

## World COPD Awareness Day

17 November 2021

**#COPDAWARENESS** 

## Developing innovative therapies for the treatment of respiratory diseases

**November 2021** 

Verona Pharma

**Breath of Innovation™** 

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## Ensifentrine is a Phase 3, first-in-class candidate for the maintenance treatment of COPD

Inhaled PDE3 and PDE4 inhibitor

# Large market with significant unmet need

- ~\$10.5B US sales¹
- >1M patients remain symptomatic despite dual/triple treatment<sup>2-4</sup>

# **Ensifentrine** novel profile

- Novel dual MOA
- Efficacy demonstrated in two large Phase 2b trials
- Safety profile consistent with placebo

# Targeted commercial opportunity

- Pulmonologists key to adoption<sup>5</sup>
- Primary reimbursement channel is Medicare Part B<sup>6</sup>



## Verona Pharma's respiratory product pipeline

Ensifentrine is a potential "Pipeline in a product"

Program	Delivery	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestone Targets / Status
Maintenance treatment of COPD	Nebulizer					ENHANCE-2 top-line mid-year 2022 ENHANCE-1 top-line near end of 2022
Maintenance treatment of COPD	DPI/MDI					Positive Phase 2 data DPI & pMDI formulations (FEV $_1$ improvement & Safety similar to placebo)
Maintenance treatment of COPD (w/ LAMA or LABA)	Inhaled					Future life cycle management
Asthma	Nebulizer					Positive Phase 2 data <sup>1</sup>
Asthma	DPI/MDI					Phase 2 ready
Cystic Fibrosis	Nebulizer					Proof of concept <sup>2</sup>
Cystic Fibrosis	DPI/MDI					Phase 2 ready



## Well capitalized with cash runway through at least 2023

Clinical program, NDA submission, and pre-commercial efforts are fully supported

#### **Financial highlights**

Cash and equivalents (Quarter end September 30)	\$166.5M
Operating expenses* (Quarter end September 30)	\$28.5M
Market cap (Nasdaq: VRNA) (as of November 8, 2021)	\$310.3M
Shares outstanding (as of November 5, 2021)	60.0M ADSs

































<sup>\*</sup>net of non-cash share based comp

## COPD: a global problem

>384 million patients suffering worldwide and the 3<sup>rd</sup> leading cause of death<sup>1</sup>

Prevalence of COPD in US:

