Officer, Acorda Therapeutics Former President & CEO, Tobira Therapeutics

#### Rhonda F. Farnum **Senior Vice President**, **Chief Business Officer**

Former Executive Director of Marketing, Amgen Former VP (Hematology), Onyx Pharmaceuticals & Former Commercial Leadership, Genentech



#### **Richard A. Graham** Senior Vice President,

**Research and Development** 

Former Senior Director, Head of Translational Medicine, **Onvx Pharmaceuticals** Former Clinical Pharmacologist and Project Team Leader, Genentech and GlaxoSmithKline



#### **Brett A. Grimaud** Senior Vice President,

Former Senior Director, Theravance, Inc. (now INVA) Former Senior Attorney, Gunderson Dettmer



# **General Counsel and Secretary**

#### **Stacy Pryce Senior Vice President**, **Chief Strategy Officer**

Former VP Business Development, Aerogen Former Senior Director, Alliance Management & **Business Development Vertex Pharmaceuticals** 





### The Board of Directors Experienced leaders from a diverse range of relevant backgrounds



**Rick Winningham** Chairman & CEO, Theravance Biopharma

- Demonstrated leadership and senior management experience in the biopharmaceutical industry
- Former Chairman & CEO at Theravance, Inc. (now INVA) and former President of Oncology / Immunology / Oncology Therapeutics Network and President of Global Marketing at Bristol Mvers Sauibb



William Young Senior Advisor, Blackstone Life Sciences

- Extensive leadership experience at numerous pharmaceutical and biotechnology organizations as well as financial / investing expertise gained as a venture capitalist
- Former Chairman & CEO at Monogram Biosciences and Venture Partner at Claris Ventures



- Extensive leadership experience with regulatory and clinical expertise in the life sciences industry
- Former President and Chief Scientific Officer at PharmApprove and CEO at Phytomedics



**Eran Broshy** Former Chairman & CEO, inVentiv Health

- Demonstrated leadership in managed healthcare in addition to the broader healthcare industry
- Former Partner and Head of the Americas Healthcare Practice at The Boston Consulting Group and CEO at Coelacanth



Burton Malkiel, Ph.D. CIO & Chair of the Investment Committee, Wealthfront

- Demonstrated leadership and knowledge of financial and financing matters
- Former Appointee to the President's Council of Economic Advisors



- Former President & CEO. Lux Biosciences
- · Extensive management experience in the pharmaceutical and biotherapeutics industries with expertise in later stage drug development and commercialization
- Former President & CEO at Alpharma and Guilford Pharmaceuticals



**Donal O'Connor** Former Senior Partner. PwC Ireland

- · Extensive experience across the financial and pharmaceutical industries, including with Irish entities, in addition to accounting and financial expertise
- Former Chairman of Anglo Irish Bank and Board member at the Irish Auditing and Accountancy Supervisory Authority



- Deepa Pakianathan, Ph.D. CEO. Redd Pharmaceuticals
- Knowledge and experience in overseeing the business development and strategy of multiple healthcare companies with experience gained as a biotechnology investor, research analyst and research scientist
- Managing Member at Delphi Ventures



### **Investment Highlights**

- Transformed and focused therapeutics company
- Attractive pipeline and programs with YUPELRI<sup>®</sup>, ampreloxetine and retained potential significant TRELEGY value
- Strong, debt-free balance sheet
- Finalizing capital return program
- Sustainable, annual cash flow generation 2023
- Experienced Board and Management team with the right mix of skills and experience to drive value



# YUPELRI<sup>®</sup> (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.<sup>1</sup> LAMAs are a cornerstone of maintenance therapy for COPD and YUPELRI<sup>®</sup> is positioned as the first once-daily single-agent bronchodilator product for COPD patients who require, or prefer, nebulized therapy. YUPELRI<sup>®</sup>'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.

