

JUNE 27<sup>TH</sup>, 2024

# FDA Approval: Ohtuvayre™ (ensifentrine)



**Verona Pharma**<sup>®</sup>  
Breath of Innovation

**Ohtuvayre**<sup>™</sup>  
(ensifentrine) Inhalation  
Suspension  
3 mg/2.5 mL

## Introduction

**David Zaccardelli, PharmD**  
*President & CEO*



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## Mechanism of Action, Clinical Data, & FDA Approved Label

**Tara Rheault, PhD**  
*Chief Development Officer*



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## Commercialization Strategy

**Chris Martin**  
*Chief Commercial Officer*



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## Q&A

**David Zaccardelli PharmD, Tara Rheault PhD, Chris Martin,  
Mark Hahn (CFO), Kathy Rickard, MD (CMO)**



**Pulmonary Specialist: Mike Wells MD**  
*Associate Professor in the Division of Pulmonary, Allergy, and  
Critical Care Medicine and the Medical Director for the Lung  
Health Center at the University of Alabama at Birmingham (UAB)*



# Forward-looking statements



This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation other than statements of historical fact should be considered forward-looking statements. Words such as “anticipate,” “believe,” “plan,” “expect,” “intend,” “may,” “potential,” “prepare,” “possible” and similar words and expressions are intended to identify forward-looking statements. These forward-looking statements include, but are not limited to, statements regarding the potential benefits, efficacy, and approval of our drug Ohtuvayre™, including, but not limited to, statements relating to the potential to change the treatment paradigm for COPD patients, the anticipated timing of commercial availability and our ability to successfully market and sell Ohtuvayre.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from our expectations expressed or implied by the forward-looking statements, including, but not limited to, the following: our limited operating history; our need for additional funding to complete development and commercialization of Ohtuvayre which may not be available and which may force us to delay, reduce or eliminate our development or commercialization efforts; our reliance on the success of Ohtuvayre, our only commercial product; our reliance on third-party manufacturers and suppliers; the efficacy of Ohtuvayre™ compared to competing drugs; our ability to successfully commercialize Ohtuvayre; serious adverse, undesirable or unacceptable side effects associated with Ohtuvayre which could adversely affect our ability to commercialize Ohtuvayre; failure to develop Ohtuvayre for additional indications, alternate delivery methods, or as a combination therapy; failure to obtain approval for and commercialize Ohtuvayre in multiple major pharmaceutical markets; lawsuits related to patents covering Ohtuvayre and the potential for our patents to be found invalid or unenforceable; lawsuits related to our licensing of patents and know-how from third parties for the commercialization of Ohtuvayre; changes in our tax rates, unavailability of certain tax credits or reliefs or exposure to additional tax liabilities or assessments that could affect our profitability, and audits by tax authorities that could result in additional tax payments for prior periods; and our vulnerability to natural disasters, global economic factors, geo-political actions and unexpected events, including health epidemics or pandemics. These and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the period ended March 31, 2024 filed with the Securities and Exchange Commission (“SEC”) on May 10, 2024, and our other reports filed with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change, except as required under applicable law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.

# Label supports broad use of Ohtuvayre in COPD patients

**Ohtuvayre™**  
(ensifentrine) Inhalation Suspension

3 mg/2.5 mL

***Broad Use / Novel MOA***

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***Pre-commercial activities set the stage for rapid launch***

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***Commercial team / infrastructure in place for Launch***

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**First inhaled COPD treatment providing bronchodilation and non-steroidal anti-inflammatory effects**

APPROXIMATELY 50% PATIENTS REMAIN PERSISTENTLY SYMPTOMATIC



# COPD patients need new treatment options<sup>1,2</sup>

**~8.6M** Maintenance Treated COPD Patients<sup>3</sup>

**50%**

*Persistently Symptomatic COPD Patients  
Regardless of Therapy<sup>2</sup>*

**~4.3M**

*Persistently symptomatic patients*



**Launch  
Focus**

<sup>1</sup>Chen, et al., Int J Chron Obstruct Pulmon Dis. 2018;13:1365-1376; <sup>2</sup>Phreesia COPD Patient Perceptions Survey; <sup>3</sup>Data on File – Forecast Project