~25M patients<sup>2</sup>

~6M treated chronically



**~\$10.5B** in maintenance COPD sales<sup>5</sup>

Prevalence of COPD in China: ~100M patients<sup>3</sup>



~\$1B in sales (expected to double by 2030)<sup>5</sup>

Prevalence of COPD in EU: ~70M patients4

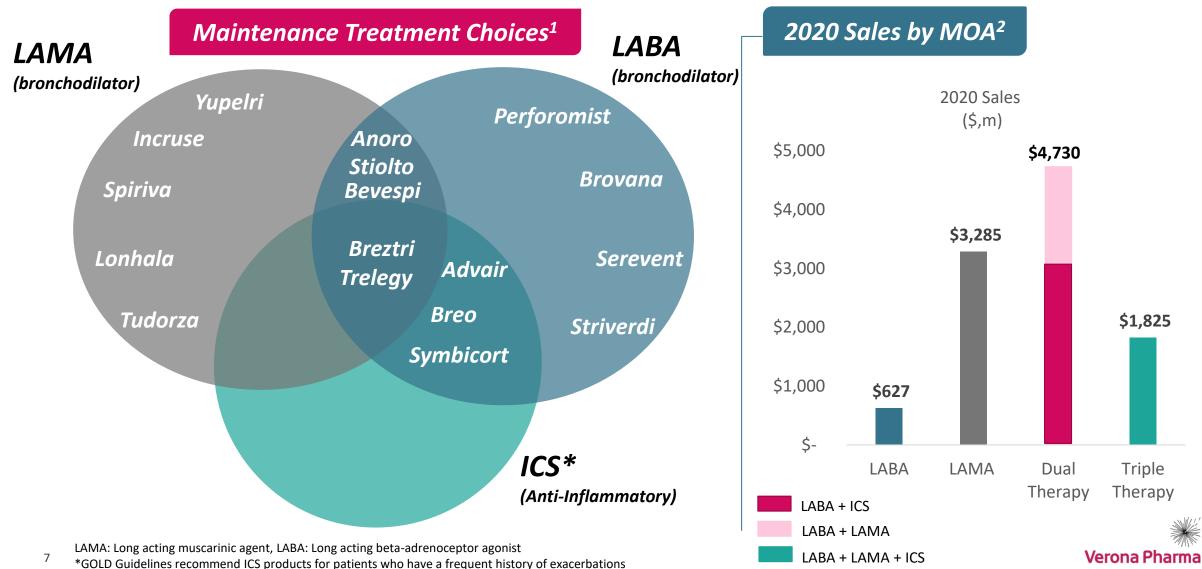


**~\$2.7B** in sales<sup>5</sup>



## **Current COPD treatments limited to 3 MoAs**

LAMAs & dual therapies generate the majority of product sales



¹https://www.copdfoundation.org/Learn-More/I-am-a-Person-with-COPD/Treatments-Medications.aspx; ² IQVIA MIDAS, IQVIA MIDAS Medical

## COPD places a tremendous burden on **US** medical system & patients

#### **US Medical System**

#### **Patients**



~1.9M Emergency room visits<sup>1</sup>

COPD patients have limited activity<sup>3</sup>



~740K Hospitalizations<sup>1</sup>

COPD patients feel socially limited<sup>3</sup>



~\$50B in costs (Direct/Indirect)<sup>2</sup>

COPD patients limited at work<sup>3</sup>



## Execution driven leadership team

### Decades of respiratory and commercialization experience



Verona's team has expertise in developing / commercializing many COPD drugs including:























# Ensifentrine: Novel profile providing both bronchodilator and anti-inflammatory effects

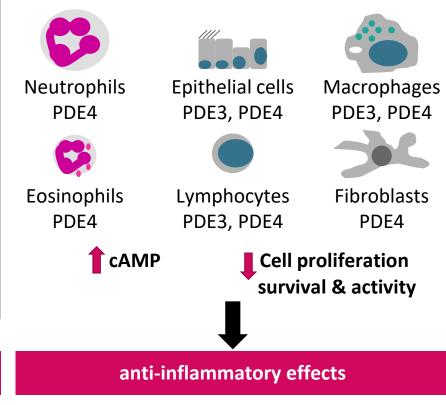
Ensifentrine impacts 3 key mechanisms in respiratory disease

#### Airway Smooth Muscle<sup>1-4</sup>

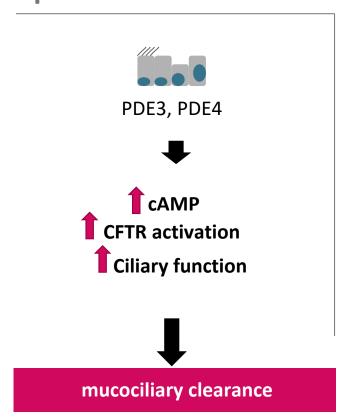
# PDE3, PDE4 **Bronchial relaxation**

bronchodilation

#### Inflammatory Cells<sup>5,6</sup>



#### **Epithelial Cells**<sup>7,8</sup>





## Ensifentrine: Two large Phase 2b trials to support development

Study 203 & 205 provide robust efficacy and safety for development

Study 203 Ensifentrine monotherapy N=403 Ensifentrine 0.75mg, 1.5mg, 3mg, 6mg BID N=324

Placebo BID N=79

Study 205 Ensifentrine plus Tiotropium (LAMA) N=413 Ensifentrine 0.375mg, 0.75mg, 1.5mg, 3mg BID N=329

Placebo BID

N = 84

4 Weeks

#### **Patient population:**

- Study 203:
  - Monotherapy (EU only sites)
  - ~40% of patients on ICS
- Study 205:
  - LAMA (tiotropium) background (US only sites)
  - Symptomatic: mMRC ≥ 2
- 30-80% predicted FEV<sub>1</sub>

