



**Verona Pharma**

## **Investor and Analyst R&D Forum**

Developing respiratory drugs to improve health and quality of life



**May 8, 2019, London**

(AIM: VRP) (NASDAQ: VRNA)  
[www.veronapharma.com](http://www.veronapharma.com)



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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 candidate, the timing or likelihood of regulatory filings and approvals for any of its product candidates, and estimates regarding the Company’s expenses, future revenues and future capital requirements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other comparable terminology.

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 any future results, performance or achievements 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 20-F filed with the Securities and Exchange Commission (the “SEC”) on March 19, 2019, and in its other reports filed with the SEC. 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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**Welcome**

**Jan-Anders Karlsson, CEO, Verona Pharma**



# Agenda

Time	Details
09:00 – 09:15 am	<b>Welcome</b> ( <i>Jan-Anders Karlsson, CEO, Verona Pharma</i> )
09:15 – 09:30 am	<b>The Patient Perspective, British Lung Foundation</b> ( <i>Chris Warburton, Patient Advocate</i> )
09:30 – 10:30 am	<b>Clinical Expert Perspective</b> ( <i>chaired by Brian Leaker, Royal Free Hospital</i> ) <ul style="list-style-type: none"><li>• COPD treatment challenges/unmet need (<i>Robert Wise, M.D. 15 min</i>)</li><li>• US payer landscape (<i>15 min</i>)</li><li>• Treatment pipeline (<i>Gerard Criner, M.D. 15 min</i>)</li><li>• Ensifentrine clinical progress (<i>Kathleen Rickard, CMO 15 min</i>)</li></ul>
10:30 – 11:15 am	<b>Speaker Panel Q&amp;A</b>
11:15 – 11:30 am	<b>Close</b> ( <i>Jan-Anders Karlsson</i> )

