

# Developing innovative therapies for the treatment of respiratory diseases

#### May 2024

Ensifentrine is an investigational drug and has not been approved by the FDA (or any other regulatory authority).

Nasdaq: VRNA | www.veronapharma.com



### **Forward-looking statements**

This presentation contains "forward-looking" statements that are based on the beliefs and assumptions and on information currently available to management of Verona Pharma plc (together with its consolidated subsidiaries, the "Company"). All statements other than statements of historical fact contained in this presentation are forward-looking statements. Forward-looking statements include information concerning the initiation, timing, progress and results of clinical trials of the Company's product candidates, the timing or likelihood of regulatory filings and approvals of its product candidates, and estimates regarding the Company's expenses, future revenues and future capital requirements.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the Company's actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. These risks, uncertainties and other factors include those under "Risk Factors" in the Company's annual report on Form 10-K for the year ended December 31, 2023, and current reports on Form 8-K and our other filings with the Securities and Exchange Commission. Forward-looking statements represent the Company's beliefs and assumptions only as of the date of this presentation. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, the Company assumes no obligation to publicly update any forward-looking statements for any reason after the date of this presentation, or to conform any of the forward-looking statements to actual results or to changes in its expectations.

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The Company's product candidate, ensifentrine, is an investigational drug under review by the US Food and Drug Administration (FDA). It has not been evaluated as safe or effective or approved for commercialization by any regulatory authority.



Ensifentrine is an investigational first-in-class drug candidate US FDA review for maintenance treatment of COPD PDUFA Action Date of June 26, 2024

## Large market with significant unmet need

- ~\$10B US sales<sup>1</sup>
- Millions of patients remain symptomatic and unsatisfied with current therapies<sup>2-6</sup>

## **Ensifentrine novel profile**

- Novel, selective MOA, dual inhibitor of PDE3 and PDE4
- Positive Phase 3 data on key lung function measures, symptoms and exacerbations
- Well-tolerated over 24 and 48 weeks

## Targeted commercial opportunity

- Pulmonologists key to adoption with potential for broad utilization<sup>5</sup>
- Medical Benefits (Primarily Medicare Part B) is expected to be an important reimbursement channel<sup>7</sup>



<sup>1</sup>As of year end 2021, IQVIA MIDAS, IQVIA MIDAS Medical; <sup>2</sup>Ferguson et al. Lancet Respir Med 2018;6:747-58; <sup>3</sup>Mahler D, et al., Eur Respir J, 2014;43:1599-1609; <sup>4</sup>Vestbo J, et al., The Lancet, 2017;389:19-29; <sup>5</sup>Verona I US MCOPD Integrated Conjoint Survey; <sup>6</sup>Phreesia COPD Patient Survey 2022; <sup>7</sup>Verona\_IQVIA\_LAAD Quarterly Reporting Report

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## Verona Pharma's respiratory product pipeline

Ensifentrine provides multiple product opportunities

Product	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	US FDA review
	Maintenance treatment of COPD					
Ensifentrine (Nebulizer)	Non-CF bronchiectasis					
	Cystic Fibrosis					
	Asthma					
Ensifentrine + LAMA (Nebulizer)	Maintenance treatment of COPD					
	Maintenance treatment of COPD					
Ensifentrine (DPI / MDI)	Asthma					
	Cystic Fibrosis					

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LAMA: Long-acting muscarinic agent

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DPI: Dry powder inhaler, pMDI: Pressurized metered-dose inhaler

## Strong financial position for potential launch

#### **Financial highlights**

Cash and Equivalents (as of March 31, 2024)	\$254.9M
Operating expenses (quarter ended March 31, 2024)	\$27.2M
Market cap (Nasdaq: VRNA) (as of May 7, 2024)	\$1.2B
Shares outstanding* (as of May 7, 2024)	81.1M ADSs

\*Approximately 648.7M ordinary shares outstanding.

\*\*Capped at 1.75x of the amount funded.

\*\*\*Runway expectations based on cash and equivalents as of March 31, 2024, and future draws on Oaktree OMERS debt facility and RIPSA.

- **\$400M** debt facility (\$345M potential future draws)
- **\$250M** Revenue Interest Purchase and Sale Agreement\*\*
- **2026** funded beyond 2026\*\*\*