#### **Key Endpoints**

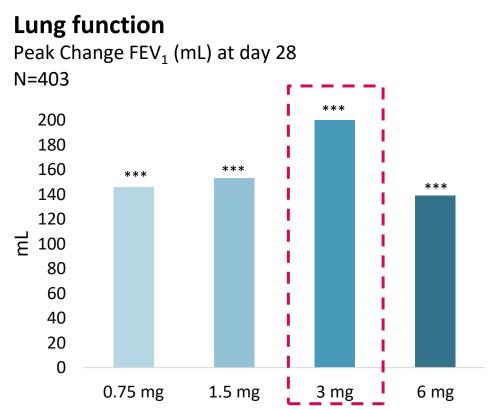
- Peak FEV<sub>1</sub>
- FEV<sub>1</sub> (AUC over 12 hours) at week 12
- Symptoms & QOL (E-RS: COPD, SGRQ)
- Other FEV₁ (trough, peak)



## Ensifentrine: Efficacy demonstrated in two large Phase 2b trials

Improvements in lung function seen at Phase 3 trial dose

#### Study 203: Ensifentrine Monotherapy<sup>1</sup>

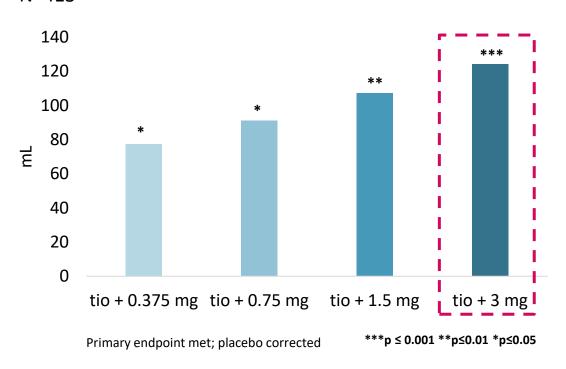


<sup>\*</sup>Peak Change from Day 1 in Baseline in FEV<sub>1</sub> (mL) on Day 28, \*\*\*p ≤ 0.001 Week 4, Primary endpoint met; placebo corrected

#### Study 205: Ensifentrine + Tiotropium<sup>2</sup>

#### **Lung function**

Peak Change FEV<sub>1</sub> (mL) at week 4 N=413

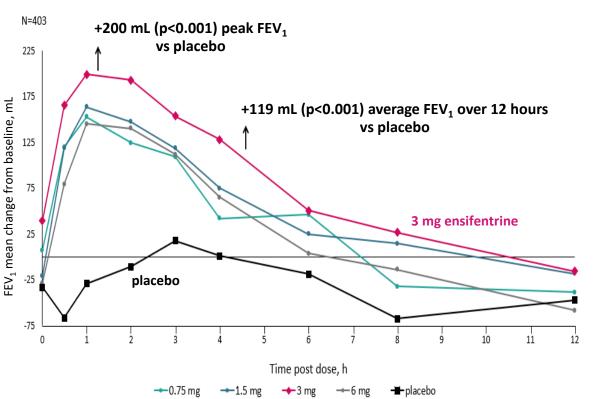




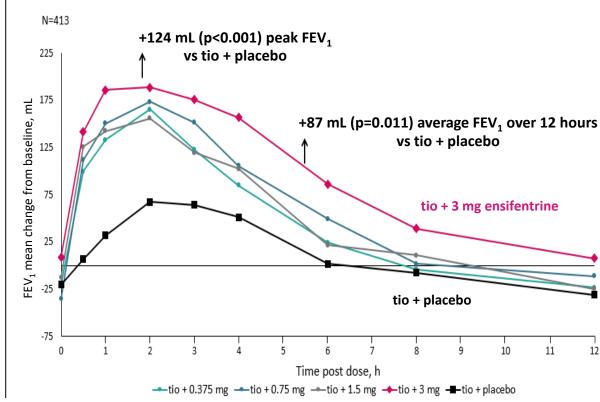
## Ensifentrine: Spirometry across Phase 2b program

