# Theravance<sup>®</sup> K Biopharma

Medicines That Make a Difference<sup>®</sup>

### **Corporate Presentation**

#### January 2020

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#### **Forward looking statements**

Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, the company cautions investors that any forward-looking statements or projections made by the company are subject to risks and uncertainties that may cause actual results to differ materially from the forward-looking statements or projections.

Examples of forward-looking statements in this presentation may include the Company's strategies, plans and objectives, the Company's regulatory strategies and timing of clinical studies (including the data therefrom), the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations for product candidates through development, potential regulatory approval and commercialization (including their differentiation from other products or potential products), product sales or profit share revenue and the Company's expectations for its 2019 operating loss, excluding share-based compensation.

The company's forward-looking statements are based on the estimates and assumptions of management as of the date of this presentation and are subject to risks and uncertainties that may cause the actual results to be materially different than those projected, such as risks related to potential future disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that an arbitration award or litigation result could be adverse to the Company, delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's compounds or product candidates are unsafe or ineffective, risks that product candidates do not obtain approval from regulatory authorities, the feasibility of undertaking future clinical trials for our product candidates based on policies and feedback from regulatory authorities, 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.

Other risks affecting the company are described under the heading "Risk Factors" and elsewhere in the company's Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 8, 2019, and other periodic reports filed with the SEC.



#### **Strategic objective**

Transform the treatment of serious diseases through the discovery, development, and commercialization of *organ-selective medicines* designed to maximize patient benefit while minimizing patient risk





### **Creating transformational value for stakeholders**

Innovative and productive research engine feeding pipeline of organ-selective assets



Proven **development expertise** and established **commercial infrastructure** 

**Strategic partnerships** complement internal capabilities and balance technical, execution and financial risks



**Strong capital position** augmented by TRELEGY ELLIPTA<sup>1</sup> royalties and YUPELRI<sup>®</sup> launch





1. TBPH holds 85% economic interest in upward-tiering royalty stream of 6.5% – 10% payable by GSK (net of TRC expenses paid and the amount of cash, if any, expected to be used by TRC pursuant to the TRC Agreement over the next four fiscal quarters). 75% of royalties received pledged to service PhaRMA<sup>SM</sup> notes, 25% of royalties received retained by TBPH. All statements concerning TRELGY ELLIPTA based on publicly available information.

# Key programs supported by proven development and commercial expertise

	Program	Indication	Research	Phase 1	Phase 2	Phase 3	Filed	Marketed	Collaborator	
Organ-selective	YUPELRI® (revefenacin) LAMA	COPD						Marketed	III Mylan	
	<b>TD-1473</b> GI JAKi	UC		Phas	se 2b/3					
		CD		Phase 2					– Janssen 🖌	
	<b>TD-8236</b> Inhaled JAKi	Inflammatory lung diseases		Pha	ase 2				Wholly-owned	
	<b>TD-5202</b> Irreversible JAK3i	Inflammatory intestinal diseases	Pha	ase 1					Janssen	
	New programs	Multiple	Research						Wholly-owned	
	Ampreloxetine (TD-9855) NRI	Symptomatic neurogenic orthostatic hypotension		Phase 3				Wholly-owned		
Economic Interests	Program	Indication	Research	Phase 1	Phase 2	Phase 3	Filed	Marketed	Rights	
	TRELEGY ELLIPTA FF/UMEC/VI	COPD						Marketed	GSK &	
		Asthma				F	iled		Innoviva, Inc.	
	Skin-selective JAKi	Dermatological diseases	Research						Pfizer	

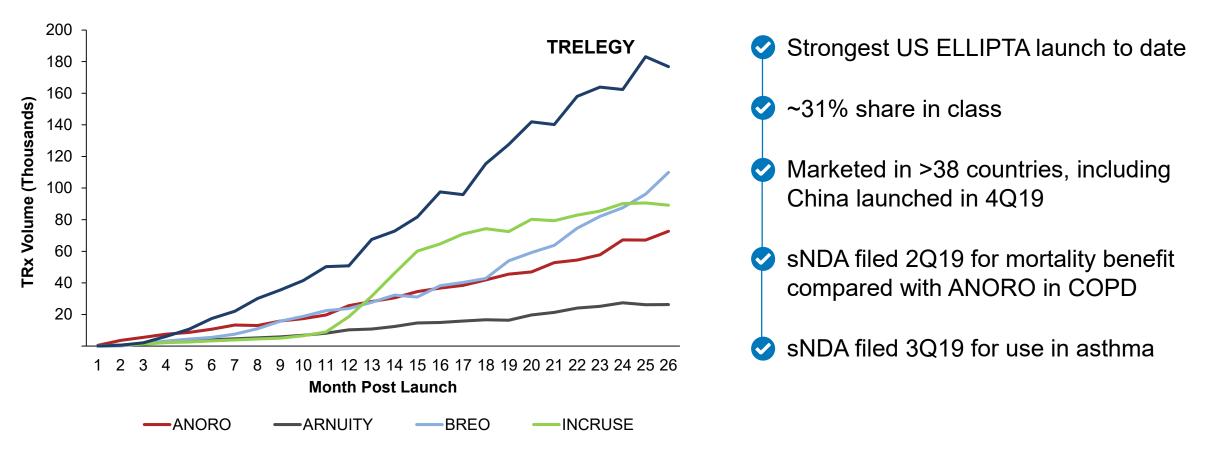
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### **Economic interest** GSK's TRELEGY ELLIPTA (FF/UMEC/VI): First and only once-daily single inhaler triple therapy