## COPD affects >390 million patients worldwide<sup>1</sup>

Despite available treatments COPD is still the third leading cause of death

Prevalence of COPD in US: ~8.6M treated chronically<sup>2</sup>

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

**~\$10B** in maintenance COPD sales<sup>5</sup>



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

Prevalence of COPD in EU: ~70M patients<sup>4</sup>



#### ~2B Euros in sales (2020)<sup>5</sup>

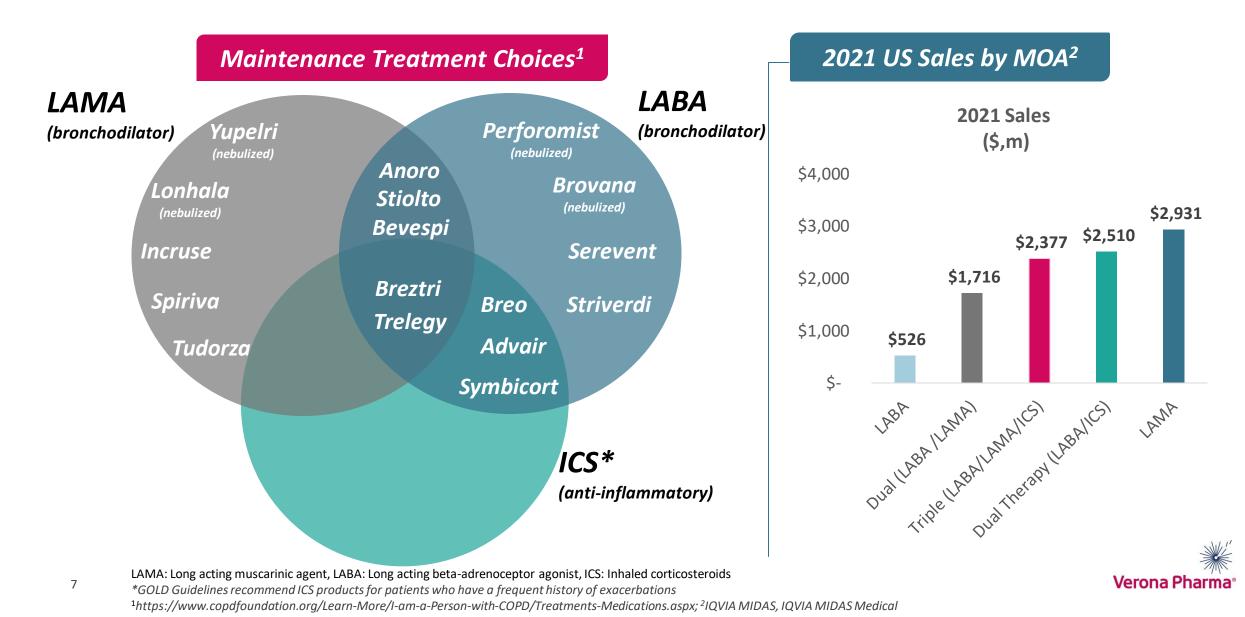


<sup>1</sup>Adeloye et al., The Lancet Respir Med, 2022;10(5):447-458; <sup>2</sup>Verona IQVIA Ensifentrine Market Research; <sup>3</sup>Wang et al., The Lancet, April 2018;391; <sup>4</sup>NCD Alliance estimates, <u>https://ncdalliance.org/news-events/news/66-million-people-may-live-with-copd-in-europe-yet-it-remains-unknown</u>; <sup>5</sup>IQVIA MIDAS, IQVIA MIDAS Medical

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

LAMAs & dual therapies generate the majority of US sales



## **Execution driven leadership team**

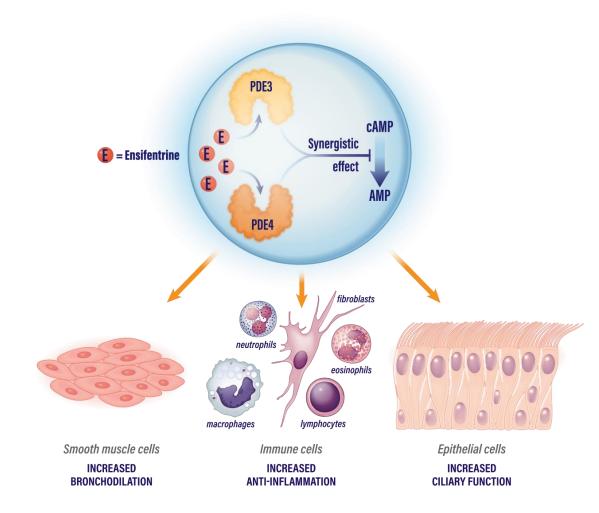
Decades of respiratory and commercialization experience





## **Ensifentrine: Novel mechanism of action**

Resulting in downstream bronchodilatory, anti-inflammatory, and ciliary effects



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#### **Direct mechanisms:**

• Modulation of intracellular cAMP in cells that express PDE3, PDE4, or both

#### Indirect mechanisms:

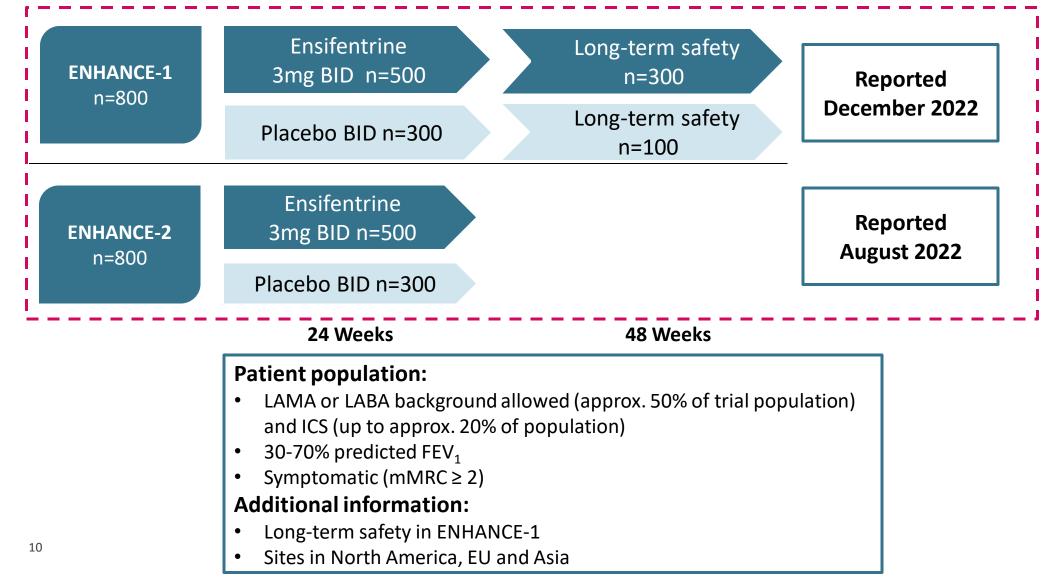
- Reduction in macrophage activation that impacts cellular adhesion, chemotaxis, and survival of neutrophils and eosinophils
- CFTR activation and increased ciliary beat frequency in vitro



## **Pivotal Phase 3 program**

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

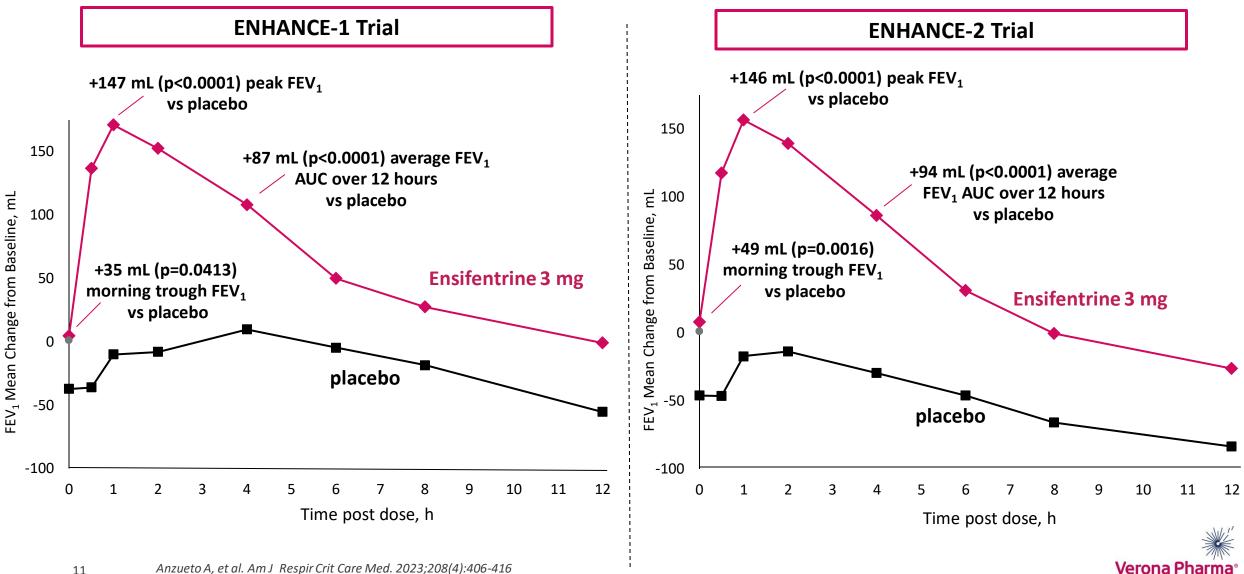
Ensifentrine as a Novel in HAled Nebulized COPD th Erapy in moderate to severe COPD