12-Hour spirometry profile at week 4 supports twice daily dosing





#### Study 205: Ensifentrine + Tiotropium<sup>2</sup>





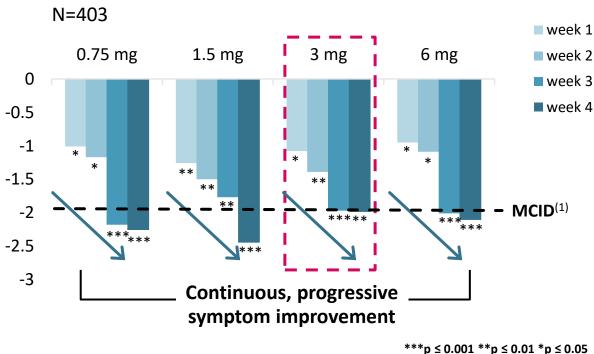
## Ensifentrine: Symptom improvement in two large Phase 2b trials

#### Improvements seen at Phase 3 trial dose

#### Study 203: Ensifentrine Monotherapy<sup>1</sup>

#### **Symptom relief**

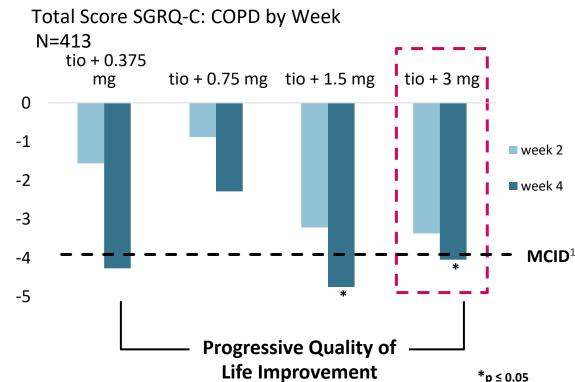
Total Score E-RS: COPD by Week



Placebo corrected
(1) Minimal clinically important difference

#### Study 205: Ensifentrine + Tiotropium<sup>2</sup>

#### **Symptom & QOL relief**



Placebo corrected



<sup>&</sup>lt;sup>1</sup>Minimal clinically important difference (-4 units)

## Safety profile similar to placebo

Ensifentrine well tolerated at all doses in trials involving over 1,300 patients



Adverse events generally balanced between ensifentrine and placebo

#### **Safety Database:**

- 18 clinical trials
- 980 COPD patients on nebulized ensifentrine across 6 studies



Gastrointestinal profile similar to placebo



Cardiovascular profile similar to placebo



No consistent or dose related changes in adverse events, blood pressure, heart rate or QT in independent cardiologist review

Ensifentrine has a favorable benefit / risk profile



## ENHANCE program incorporates many elements of Phase 2 trials

	Phase 2b Trials (Study 203 / 205) <sup>1,2</sup>	ENHANCE 1 & 2 Trials <sup>3,4</sup>
Sites	US & Europe	US, Europe, & South Korea
Dosage	0.375, 0.75, 1.5, 3, 6 mg BID	3 mg BID
Number of patients	400 / study	800 / study
Length of study	4 weeks (efficacy & safety)	12 weeks (Primary Endpoint – lung function) 24 weeks (Secondary Endpoints – symptoms / QOL) 48 weeks (safety)
Entry criteria	<ul> <li>Monotherapy / Add on to LAMA</li> <li>ICS use in ~40% (Study 203)</li> <li>30-80% predicted FEV<sub>1</sub></li> <li>Symptomatic: mMRC ≥ 2 (Study 205)</li> </ul>	<ul> <li>Monotherapy / Add on to LAMA or LABA</li> <li>ICS up to 20%</li> <li>30-70% predicted FEV<sub>1</sub></li> <li>Symptomatic: mMRC ≥ 2</li> </ul>
Key endpoints	<ul> <li>Peak FEV<sub>1</sub></li> <li>FEV<sub>1</sub> (0-12 hrs)</li> <li>Symptoms &amp; QOL (E-RS and SGRQ)</li> <li>Trough FEV<sub>1</sub></li> </ul>	<ul> <li>Peak FEV<sub>1</sub></li> <li>FEV<sub>1</sub> (0-12 hrs)</li> <li>Symptoms &amp; QOL (E-RS and SGRQ)</li> <li>Trough FEV<sub>1</sub></li> </ul>

<sup>&</sup>lt;sup>1</sup>RPL554-CO-203, Singh D, et al., Respiratory Research 2020;



<sup>&</sup>lt;sup>2</sup>RPL554-CO-205 Full Phase 2b Analysis Set, data on file; tiotropium (Spiriva®)