# HCPs indicate broad usage of Ohtuvayre

**~8.6M**

Maintenance Treated COPD Patients<sup>1</sup>



**\* Stated Preference share<sup>2</sup>**

**20%\***

**~1.6M**  
Mild  
Patients

**29%\***

**~2.9M**  
Moderate  
Patients

**38%\***

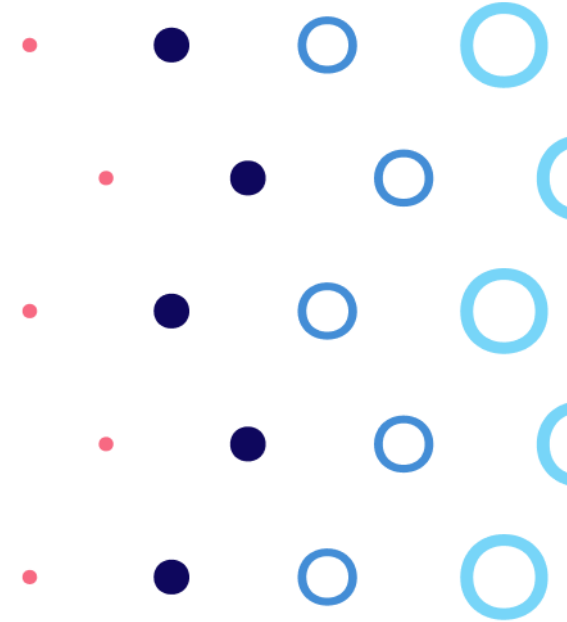
**~2.5M**  
Severe  
Patients

**43%\***

**~1.6M**  
Very Severe  
Patients

<sup>1</sup>Data on File – Forecast Project; <sup>2</sup>Data on File ATU 2024  
TPP Tested consistent with label

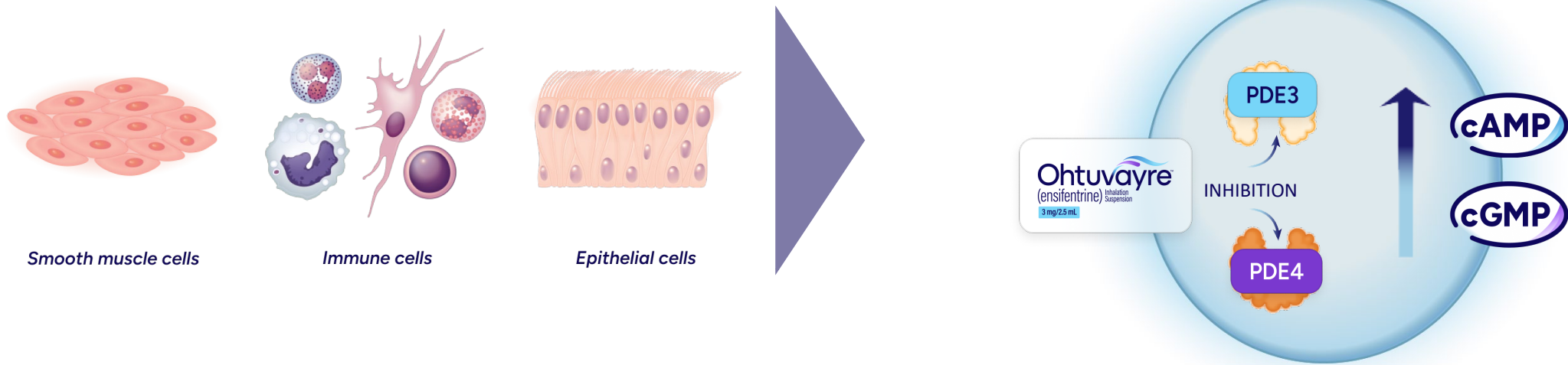
# Mechanism of Action & Clinical Data



# Ohtuvayre™ is a novel selective inhibitor of PDE3 and PDE4

PDE3 and PDE4 enzymes are present in lung cells associated with COPD pathology:

Selective inhibition of PDE3 and PDE4 results in accumulation of intracellular levels of signaling molecules, cAMP and cGMP



## This mechanism of action produces:

- Bronchodilation
- Decreased inflammatory response
- Increased ciliary function

cAMP = cyclic adenosine monophosphate; cGMP = cyclic guanosine monophosphate; PDE3 = phosphodiesterase 3; PDE4 = phosphodiesterase 4.