### **Economic interest in GSK's TRELEGY ELLIPTA**

UPWARD-TIERING ROYALTIES OF ~5.5% TO 8.5% OF WORLDWIDE NET SALES<sup>1</sup>



#### Launched in US in November 2017

Source: GSK, IQVIA NPA weekly TRx data. This information is an estimate derived from the use of information under license from the following IQVIA information service: NPA for the time period Sep 2013 through Nov 2019. IQVIA expressly reserves all rights, including rights of copying, distribution, and republication.



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## YUPELRI® (revefenacin) inhalation solution First and only once-daily, nebulized maintenance medicine for COPD

#### YUPELRI® (revefenacin) inhalation solution FDA-APPROVED FOR THE MAINTENANCE TREATMENT OF COPD



First and only once-daily, nebulized maintenance medicine for COPD

Once-daily LAMAs are first-line therapy for moderate to severe COPD<sup>1</sup>

9% of COPD patients (~800,000) use nebulizers for ongoing maintenance therapy; 41% use nebulizers at least occasionally for bronchodilator therapy<sup>2</sup>

Nebulized therapy associated with reduced hospital readmissions in low PIFR patients<sup>3</sup>

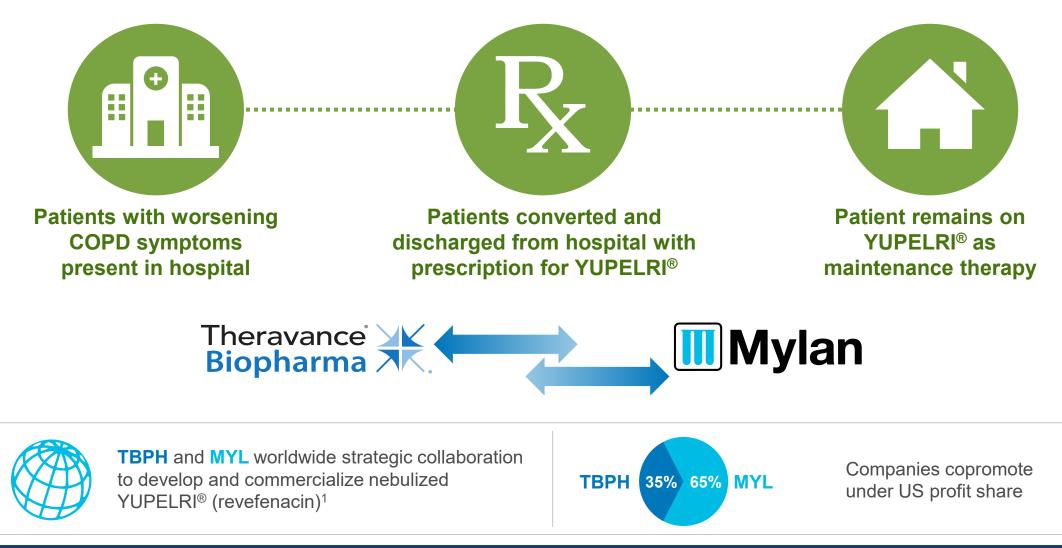
Theravance Biopharma 1. Global Strategy for Diagnosis, Management, and Prevention of COPD, 2018; 2. TBPH market research (N = 160 physicians); refers to US COPD patients 3. Loh CH, et al. Ann Am Thorac Soc. 2017 Aug;14:1305-11; 4. IMS Health information service: NSP for period MAT May, 2015. Excludes nebulized short-acting beta agonists. IMS expressly reserves all rights, including rights of copying, distribution and republication. LAMA, longacting muscarinic antagonist; PIFR, peak inspiratory flow rate; LABA, long-acting beta agonist.