# Ensifentrine is a first-in-class candidate for respiratory diseases

*Plan to enter Phase 3 in 2020*

**Inhaled PDE<sub>3</sub> and PDE<sub>4</sub> inhibitor**

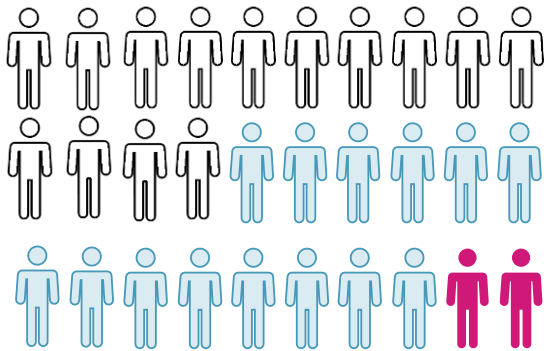


Bronchodilator and anti-inflammatory agent  
in a single compound

**Potential US \$1 billion COPD nebulizer market opportunity**

# COPD: The silent epidemic

~30 million patients in  
US alone



~16M  
Diagnosed

~2M  
Severe/  
very severe

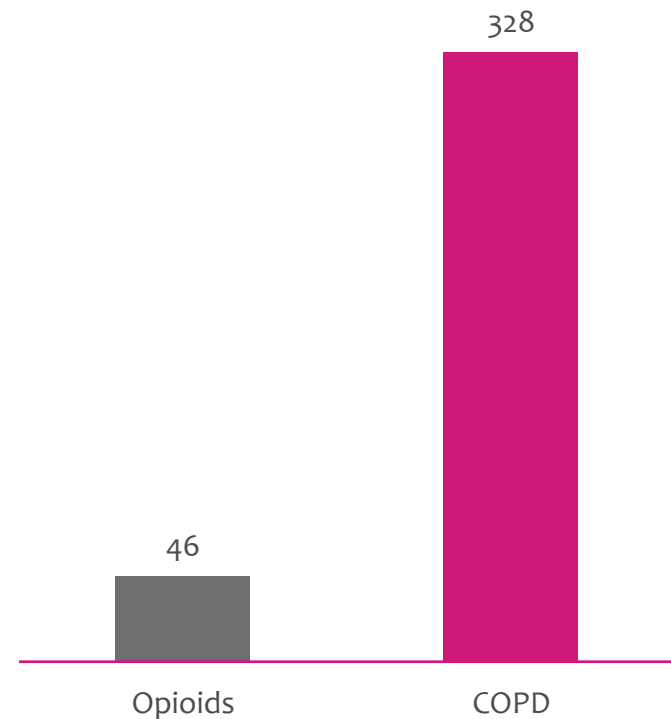
## Cost

~\$50 billion/year by 2020

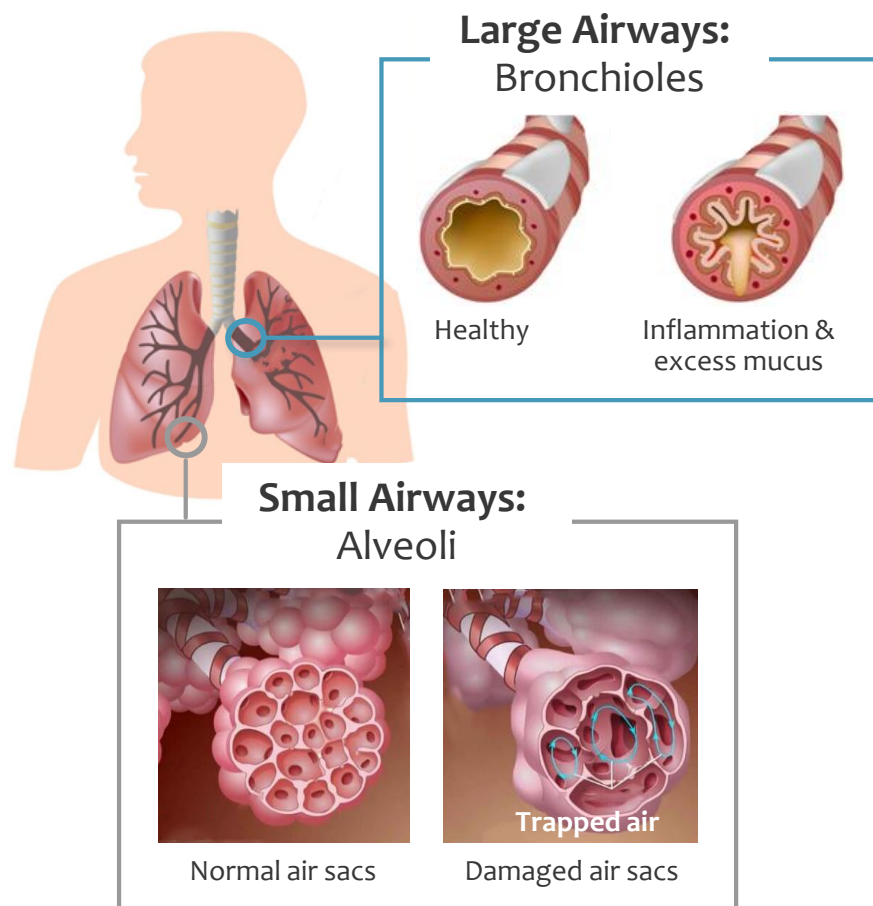
Indirect & direct

3<sup>rd</sup> leading medical cause of death  
by disease in US

Deaths/Day



# COPD: A significant unmet need



## Consequences and symptoms

---

- Debilitating breathlessness
  - Coughing, sputum
  - Poor lung function
  - Fatigue/struggle with daily tasks
  - Exacerbations/flare-ups
-



# Nebulized ensifentrine in COPD: Potential \$1 billion market opportunity in US

6M treated



2M on dual/triple therapy



800,000 symptomatic patients on dual bronchodilator/triple therapy need additional treatment

Current market data	Potential patient population
About 1/3 of moderate to severe patients use nebulizer	>250,000
Avg. Annual WAC Price of existing nebulized COPD drugs	\$12,000

Attractive Medicare Part B Reimbursement

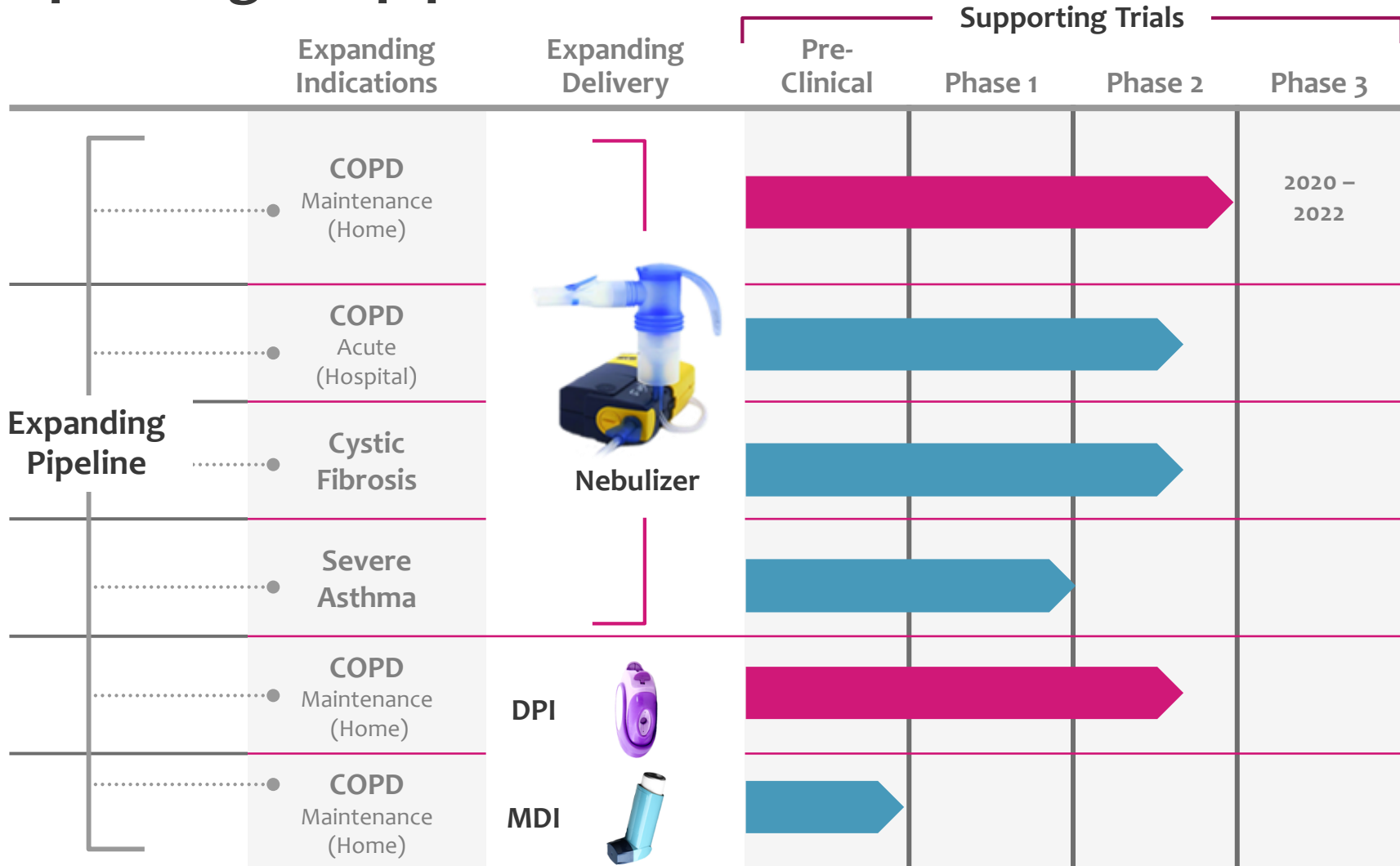
Top-prescribing physicians can be reached with targeted specialist salesforce