<sup>1</sup>Calzetta L, et al., J Pharmacol Exp Ther. 2013;346(3); <sup>2</sup>Calzetta L, et al., Pulm Pharmacol Ther 2015;32:15-23; <sup>3</sup>Matera MG, et al., Am J Respir Crit Care Med 2013;187:A1495; <sup>4</sup>Venkatasamy R, et al., Br J Pharmacol 2016;173(15):2335-2351; <sup>5</sup>Boswell-Smith V, et al., J Pharmacol Exp Ther 2006;318(2):840-848; <sup>6</sup>Franciosi LG, et al., Lancet Respir Med 2013;1(9):714-727; <sup>7</sup>Schmidt D, et al., Br J Pharmacol 2000;131(8):1607-1618; <sup>8</sup>Turner MJ, et al., Am J Physiol Lung Cell Mol Physiol 2016;310(1):L59-70



# Phase 3 data published in *American Journal of Respiratory and Critical Care Medicine*



Endpoint	ENHANCE-1 (N=760)	ENHANCE-2 (N=789)
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 vs placebo <sup>a</sup>
Symptoms (E-RS Total Score) Quality of Life (SGRQ Total Score)	-1.0 units (p=0.0111) vs placebo -2.3 units (p=0.0253) vs placebo	-0.6 units vs placebo <sup>b</sup> -0.5 units vs placebo <sup>b</sup>
Exacerbation rate Time to first COPD exacerbation	36% reduction in rate <sup>c</sup> 38% reduction in risk <sup>c</sup>	43% reduction in rate <sup>c</sup> 42% reduction in risk <sup>c</sup>
Incidence of adverse events (AEs ≥1% and greater than placebo)		Back Pain 1.8% vs 1.0% Hypertension 1.7% vs 0.9% UTI 1.3% vs 1.0% Diarrhea 1.0% vs 0.7%

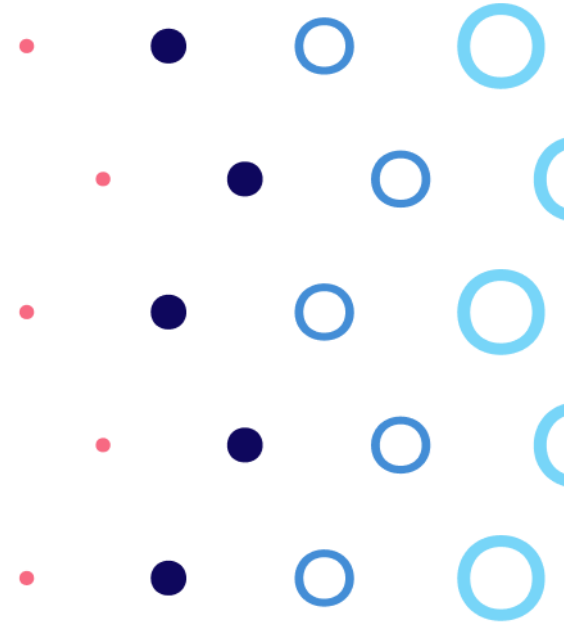
<sup>a</sup> Result was not statistically significant due to failure higher in the analysis hierarchy

<sup>b</sup> Not significant

<sup>c</sup> Pre-specified other endpoints were not part of the formal testing hierarchy

UTI = Urinary tract infection

# FDA Approved Label



# Ohtuvayre™ Label: Supports broad use in COPD patients

## -----INDICATIONS AND USAGE-----

OHTUVAYRE is a phosphodiesterase 3 (PDE3) inhibitor and phosphodiesterase 4 (PDE4) inhibitor indicated for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients.



Maintenance treatment of COPD



No limitations based on background medications or patient subgroups

**Indication supports use in all  
COPD patient types**

# Ohtuvayre™ label: Novel MoA described

## 12.1 Mechanism of Action

Ensifentrine is a small molecule that is an inhibitor of the PDE3 and PDE4 enzymes. PDE3 primarily hydrolyzes the second-messenger molecule cyclic adenosine monophosphate (cAMP) but is also capable of hydrolyzing cyclic guanosine monophosphate (cGMP). PDE4 hydrolyzes cAMP only. Inhibition of PDE3 and PDE4 results in accumulation of intracellular levels of cAMP and/or cGMP, resulting in various downstream signalling effects.