<sup>&</sup>lt;sup>3</sup> https://clinicaltrials.gov/ct2/show/NCT04535986?term=ensifentrine&draw=2&rank=1

<sup>&</sup>lt;sup>4</sup> https://clinicaltrials.gov/ct2/show/NCT04542057?term=ensifentrine&draw=2&rank=2

## Pivotal Phase 3 program nearing completion

Two pivotal efficacy and safety studies: ENHANCE-1 and ENHANCE-2

Ensifentrine as a Novel inHAled Nebulized COPD thErapy in moderate to severe COPD

ENHANCE-1 N=800 Ensifentrine
3mg BID N=500

Long-term safety N=300

Placebo BID N=300

Long-term safety N=100

48 Weeks

ENHANCE-2 N=800 Ensifentrine
3mg BID N=500

Placebo BID N=300

24 Weeks

#### **Primary Endpoint**

 FEV<sub>1</sub> (AUC over 12 hours) at week 12

#### **Secondary Endpoints**

- Symptoms (E-RS: COPD)
- Quality of Life (SGRQ)
- Other FEV₁ (trough, peak)

#### **Other Endpoints**

Exacerbations in pooled analysis

#### **Patient population:**

- LAMA or LABA background allowed (up to 50% of trial population) and ICS (up to 20% of population)
- 30-70% predicted FEV<sub>1</sub>
- Symptomatic (mMRC ≥ 2)

#### Additional information:

- Long-term safety established in ENHANCE-1
- Sites in the US, EU and Asia



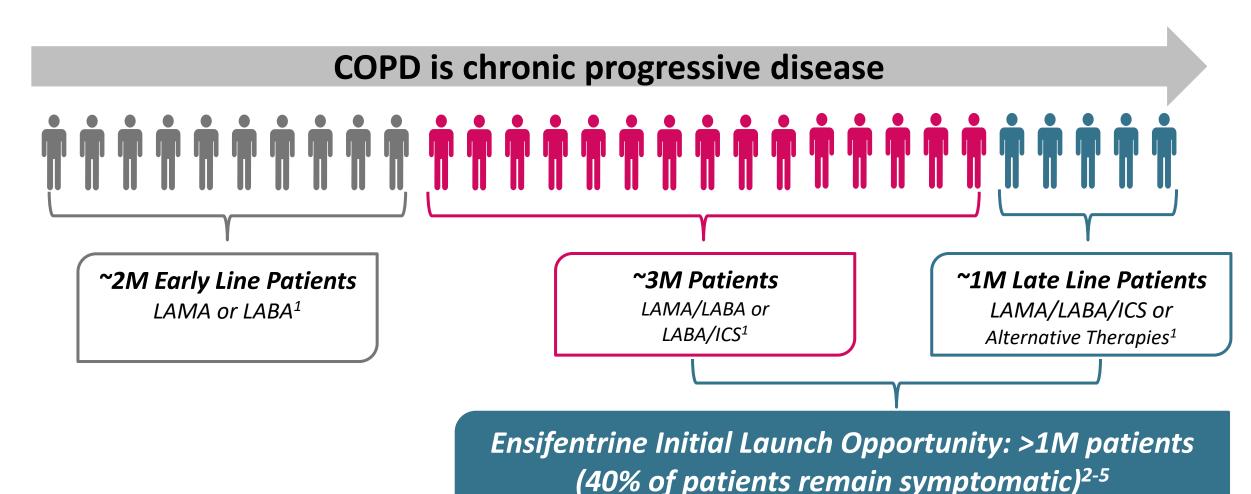


# **Ensifentrine Commercial Opportunity**



## Significant market opportunity for ensifentrine at launch

~4M COPD patients maintained on dual/triple therapy¹





Average annual WAC pricing of existing nebulized products: ~\$12k / year<sup>6</sup>