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## Primary endpoint met in both ENHANCE trials

Statistically significant peak & morning trough FEV<sub>1</sub> measures



Anzueto A, et al. Am J Respir Crit Care Med. 2023;208(4):406-416 11

## **Exacerbation rate reduced in both ENHANCE trials**

Consistent and clinically meaningful results

	ENH	ANCE-1 Tria	I			ENHAN	NCE-2 Trial		]
Treatment	Annualized Event Rate LS mean, (95% CI)	Rate Ratio (95% Cl)	Exacerbation Rate Reduction	p-value	Treatment	Annualized Event Rate LS mean, (95% CI)	Rate Ratio (95% Cl)	Exacerbation Rate Reduction	p-value
Ensifentrine 3 mg (n = 477)	0.26 (0.17, 0.40)	0.64 (0.40, 1.00)	36%	0.0503	Ensifentrine 3 mg (n = 498)	0.24 (0.18, 0.32)	0.57 (0.38, 0.87)	43%	0.0090
Placebo (n = 283)	0.41 (0.27, 0.63)				Placebo (n = 291)	0.42 (0.30, 0.57)			

Exacerbation was defined as a *worsening of symptoms* requiring:

• Minimum of 3 days of treatment with oral/systemic steroids and/or antibiotics **OR** hospitalization



## Pooled data: significant 40% reduction in exacerbation rate

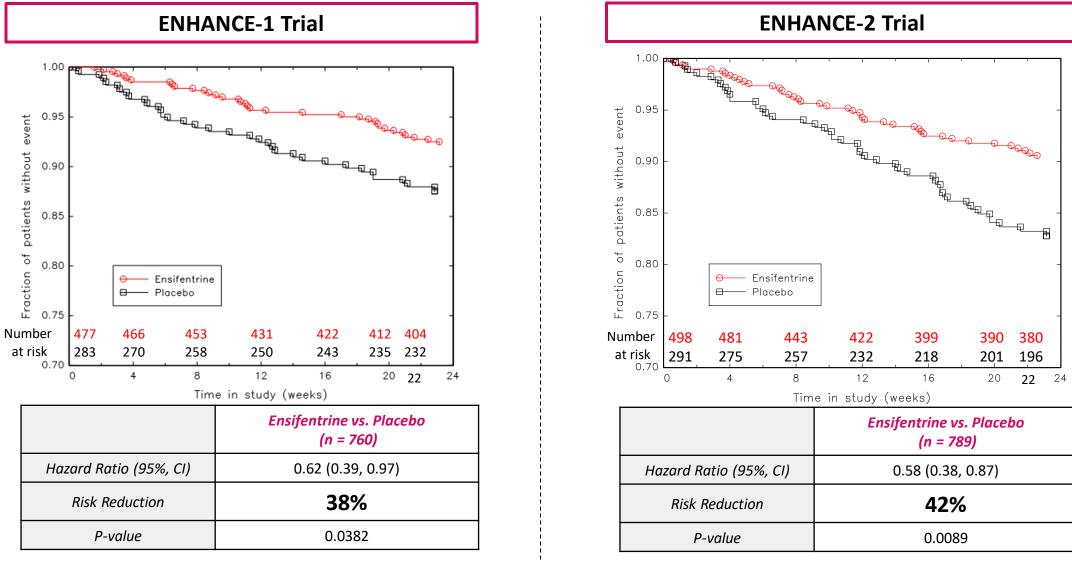
Protocol specified pooled analysis including ENHANCE-1 and ENHANCE-2

Treatment	Annualized Event Rate LS mean, (95% CI)	Rate Ratio (95% CI)	Exacerbation Rate Reduction	P-value
Ensifentrine 3 mg (n = 975)	0.27 (0.19, 0.39)	0.60 (0.44, 0.82)	40%	0.0012
Placebo (n = 584)	0.45 (0.31, 0.65)			



## Time to first exacerbation significantly delayed across trials

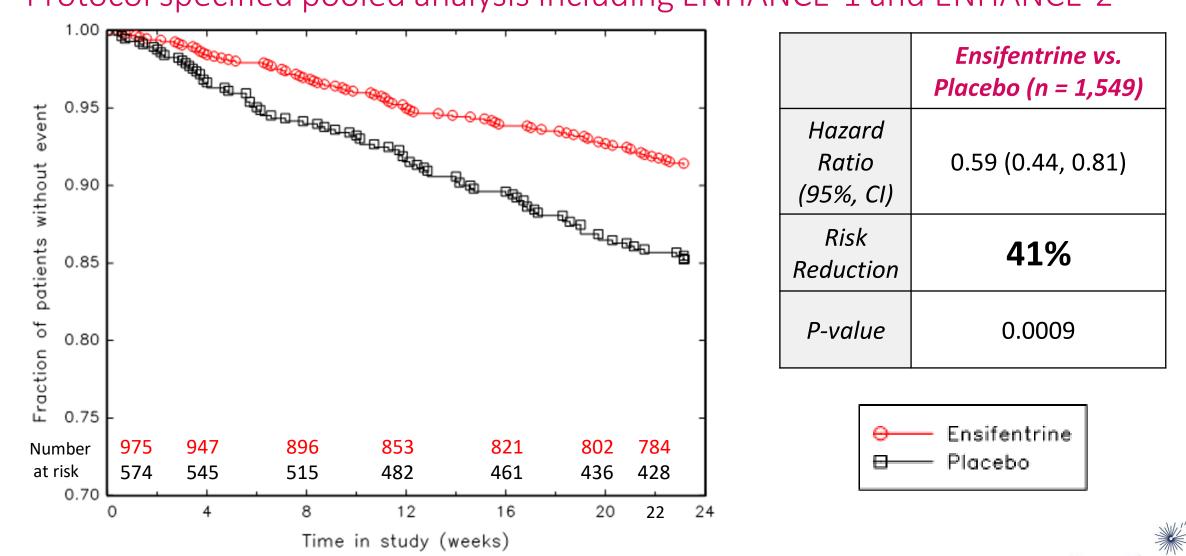
Consistent and clinically meaningful reduction in risk of a COPD exacerbation