### **YUPELRI®** commercial strategy

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Biopharma XK Medicines That Make a Difference\*

COMBINED SALES INFRASTRUCTURES TARGET HCPS AT KEY INTERSECTIONS



1. For COPD and other respiratory diseases. TBPH is eligible to receive up to \$259 million in development and sales milestone payments, as well as a profit-sharing arrangement with MYL on US sales and double-digit royalties on ex-US sales. TBPH retains worldwide rights to revefenacin delivered through other dosage forms (e.g. metered dose inhaler or dry powder inhaler).

#### YUPELRI<sup>®</sup> launch metrics STRONG CUSTOMER ACCEPTANCE AND MARKET UPTAKE

#### *FORMULARY*

85 wins
(equates to 220 accounts)

~70 reviews scheduled
(>400 potential accounts)

 100% medical support requests fulfilled <30 days</li>

#### **PATIENT**

 Field force productivity goals exceeded

~30,000 patients<sup>2</sup> prescribed (through Q4 2019)

#### ACCESS

- 100% Medicare Part B<sup>1</sup>

~50% commercial

– Permanent J-CODE issued<sup>3</sup>

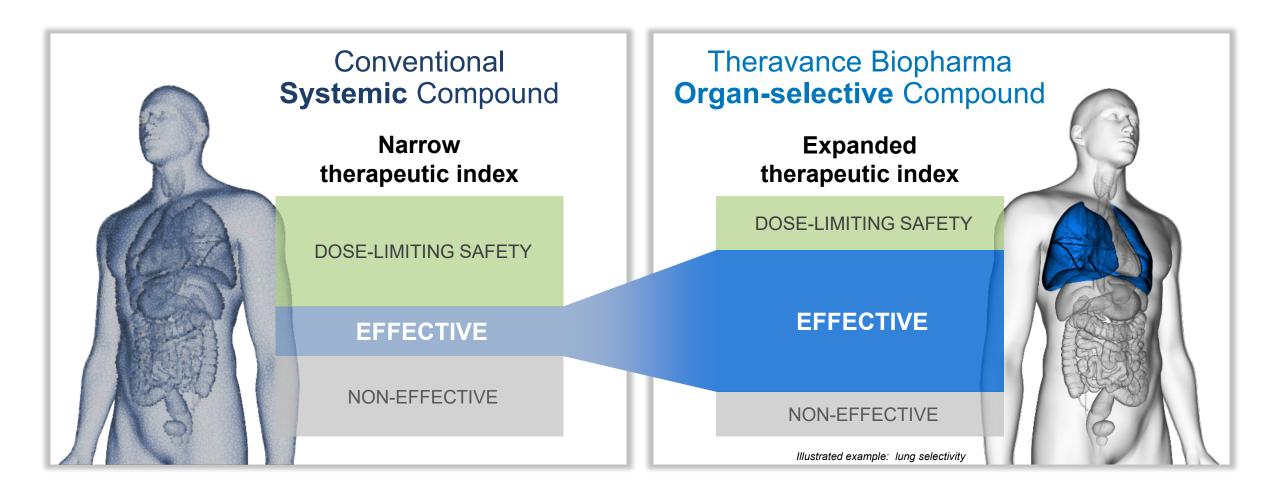


Majority of YUPELRI® volume flows through durable medical equipment channel (approximately 3 month lag in data capture); remaining volume flows through hospitals, retail and long-term care pharmacies. Wholesale acquisition cost (WAC): \$1,066 per month (or ~\$35 per day). 1. For patients with supplemental insurance. 2. TBPH estimate derived from integrating multiple data sources. 3.Effective July 1, 2019.

# **Our science**

Organ-selective approach designed to optimize therapeutic index

Organ-selective approach leverages proven and deep expertise in developing lung-selective medicines for respiratory disease

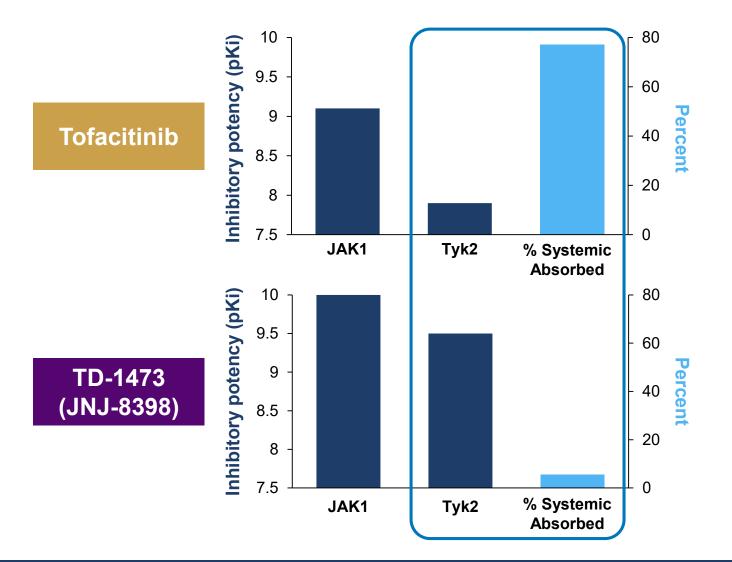




# TD-1473 (JNJ-8398)

Oral gut-selective pan-JAK inhibitor Goal: Treat inflammatory intestinal diseases