Dual inhibition of PDE3 and PDE4

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cAMP and cGMP downstream effects include bronchodilation and anti-inflammatory effects

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**Novel MOA language  
differentiates from other  
COPD treatments**

# Ohtuvayre™ label: Twice daily dosing with a standard jet nebulizer

## -----DOSAGE AND ADMINISTRATION-----

Recommended Dosage: 3 mg (one ampule) twice daily administered by oral inhalation using a standard jet nebulizer with a mouthpiece.



Twice daily dosing



Use with standard jet nebulizer



~5-7 min nebulization time\*

**BID dosing with any standard jet nebulizer**

\*using the PARI LC Sprint® jet nebulizer attached to a PARI Vios Pro® compressor

# Ohtuvayre™ label: Low incidence of adverse events

**Table 1. Adverse Reactions with OHTUVAYRE with incidence  $\geq$  1% and More Common than Placebo in Patients with COPD in the Pooled 24-Week Safety Population (ENHANCE-1 and ENHANCE-2)**

Adverse Reaction	OHTUVAYRE N=975 n (%)	Placebo N=574 n (%)
Back pain	18 (1.8%)	6 (1.0%)
Hypertension	17 (1.7%)	5 (0.9%)
Urinary tract infection	13 (1.3%)	6 (1.0%)
Diarrhea	10 (1.0%)	4 (0.7%)



48-week safety similar to 24-week



Low rate of discontinuation due to AEs  
(7.6% Ohtuvayre vs. 8.2% placebo)

**Data supports overall  
positive benefit to risk  
profile**

# Ohtuvayre™ label: Warnings and precautions

## -----WARNINGS AND PRECAUTIONS-----

- Should not use OHTUVAYRE to treat acute symptoms of bronchospasm.
- If paradoxical bronchospasm occurs, discontinue OHTUVAYRE and institute alternative therapy.
- An increase in psychiatric adverse reactions, including suicidality, were reported with use of OHTUVAYRE. Carefully weigh the risks and benefits of treatment with OHTUVAYRE in patients with a history of depression and/or suicidal thoughts or behavior.



Bronchospasm warning consistent with other inhaled COPD products

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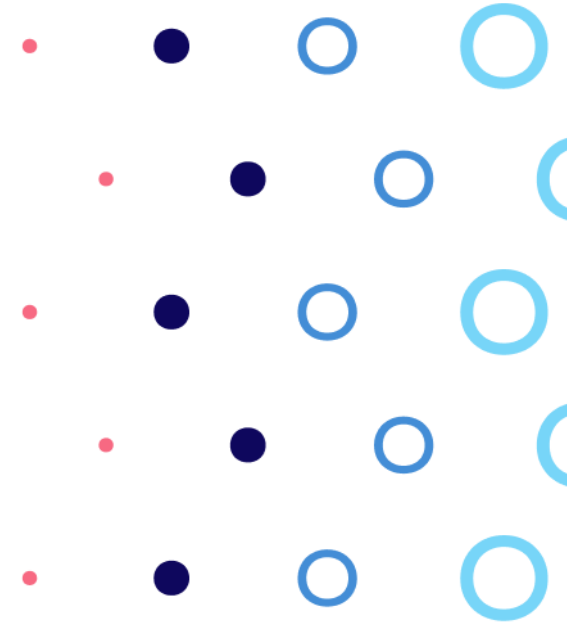


Psychiatric adverse reactions warning similar to other PDE4 inhibitors including Daliresp and Otezla

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**Consistent with inhaled COPD products and PDE4 inhibitors**