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Anzueto A, et al. Am J Respir Crit Care Med. 2023;208(4):406-416

### **Pooled data: significant 41% risk reduction in time to first exacerbation** Protocol specified pooled analysis including ENHANCE-1 and ENHANCE-2

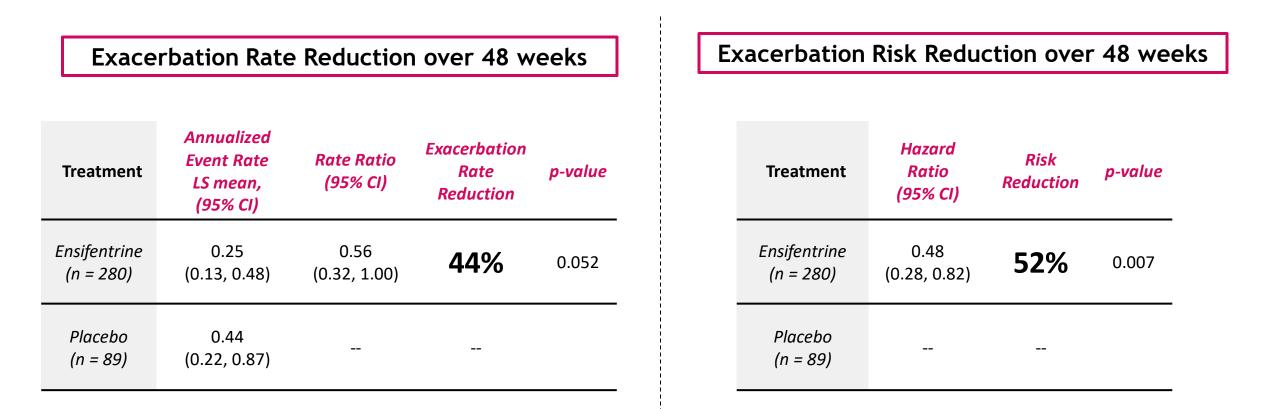


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<sup>15</sup> Barjaktarevic I, et al. Am J Respir Crit Care Med. 2023;207:A5008

## Ensifentrine reduced exacerbation rate and risk over 48 weeks in ENHANCE-1

Consistent reductions in moderate/severe COPD exacerbation rate and risk



LS = least-squares.

Exacerbation was defined as a **worsening of symptoms** requiring a minimum of 3 days of treatment with oral/systemic steroids and/or antibiotics OR hospitalization

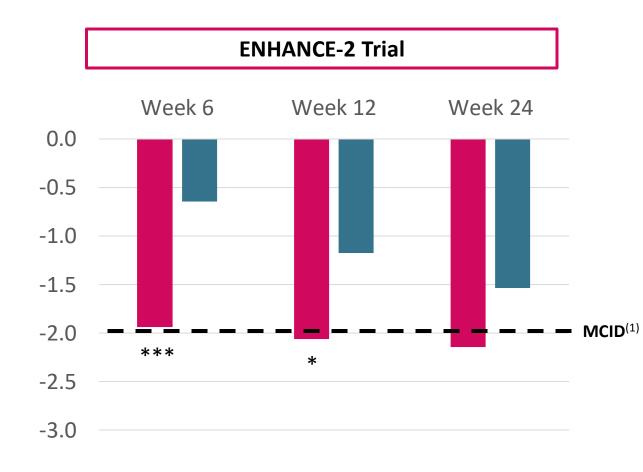


16 Anzueto A, et al. Am J Respir Crit Care Med. 2023;208(4):406-416

## **Ensifentrine improved symptoms across trials**

Early and sustained improvement in E-RS total score





EnsifentrinePlacebo

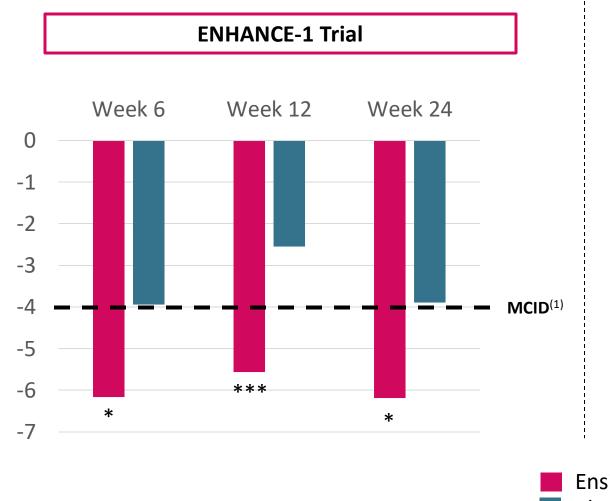
(1) Minimal clinically important difference

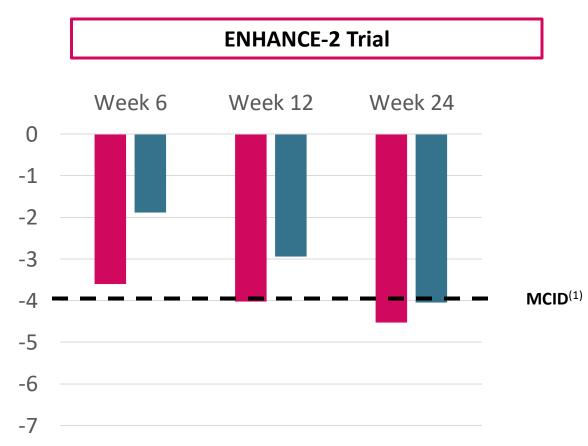
\*\*\*  $P \le 0.001 ** P \le 0.01 * P \le 0.05$ 