# Improved preclinical profile of a novel, potent, gut-selective pan-JAK inhibitor





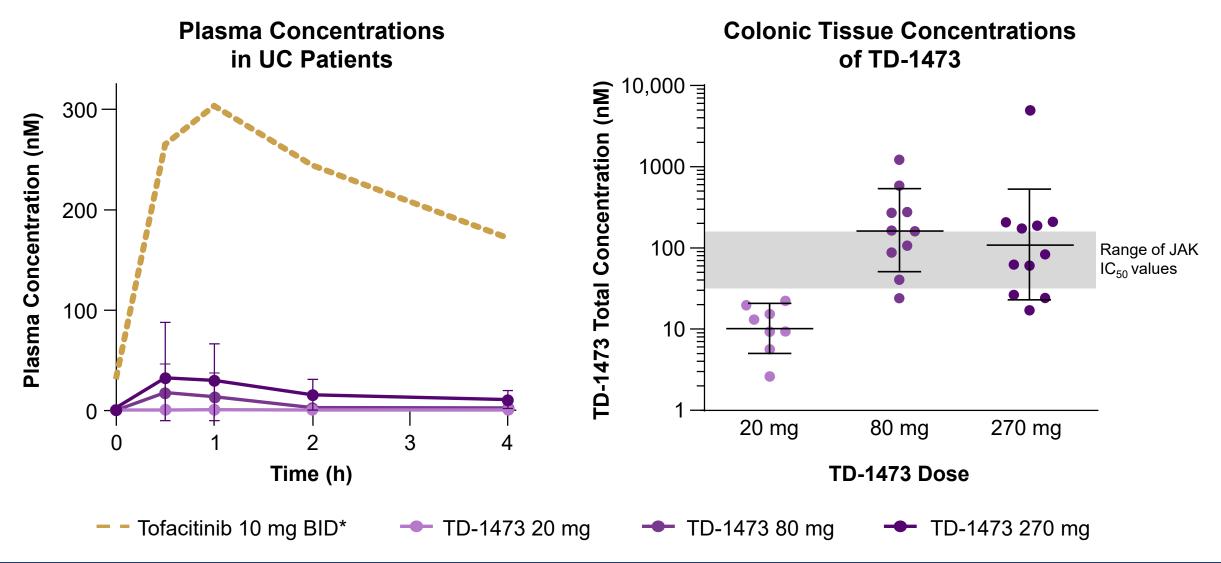


Tyk2: tyrosine kinase 2.

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Biopharma XK Medicines That Make a Difference\*

# Systemic exposures low; tissue concentrations at or above JAK inhibition levels



Tofacitinib concentrations extracted from J Pharmacol Exp Ther 348:165–173, January 2014. BID: twice daily; Hr: hours; IC<sub>50</sub>: concentration to produce 50% maximal inhibition; PK: pharmacokinetics

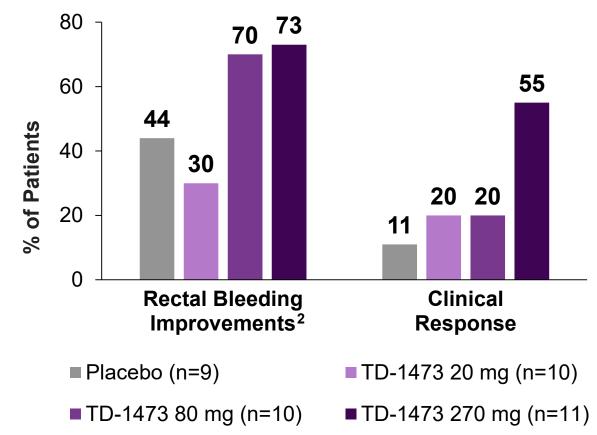
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Biopharma XK Medicines That Make a Difference\*