# Ohtuvayre™ Commercial Strategy





# COPD patients need new treatment options<sup>1,2</sup>



**~8.6M** Maintenance Treated COPD Patients<sup>3</sup>

**50%**

*Persistently Symptomatic COPD Patients  
Regardless of Therapy<sup>2</sup>*

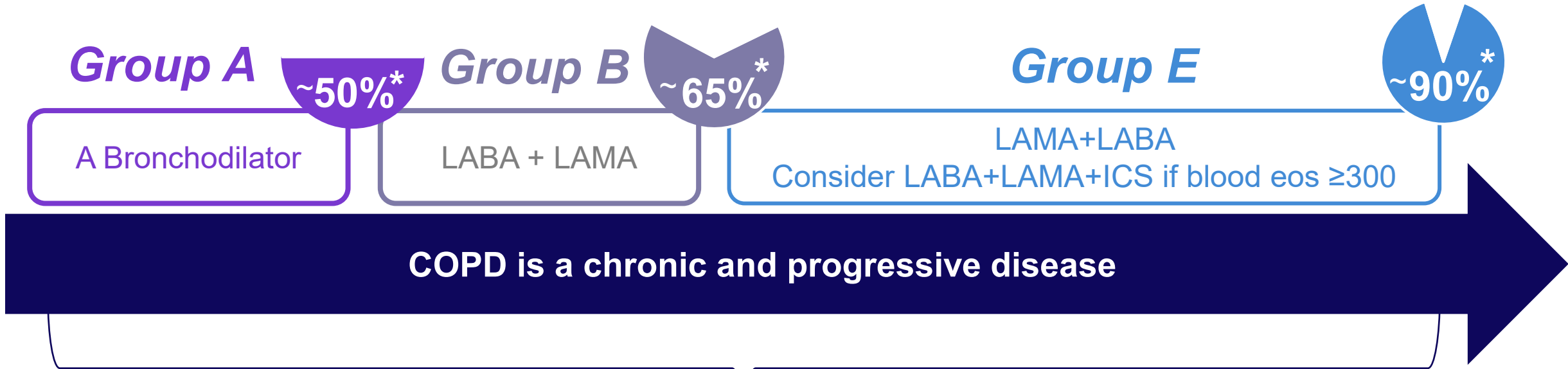
**Persistent Symptoms  
drive referrals to  
Pulmonologists**

**~4.3M**

*Persistently symptomatic patients*

**Ohtuvayre™** Launch  
**(ensifentrine) Inhalation** Focus  
**Suspension**  
3 mg/2.5 mL

# HCPs have high willingness to use Ohtuvayre™ across all COPD patient groups<sup>1</sup>



**80%\***



**Overall Intent to Prescribe**

\* HCPs intent to Prescribe Ohtuvayre™

<sup>1</sup>Data on File ATU 2024

Market Research Question: assume this patient was complaining of the following symptoms. Based on their clinical characteristics and current treatment, would you consider **prescribing Product X** to this patient, assuming it is now available?  
TPP Tested consistent with current label

# Patients have significant symptom burden and want different treatment options

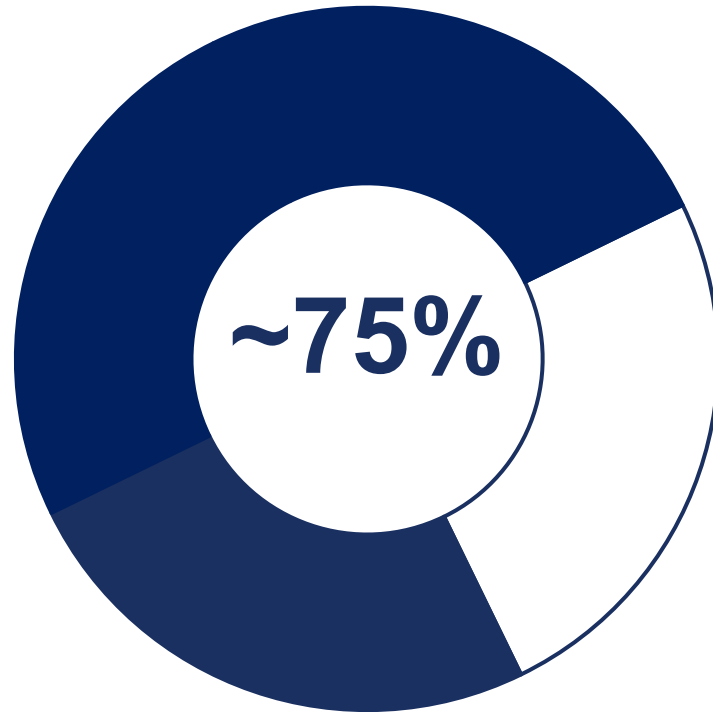
**>50%** patients report persistent monthly symptoms<sup>1,2</sup>