## **Ensifentrine improved quality of life across trials**

Early and sustained improvement in SGRQ total score





EnsifentrinePlacebo

(1) Minimal clinically important difference
\*\*\* P ≤ 0.001 \*\* P ≤ 0.01 \* P ≤ 0.05



### Adverse events reported at low rates over 24 and 48 weeks

Few events greater than 1% and greater than placebo

ENHANCE-1 Trial <sup>1</sup>					
	Event	Ensifentrine 3 mg (n = 477)	Placebo (n = 283)		
Subjects with at least one TEAE, n (%)		221 (46.3)	114 (40.3)		
	Hypertension, n (%)	14 (2.9)	4 (1.4)		
Any TEAE	Back pain, n (%)	12 (2.5)	1 (0.4)		
>1% and greater than placebo	URT*, n (%)	10 (2.1)	5 (1.8)		
	Pneumonia, n (%)	7 (1.5)	1 (0.4)		
	Toothache, n (%)	6 (1.3)	2 (0.7)		
	Atrial fibrillation, n (%)	6 (1.3)	2 (0.7)		

\* Upper respiratory tract infection

ENHANCE-2 Trial <sup>2</sup>					
Event Event Event Event Event Event Event Event Event Ensifentrine Placebo (n = 291)					
Subjects with at least one TEAE, n (%)		176 (35.3)	103 (35.4)		
	Worsening of COPD, n (%)	11 (2.2)	5 (1.7)		
Any TEAE ≥1% and	Nasopharyngitis, n (%)	9 (1.8)	3 (1.0)		
greater than placebo	Diarrhea, n (%)	8 (1.6)	2 (0.7)		
	Sinusitis, n (%)	6 (1.2)	0 (0)		
	Hypertension, n (%)	5 (1.0)	1 (0.3)		



## **ENHANCE Program summary**

### ENHANCE-1 and ENHANCE-2 demonstrated consistent results in COPD patients

Top-line Measurement	ENHANCE-1	ENHANCE-2		
Average FEV <sub>1</sub> AUC (0-12 hours)	+87 mL (p<0.0001) vs placebo	+94 mL (p<0.0001) vs placebo		
Peak FEV <sub>1</sub>	+147 mL (p<0.0001) vs placebo	+146 mL (p<0.0001) vs placebo		
Morning Trough FEV <sub>1</sub>	+35 mL (p=0.0413) vs placebo	+49 mL (p=0.0016) vs placebo		
Evening Trough FEV <sub>1</sub>	+58 mL (p=0.0008) vs placebo	+54 mL (p=0.0016) vs placebo		
Symptoms (E-RS Total Score)	-1.0 units (p=0.0111) vs placebo	-0.6 units (NS) vs placebo		
Quality of Life (SGRQ Total Score)	-2.3 units (p=0.0253) vs placebo	-0.5 units (NS) vs placebo		
Exacerbation rate	36% (p=0.0503) reduction in rate	43% (p=0.0090) reduction in rate		
Time to first COPD exacerbation	38% (p=0.0382) reduction in risk	42% (p=0.0089) reduction in risk		
Pooled exacerbation rate	40% (p=0.0012)	reduction in rate		
Pooled time to first COPD exacerbation	41% (p=0.0009) reduction in risk			
Incidence of educates	Low incidence of adverse events at 24 and 48 weeks			
Incidence of adverse events	No safety signals assoc	ciated with ensifentrine		



## PDUFA Date: June 26, 2024

Accelerating preparations for ensifentrine launch, if approved

Milestone	Expected Timing
PDUFA date*	June 26, 2024
Planned US Launch	Q3 2024



## Non-cystic fibrosis bronchiectasis (NCFBE) is a chronic disease marked by recurrent infection and progressive lung damage

#### ~370,000 US Patients<sup>1,2</sup> No Approved Treatments

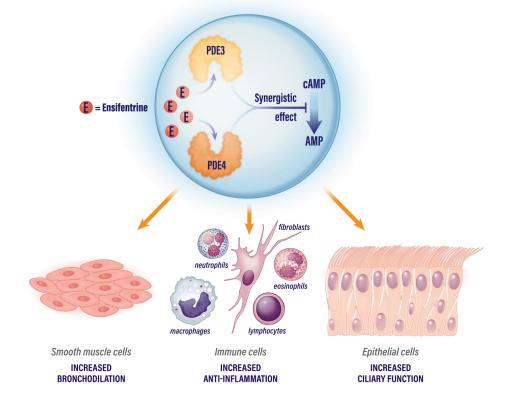
#### **Key Issues**

- Exacerbations (neutrophilic driven)
- Cough & sputum production

#### **Unmet Needs**

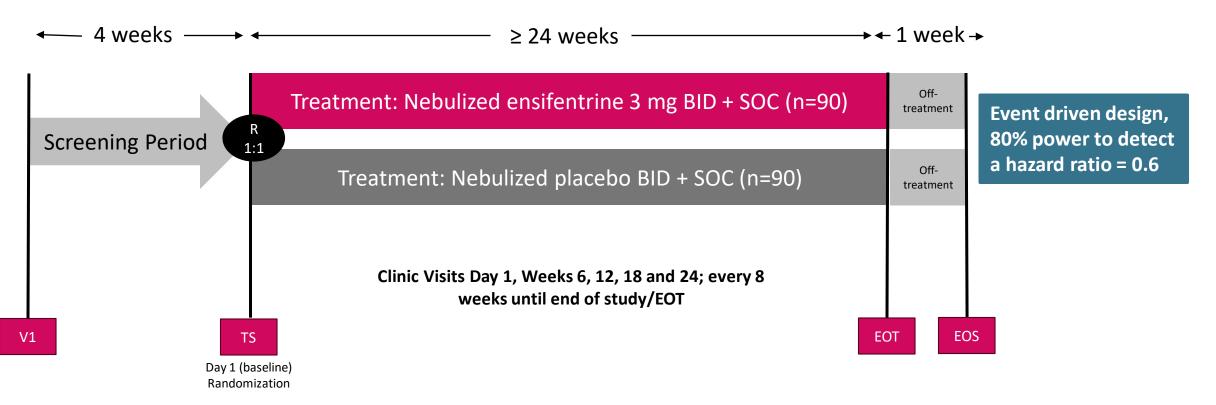
- High level of unmet need due to lack of approved options
- Anti-inflammatory drugs (international guidelines on bronchiectasis discourage use of corticosteroids)