### Potential for increased efficacy and safety with gut selectivity

TD-1473 (JNJ-8398)<sup>1</sup>

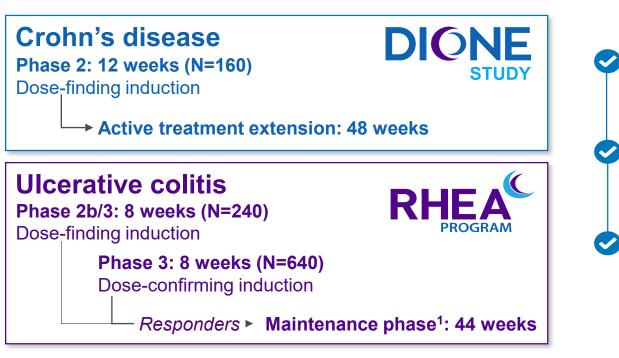
Phase 1 data in UC; 4 weeks of treatment





Presented at the European Crohn's and Colitis Organization meeting, March 8, 2019, Copenhagen, Denmark.
Component of total Mayo score clinical response.

#### TD-1473: Gut-selective pan-JAK inhibitor LATE-STAGE STUDIES IN ULCERATIVE COLITIS AND CROHN'S DISEASE



- Phase 2 Crohn's and Phase 2b/3 UC studies ongoing
- Phase 2 Crohn's and Phase 2b UC data expected late-2020
  - Global collaboration with JNJ leverages joint development expertise and provides significant economics to TBPH<sup>2</sup>

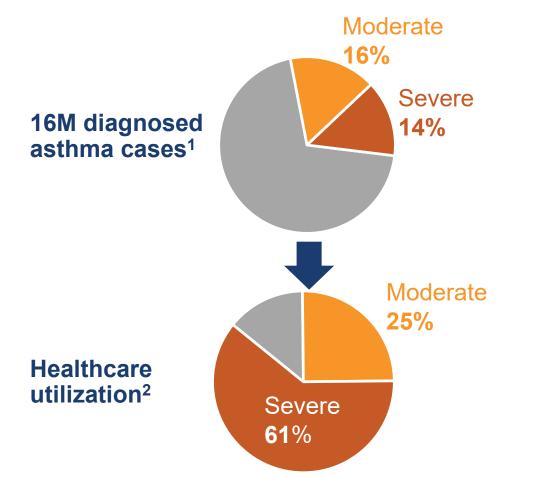


# **TD-8236**

Inhaled lung-selective pan-JAK inhibitor Goal: Treat moderate-to-severe asthma regardless of T2 phenotype

### High medical and economic burden in uncontrolled asthma

# Small portion of US patients cause ~\$58B in medical costs



## JAK/STAT cytokines implicated in moderate to severe asthma

T2-high	T2-low				
IL-4	<b>IL-23</b> /IL-12				
IL-13	IL-6				
IL-5	IL-27				
TSLP	IFN-γ				

Bold denotes biologics in development or approved

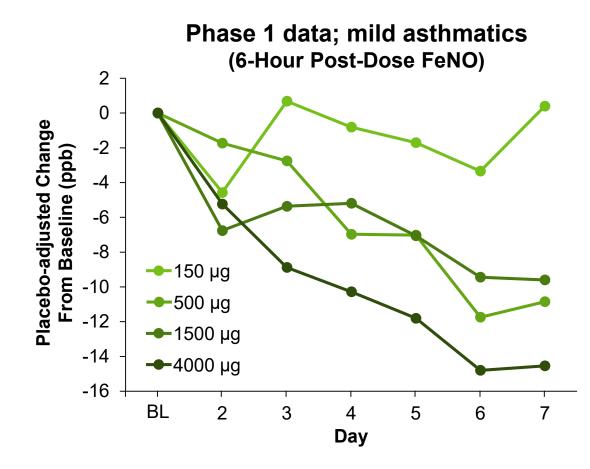
Inhaled pan-JAK inhibitor has the potential to address patient needs regardless of T2 phenotype

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1. 2018 DR/Decision Resources, LLC. All rights reserved. Reproduction, distribution, transmission or publication is prohibited; reprinted with permission; 2. Sadatsafavi, M., et al. Can Respir J 2010;17:74-80; 3. Nurmagambetov T, et al. Ann Am Thorac Soc 2018;15:348-56.

IFN: interferon; IL: interleukin; STAT: signal transducer and activator of transcription proteins; T2: type 2; TSLP: thymic stromal lymphopoietin.