**~75%** patients use a nebulizer at home<sup>3</sup>

**High** motivation to try / ask HCP about novel, steroid free COPD treatment<sup>4</sup>

# Medical benefit primary reimbursement pathway for Ohtuvayre™

Medical Benefit Reimbursement<sup>1</sup>



## Payers

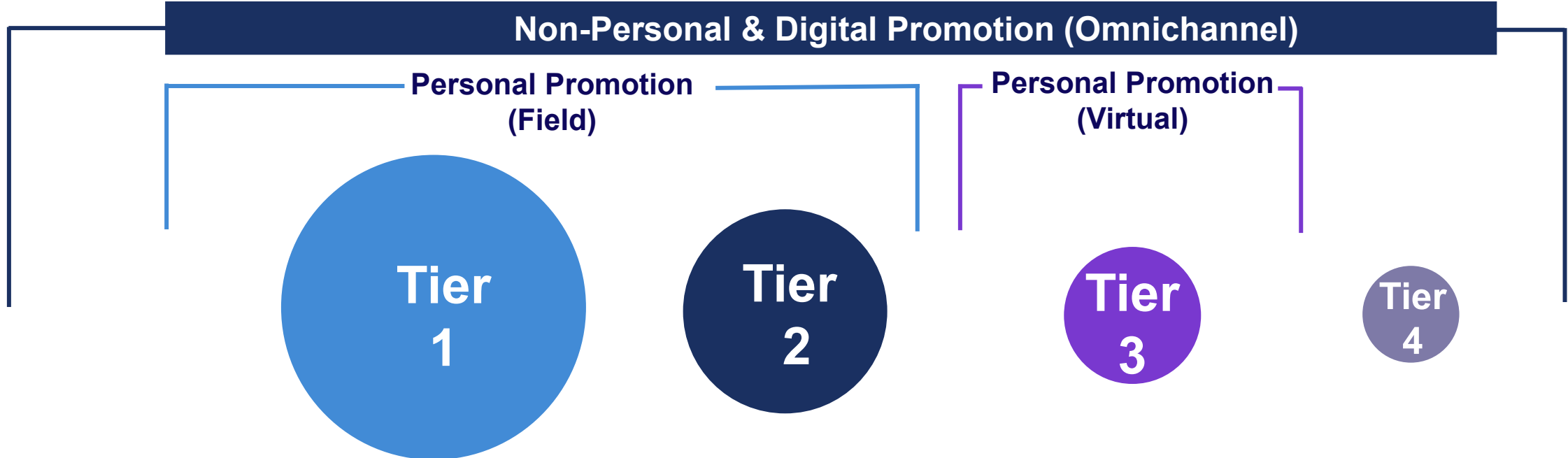
**All** clinical presentations completed with key payers

**J7699** non-specific inhalation J-Code at launch

**J-Code** to be submitted by June 28<sup>th</sup>

<sup>1</sup>Data on file - Forecast Project  
Medical Benefit Reimbursement either through traditional Medicare Part B or Medicare Advantage

# Verona will promote to the most active HCPs



HCP Count	~2,500	~12,000	~25,000	~360,000
Monthly COPD TRx	>160	>50	~20	~3

\*Data source: Data on File - Claims; Time Period: Calendar Year 2023

# Ensuring patient access and customer support



## Prescription Fulfillment

- 98% of patient lives covered
- Verona Care Coordinator & Field Reimbursement Team



## Coverage and Affordability

- Benefit verification
- Prior authorization / appeals assistance
- Financial support resources for eligible patients



## Support and Education

- Ongoing education and treatment support
- 24/7 access to clinical pharmacist

# Ohtuvayre™ pricing reflects benefit to patient and overall value to the health system



## COPD is a costly disease to the health system

~\$50B

Annual direct and indirect costs of COPD<sup>1</sup>

~\$26k

Healthcare associated costs per exacerbation<sup>2</sup>



## Cost-Effectiveness Modeling highlights Ohtuvayre value

~\$1k – \$5k\*

Various cost effectiveness models (Net monthly cost<sup>+</sup>)<sup>3,4</sup>



## Ohtuvayre Price

**\$2,950** WAC price (monthly)

\*monthly cost where Ohtuvayre offsets healthcare costs

<sup>1</sup>CDC International Journal of Chronic Obstructive Pulmonary Disease, 2020 Iheanacho et. al.; <sup>2</sup>Bogart et al. Am J Manag Care. 2020;26:e150-e154; <sup>3</sup>Data on File – Pricing Project 2024; <sup>4</sup>ICER 2024 draft report

# Ohtuvayre: Multi-billion dollar opportunity

## Ohtuvayre Opportunity

Market Size	~8.6M <sup>1</sup> Treated Patients
Pricing / Month	\$2,950 <sup>2</sup>
Months of Therapy / Year	6
GtN Discount	25%