**Ensifentrine Targets Neutrophilic Inflammation, Impacts Exacerbations & Key NCFBE Symptoms** 





## Bronchiectasis Phase 2 Design



**Primary endpoint:** Time to first protocol-defined pulmonary exacerbation **Secondary endpoints:** 

- Exacerbation rate
- Patient Reported Outcomes: E-RS cough and sputum domain, QoL-B (respiratory), SGRQ, CAAT
- Lung function (pre and post-dose)



CAAT: Chronic Airways Assessment Test; EOS: End of study; EOT: End of treatment; E-RS: Evaluating Respiratory Symptoms; QoL-B: Quality of Life Bronchiectasis; SGRQ: St. George's Respiratory Questionnaire; TS: Treatment start; V: Visit

# COPD market has progressed to fixed dosed combination products to maximize efficacy given chronic, progressive disease

#### **Rationale for Ensifentrine + Glycopyrrolate**

- Synergistic effect demonstrated on bronchial smooth muscle and isolated bronchi with ensifentrine + glycopyrrolate<sup>1</sup>
- >400 subject Phase 2b study completed with ensifentrine added on to a LAMA<sup>2</sup>
- >400 subjects were dosed with ensifentrine or placebo + LAMA in the ENHANCE program over 24 weeks
- Data supports strong improvement in lung function, symptoms, QoL and exacerbations added on to a LAMA<sup>3</sup>
- Combines 2 bronchodilator mechanisms with non-steroidal anti-inflammatory effects

#### Phase 2 program design: Two Phase 2b, randomized, double-blind, cross-over trials

- Glycopyrrolate dose ranging (n=40, >80% power)
  - 4 x 1 week treatment periods with 1 week washouts
  - 3 doses + placebo
  - Endpoints: Day 7 Trough FEV<sub>1</sub>, peak FEV<sub>1</sub>, average FEV<sub>1</sub> AUC<sub>0-12</sub>
- Fixed-dose combination versus glycopyrrolate and ensifentrine individual components (n=55, >80% power)
  - 5 x 1 week treatment periods with 1 week washouts
  - 5 dose arms: 2 combination doses + 3 individual component arms
  - Endpoints: Day 7 average FEV<sub>1</sub> AUC<sub>0-12</sub>, peak FEV<sub>1</sub> Trough FEV1





## Ensifentrine Commercial Opportunity



## **COPD** patients frequently suffer from persistent symptoms

The COPD burden is often an unspoken reality for patients; Strong interest in trying new therapies

**Recent Published Study:** ~2,000 Treated COPD Patients<sup>1</sup>

49%

**65%** 

Have symptoms for 24-30 days / month

Have moderate/great impact on everyday and emotional health

**Recent Published Study:** COPD patients on *dual/triple* therapy > 6 months<sup>2</sup>

**~56%** Dissatisfied with treatment

Most Common

Symptoms

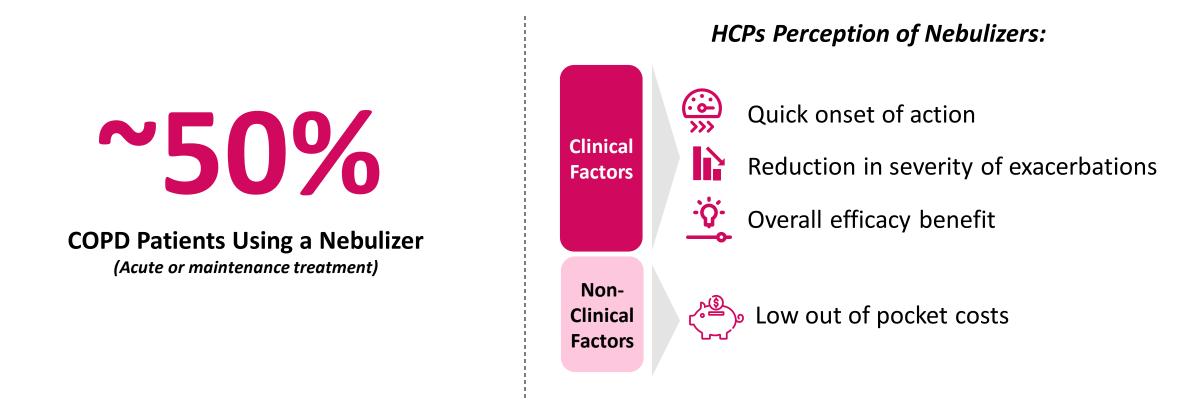
52% Dyspnea 45% Lack of Energy 30%

Lack of Sleep



## Nebulizers are very common in COPD

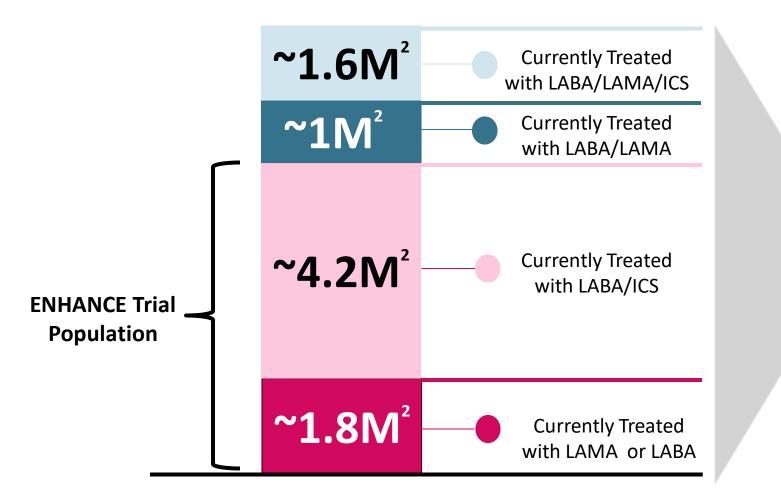
>80% of HCPs are very comfortable prescribing nebulizers in COPD