#### TD-8236: Lung-selective pan-JAK inhibitor PRELIMINARY POSITIVE FENO DATA IN MILD ASTHMATICS



Phase 1 biomarker study in moderate to severe asthmatics ongoing; data expected mid-2020

#### **TD-8236: Lung-selective pan-JAK inhibitor** PHASE 2 ALLERGEN CHALLENGE STUDY

#### TD-8236 Phase 2 Lung Allergen Challenge 12 weeks (N=21)

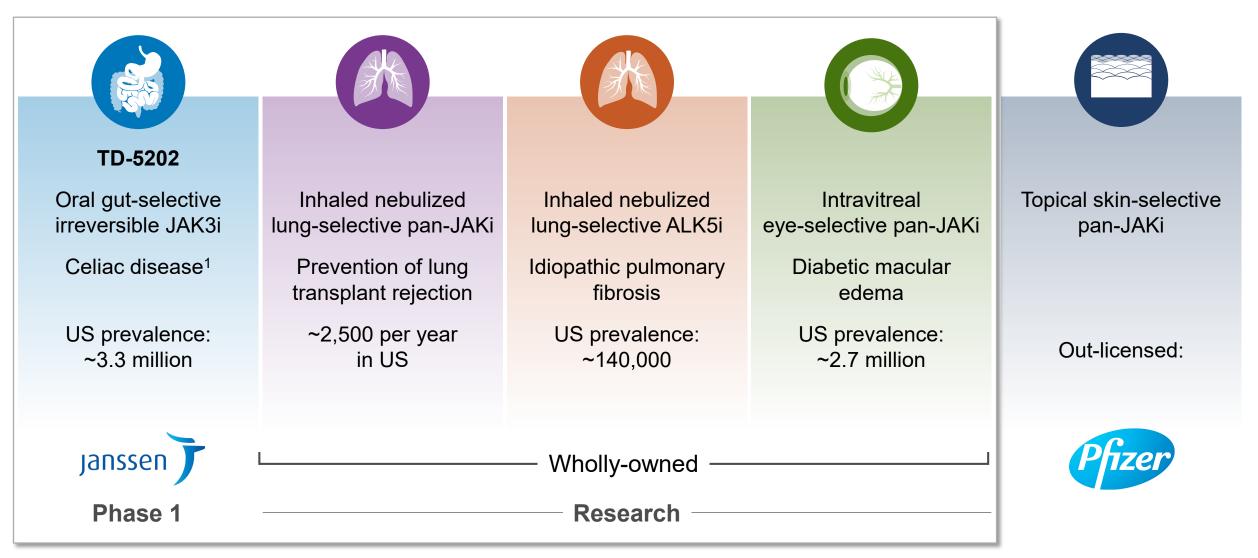
Dose characterization Randomized, double-blind, placebo-controlled, crossover study

- Phase 2 allergen challenge study underway
- Data expected 2020



# Early-stage organ-selective programs

# **Opportunity to address multiple therapeutic areas with novel organ-selective approach**



 TD-5202 is being developed in collaboration with Janssen Biotech, Inc. for inflammatory intestinal diseases e.g. celiac disease.
Theravance Biopharma and Pfizer Inc. entered into a global license agreement for skin-selective pan-JAK inhibitors. ALK5i: inhibitor of transforming growth factor β type I receptor.

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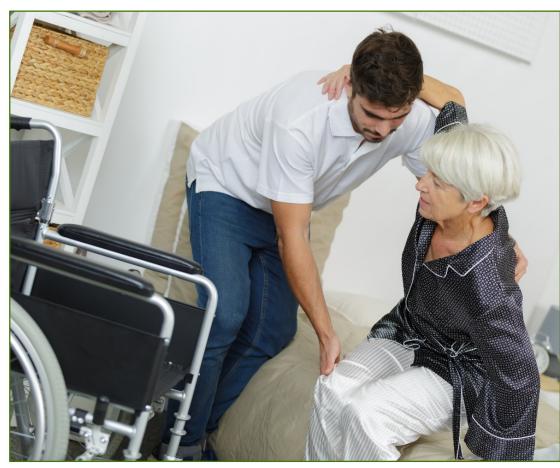
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# **Ampreloxetine (TD-9855)**

Once-daily norepinephrine reuptake inhibitor for symptomatic neurogenic orthostatic hypotension

# Reduced quality of life, significant care-giver burden and limited therapeutic options for symptomatic nOH patients



nOH is a symptom of MSA, PAF and PD

- 18% of PD<sup>1</sup> and 83% of MSA<sup>2</sup> patients have nOH
- ~350K patients in the US