Every **1%**  
share of treated patients  
~**\$1.1B**  
Net revenue

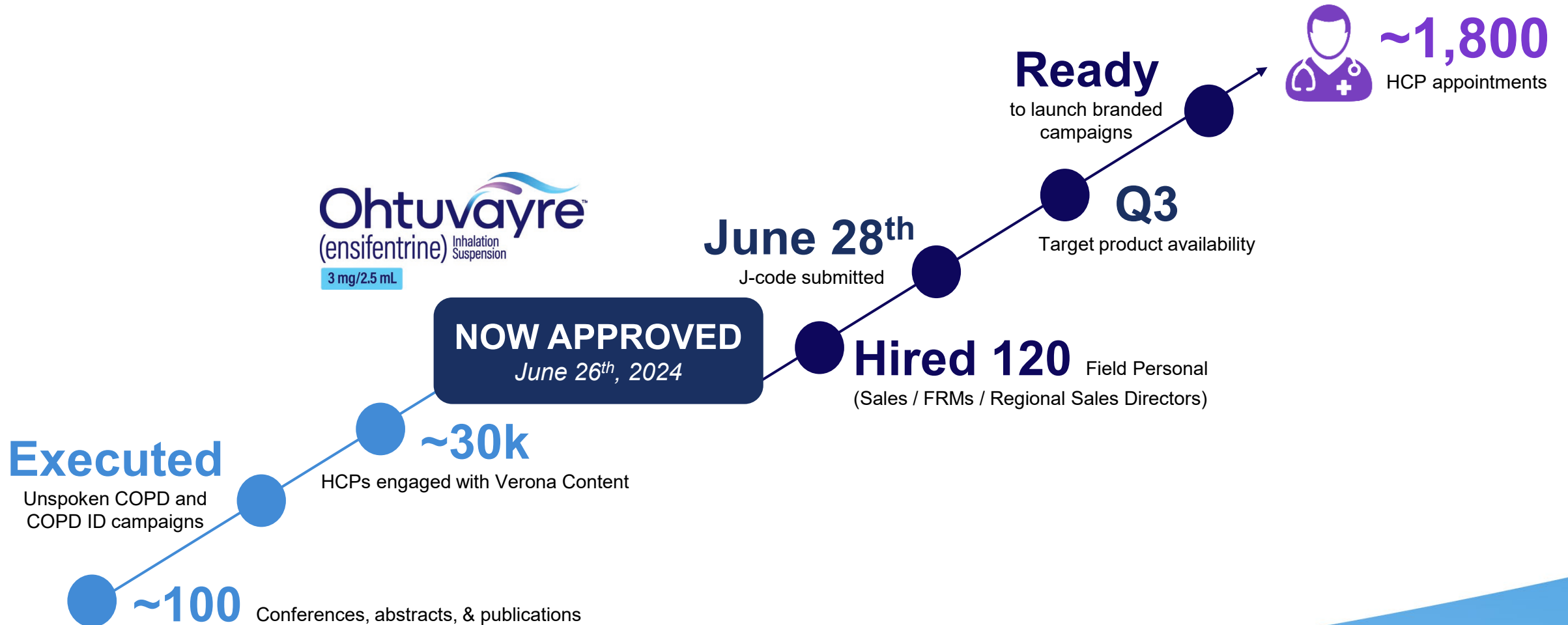
## Current COPD Patient Shares<sup>3</sup>

<b>21%</b>	Symbicort® (LABA/ICS)
<b>12%</b>	Trelegy (LAMA/LABA/ICS)
<b>11%</b>	Spiriva® (LAMA)
<b>5%</b>	Anoro (LAMA/LABA)
<b>1%</b>	Daliresp® (PDE4)

<sup>1</sup>Data on File – Forecast Project; <sup>2</sup>Verona WAC Price ; <sup>3</sup>Data on File – Patient Claims



# Verona has been preparing for this moment... and we are ready to launch



# Q&A session



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*President & CEO*



**Kathleen Rickard, MD**  
*Chief Medical Officer*



**Mark Hahn**  
*Chief Financial Officer*



**Chris Martin**  
*Chief Commercial Officer*



**Tara Rheault, PhD**  
*Chief Development Officer*



**Mike Wells, MD**  
*Associate Professor in the Division of Pulmonary,  
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