## Ensifentrine market opportunity is in a targeted HCP network

~12K Pulmonologists in the US

### **Ensifentrine initial launch opportunity**



#### ~3M Patients

LAMA/LABA or LABA/ICS<sup>1</sup>

#### ~1M Late Line Patients

LAMA/LABA/ICS or Alternative Therapies<sup>1</sup>

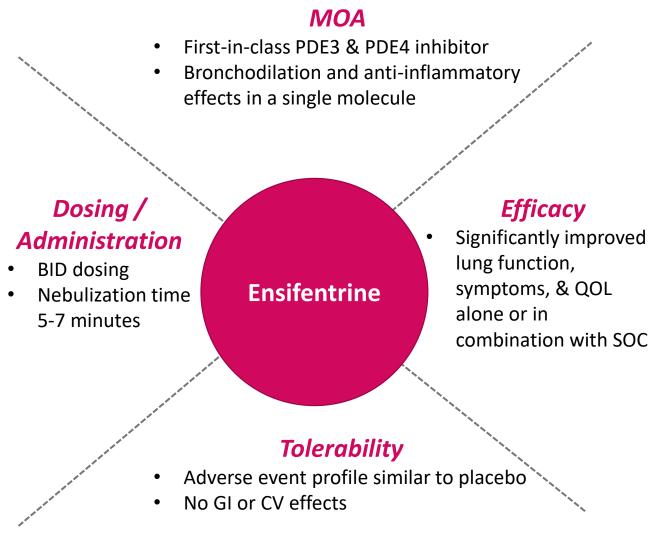
>1M patients remain symptomatic<sup>2-5</sup>

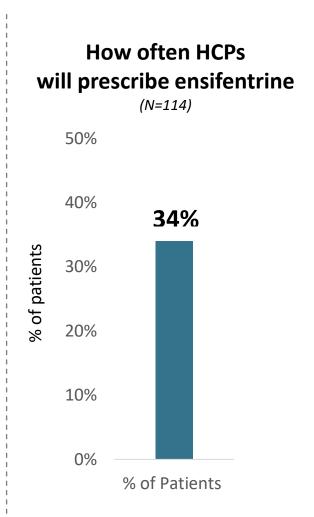
Pulmonologists and NPs/PAs will drive ensifentrine uptake<sup>6</sup>



## Ensifentrine product profile is compelling

Opportunity for broad adoption and coverage at launch





Payer Research:
35 payers covering >200m lives

>85%

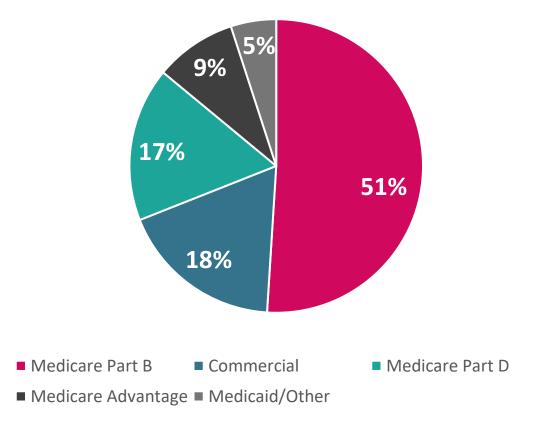
of lives will be covered



## Current nebulizer payer dynamics are favorable

Premium pricing, lower out of pocket costs, & greater access

Nebulizers Coverage by Payer Type (Brovana, Yupelri, Perforomist)



Product	Class	Avg Monthly \$ WAC price1
<i>Brovana</i> (Sunovion)	LABA	\$1,073
Perforomist (Viatris )	LABA	\$1,062
<i>Yupelri</i> (Viatris / Theravance)	LAMA	\$1,103
<i>Lonhala</i> (Sunovion)	LAMA	\$1,133

#### 100% access with Medicare Part B\*

\* Open nebulizers (Brovana, Perforomist, & Yupelri)



## Device preference can influence therapy choice<sup>1</sup>

Nebulizers have perceived advantages over other delivery methods



	1	
	Nebulizer	DPI/ MDI
Efficacy		X
Proper Usage		×
Convenience	X	
Cost / Reimbursement		×

#### Nebulizer

- **Efficacy:** Perceived to be more efficacious by some HCPs
- Proper Usage: Limited patient errors due to use of natural breath
- Cost/reimbursement: Favorable coverage and low out of pocket costs<sup>2</sup>