**Current treatments have significant limitations** 

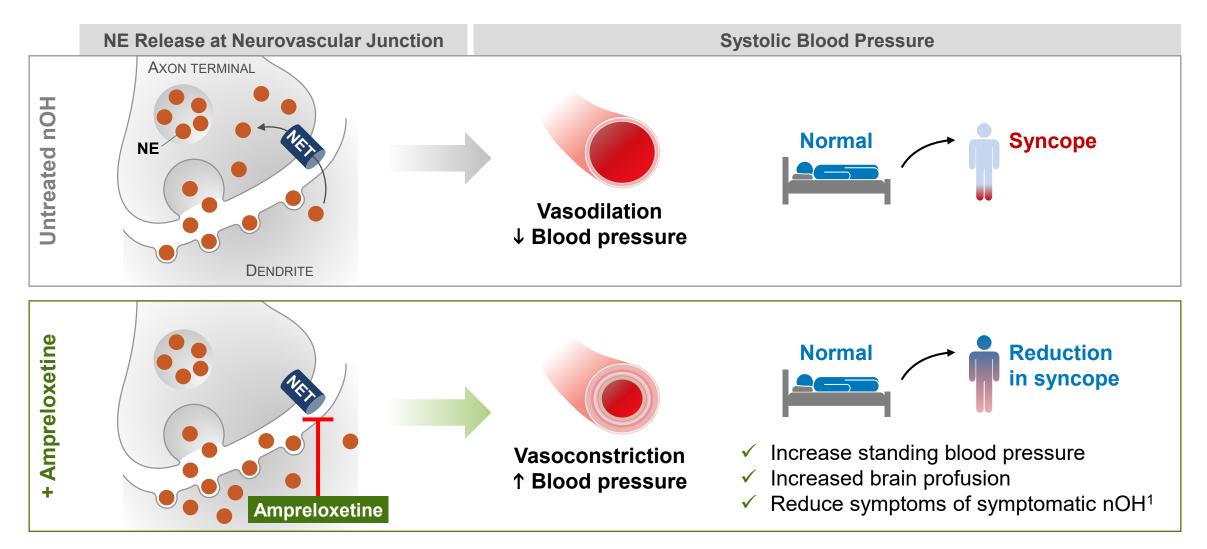
- Subset of patients do not respond
- None have demonstrated durable effect
- Require multiple daily dosing

#### High burden condition

- Impact on activities of daily living and quality of life
- Significant caregiver burden
- Economic burden to the US healthcare system

Theravance Biopharma 1. Ha AD, et al. Parkinsonism Relat Disord 2011;17:625-8; 2. Mathias C, et al. J Neurol 1999;246:893-8. nOH: neurogenic orthostatic hypotension; MSA: multiple system atrophy; PAF: pure autonomic failure; PD: Parkinson's disease.

# Designed to reduce symptoms of nOH by prolonging the effect of endogenous norepinephrine

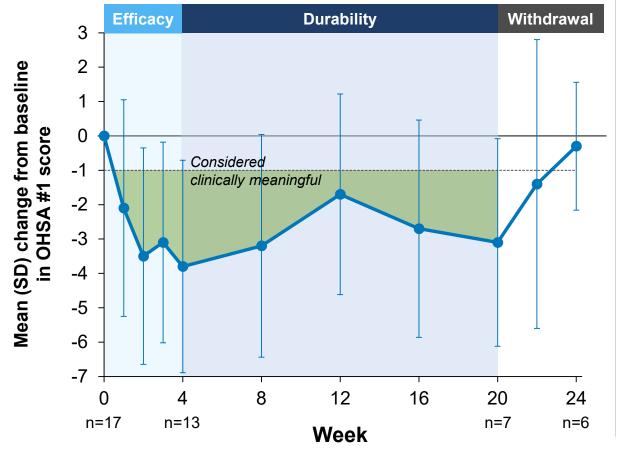




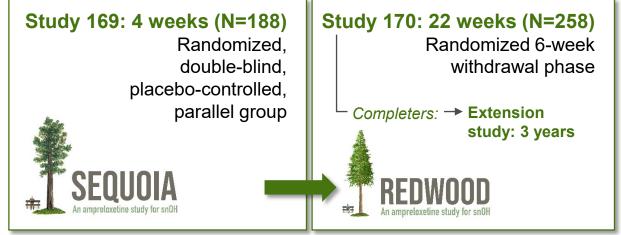
# Potential to provide meaningful and durable symptom improvement to underserved patients