## ~8.6M Maintenance treated COPD patients<sup>1</sup>

At least 50% of patients remain symptomatic regardless of treatment





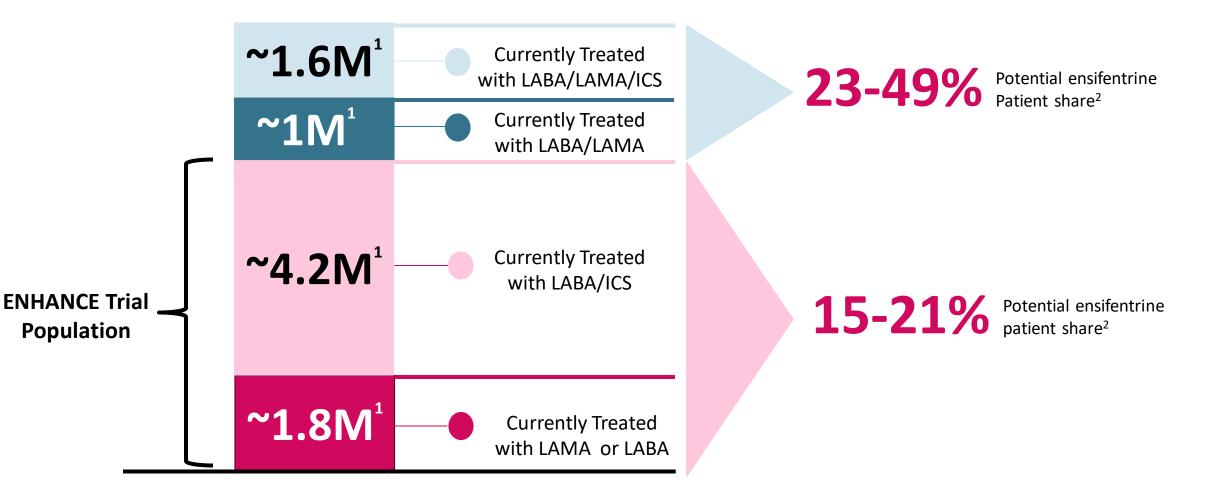
Remain persistently symptomatic regardless of therapy<sup>3,4</sup>



<sup>1</sup>IQVIA Verona\_IQVIA\_Ensifentrine Forecast Report slide 83; <sup>2</sup>IQVIA LAAD Data branded COPD claims; <sup>3</sup>Chen, et al., Int J Chron Obstruct Pulmon Dis. 2018;13:1365-1376; <sup>4</sup>Phreesia COPD Patient Perceptions Survey

## **Ensifentrine: Significant potential based on anticipated usage**

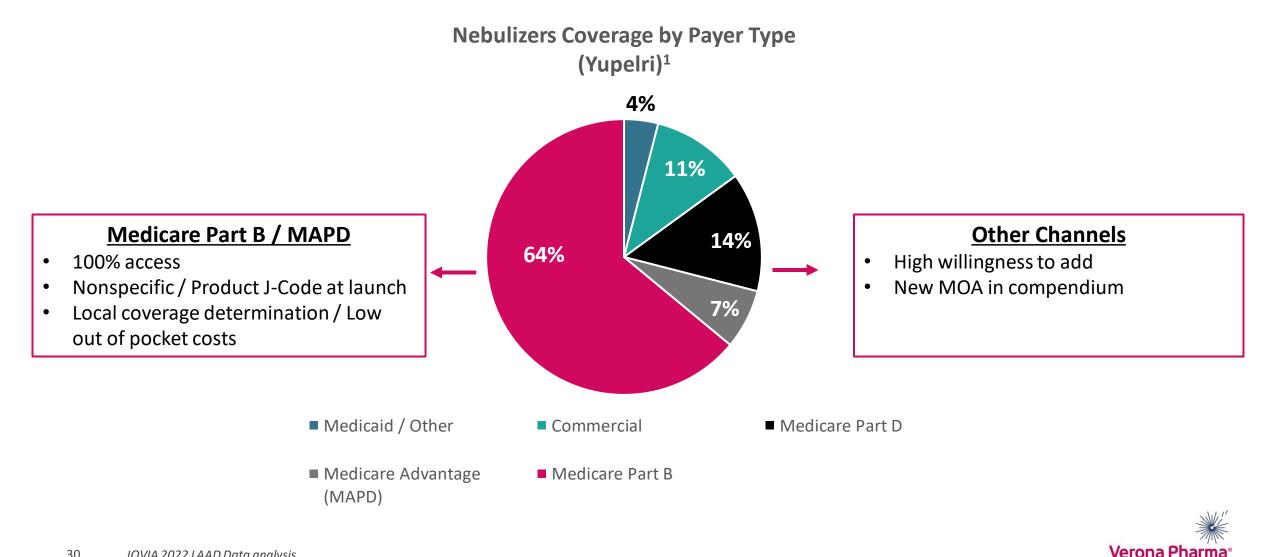
Market research indicates regardless of maintenance therapy, ensifentrine can be an add on therapy





## **Current nebulizer payer dynamics are favorable for HCPs**

Majority of other nebulizer product claims reimbursed by Medicare Part B





## **Reimbursement channel effects on launch**

HCPs access to products changed how two undifferentiated assets performed (Lonhala voluntarily removed from market: June 30<sup>th,</sup> 2023)

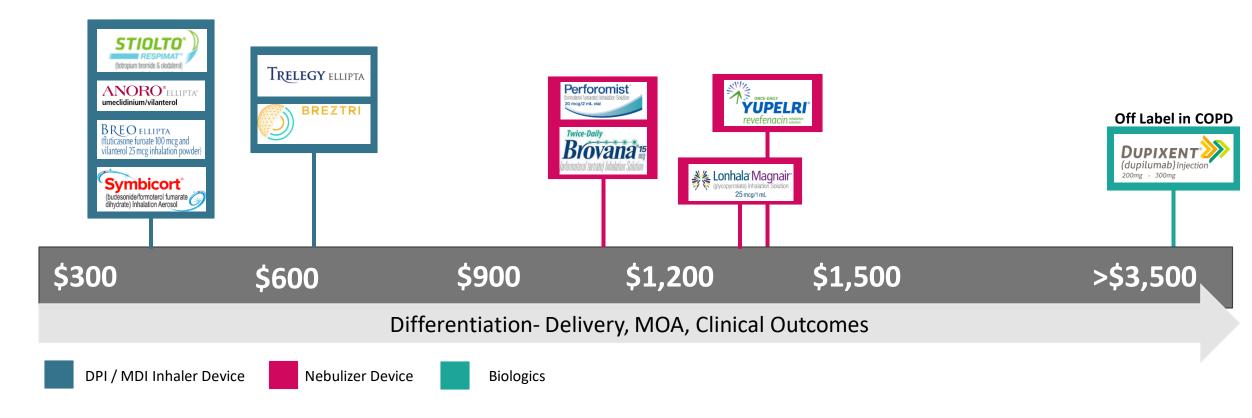
#### Medicare B (Yupelri) vs. Medicare Part D (Lonhala) Launch Comparison (TRx) 160,000 140,000 120.000 100,000 80,000 60,000 40,000 20,000 0 2018 2023 2019 2020 2021 2022 (YTD through Aug)