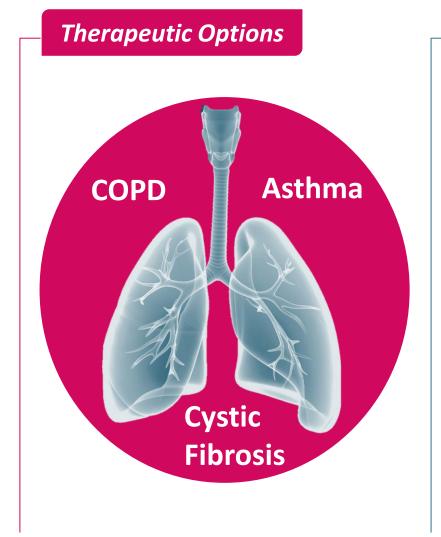
#### DPI/MDI

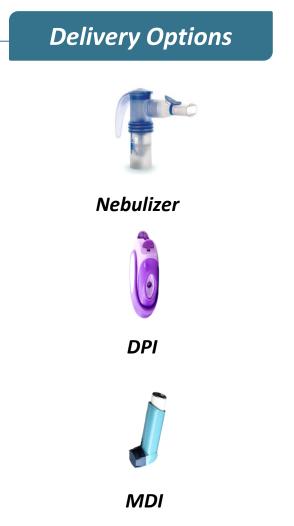
 Convenience: More portable and treatment administration is fast with minimal cleaning required

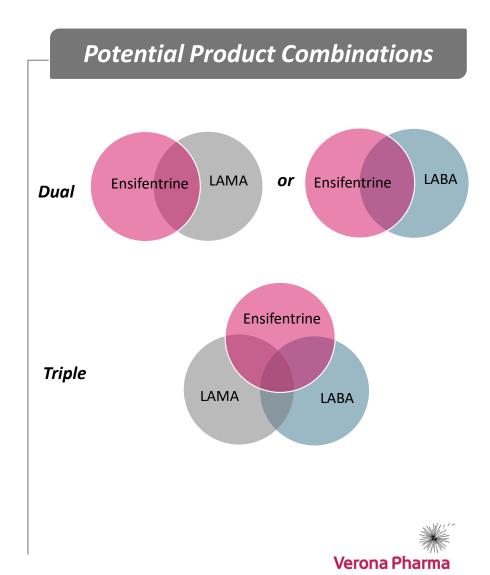


## **Ensifentrine: Significant life cycle opportunities**

Profile supports "Pipeline in a Product"







### **Ensifentrine in ROW**

Strategic partnerships to maximize ensifentrine's commercial value

United States: ~\$10.5B in Sales¹



Verona launch

China:

~\$1B in Sales

(expected to double by 2030) 1



- **\$40M upfront:** \$25M cash + \$15M equity
- **Up to \$179M** in potential milestones
- Tiered double-digit royalties





**Potential out-license** 



## Patent protection through the mid 2030s

Suspension formulation, polymorph, and manufacturing key patents

Invention	<b>Granted/Pending Application</b>	<b>Estimated Patent Expiry</b>
Polymorph	Granted US, Europe, Asia, other	2031
Suspension formulations	Granted US, Europe, Asia, other	2035
Manufacturing process	Granted Europe, US, pending China, other	2037
MDI formulation	Granted UK, pending US, Europe, China, other	2039
DPI formulation	Pending	2040
Salt forms	Granted US, pending Europe, China, other	2036
Treatment of cystic fibrosis	Granted US, Europe, pending US, other	2035
Combinations with beta-agonists	Granted US, Europe, pending Canada	2034
Combinations with anti-muscarinics	Granted US, Europe, China, pending other	2034
Composition of matter	Granted US, Europe, Asia, other	2020

Up to 5 years of additional exclusivity

through patent term extension



## Verona is well positioned to maximize the value of ensifentrine

Advanced Phase 3 asset with significant commercial opportunities

## Large market with significant unmet need

- ~\$10.5B US sales¹
- >1M patients remain symptomatic despite dual/triple treatment<sup>2-4</sup>

### **Advanced Phase 3 asset**

- Pivotal Phase 3 program nearing completion
- Earlier clinical trials studied >1,300 patients

## **Targeted commercial effort**

- Focused launch opportunity (~12k physicians)<sup>5,6</sup>
- Medicare Part B is primary method of reimbursement of nebulizers<sup>7</sup>

## Well capitalized to achieve near term milestones

Cash runway through at least 2023





## Thank you