#### Ampreloxetine

Phase 2 data in nOH; 20 weeks of treatment



#### **Phase 3 Registrational Program**



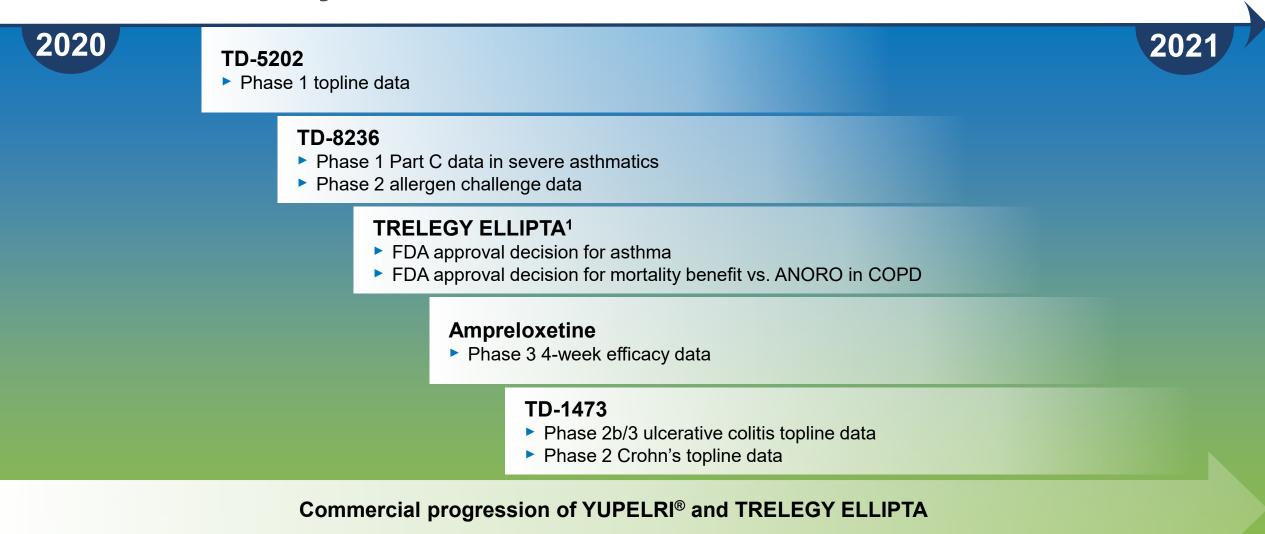
Phase 3 registrational program ongoing; 4-week efficacy data expected 2H20

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Baseline OHSA #1 (Orthostatic Hypotension Symptom Assessment Question 1) >4 points. Negative change indicates improvement in symptoms; improvement of 1 point is defined as the MCID (minimal clinically important difference) ITT: intention-to-treat; SD: standard deviation.

The Theravance Biopharma Difference

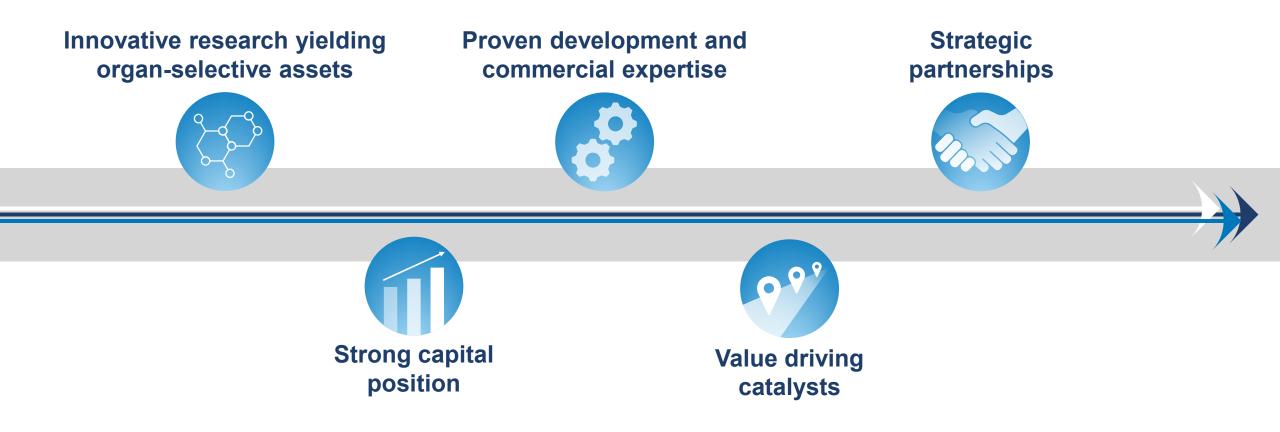
# Multiple potential milestones and value driving catalysts in 2020 and beyond





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### **Creating transformational value for stakeholders**





#### **Strategic objective**

Transform the treatment of serious diseases through the discovery, development, and commercialization of *organ-selective medicines* designed to maximize patient benefit while minimizing patient risk





### **About YUPELRI® (revefenacin) inhalation solution**

YUPELRI<sup>®</sup> (revefenacin) inhalation solution is a novel 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 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.



### 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.