■ Lonhala ■ Yupelri ■ Projected



## **Current COPD market pricing dynamics**

Priced to HCP and patient value

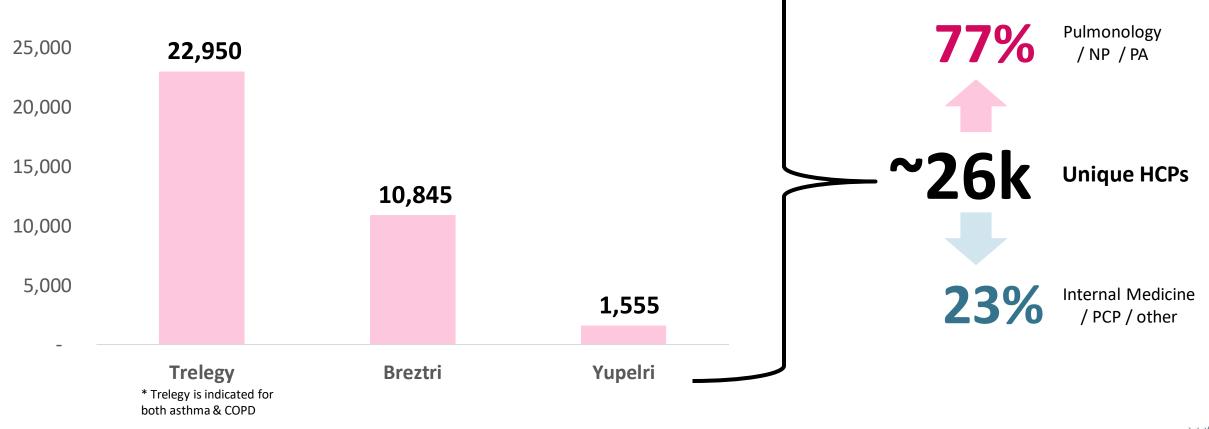




## Select group of HCPs prescribe the majority of COPD TRx's

Pulmonology / NP / PAs are drivers of prescribing in recently launched drugs

Prescriber Concentration<sup>1</sup> (# HCPs generating 70% of TRx)

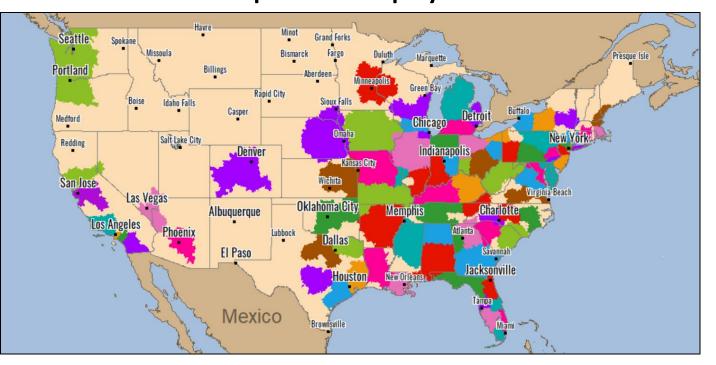


## Pulmonologists drive potential rep deployment

~100 Territories to support launch

- ~100 Field Facing Roles
  - Respiratory Sales Specialists
  - Virtual Sales Specialists
  - Field Reimbursement Managers
- Key States: ~50% of territories
  - New York
  - Pennsylvania
  - Ohio
  - Florida
  - Texas
  - California

#### Potential Respiratory Sales Specialists Deployment





## **Ensifentrine strategy in ROW**

Strategic collaborations to maximize ensifentrine's commercial value

United States: **~\$10B in Sales**<sup>1</sup>



Verona NDA under US FDA review

China: ~\$1B in Sales (expected to double by 2030) <sup>1</sup>



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

EU: ~\$2B Euros in Sales (2020)<sup>1</sup>



**Potential out-license** 



## Patent protection through the mid 2030s

Up to 5 years patent term extension on select patents

Invention	Granted/Pending Application	Estimated Patent Expiry
Polymorph	Granted US, Europe, China, Japan, other	2031
Suspension formulations	Granted US, Europe, China, Japan, other	2035
Manufacturing process	Granted Europe, US, China, Japan, other	2037
MDI formulation	Granted Europe, pending US, China, Japan, other	2039
DPI formulation	Pending	2040
Salt forms	Granted US, China, Japan, pending Europe, other	2036
Treatment of cystic fibrosis	Granted US, Europe, other	2035
Combinations with beta-agonists	Granted US, Europe, other	2034
Combinations with anti-muscarinics	Granted US, Europe, China, Japan, other	2034
Ensifentrine/glycopyrrolate formulation	Pending	2041
Composition of matter	Granted US, Europe, China, Japan, other	2020

Up to 5 years potential patent term extension on select patents



### **Verona positioned for successful ensifentrine launch, if approved** PDUFA action date: June 26, 2024

## Large Market with significant unmet need

 Millions of patients remain symptomatic and unsatisfied with current therapies<sup>1-5</sup>

## Commercial preparations well underway

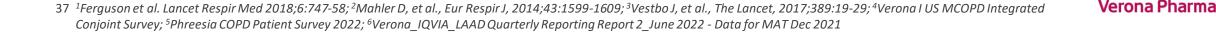
 ~100 field facing roles, infrastructure and systems established to support launch

# Differentiated molecule and reimbursement pathway

 Reimbursement primarily through medical benefit

## People and financial resources to support launch

Cash runway beyond 2026





## Thank you