Source: DRG research Q4:2018. WAC; Wholesale Acquisition Cost.





# Ensifentrine lifecycle: Expanding the pipeline over time

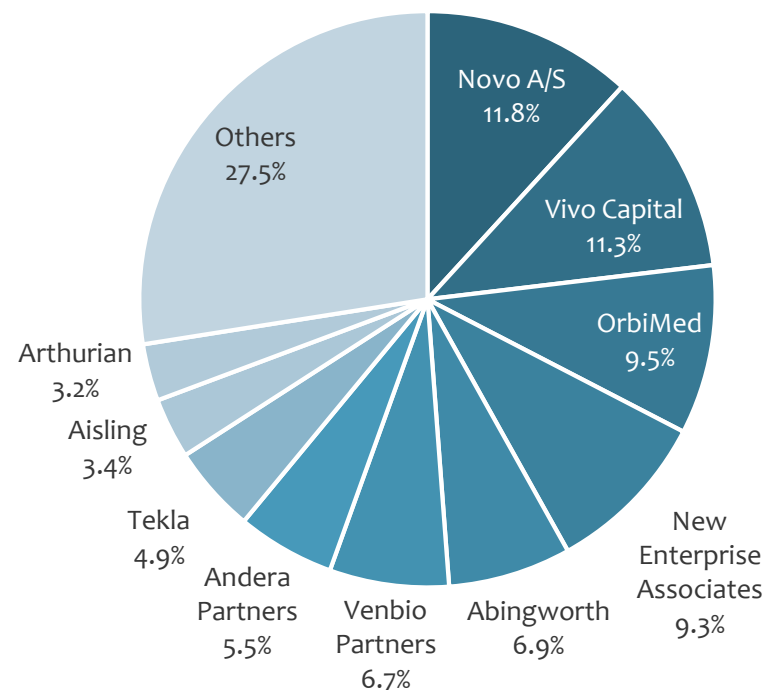


# Backed by major healthcare investors

## Financial overview March 31, 2019

Cash and cash equivalents	\$70.4M <sup>1</sup>
Operating expenses 1Q19	\$10.1M <sup>1</sup>
Market cap	\$82.3M

## Shareholdings



<sup>1</sup>Exchange rate used (US dollars per pound sterling): March, 29, 2019: \$1.3032  
Cash and cash equivalents comprises cash + cash deposits > 3 months maturity  
Cash and equivalents at March 31, 2019 amounted to £54.0M (\$70.4M)



# Multiple value creation opportunities with ensifentrine

## In COPD

### Nebulized formulation in US

- 800,000 symptomatic patients on dual bronchodilator/triple therapy need additional treatment

### Nebulized formulation in China

- Prevalence estimated to 70 million COPD patients; potential large market for nebulized drugs as about 90% of drug sales are in the hospital

### DPI or MDI formulation for COPD

- Large market, >5 million patients in the US; partnering opportunity

## In other indications

### Cystic fibrosis

- Potential first anti-inflammatory drug, independent of CF mutation status

### Severe Asthma

- Bronchodilator and anti-inflammatory agent, possibly before initiating more restrictive biologics treatments

**Nebulizer first NDA filing in US planned 2022**

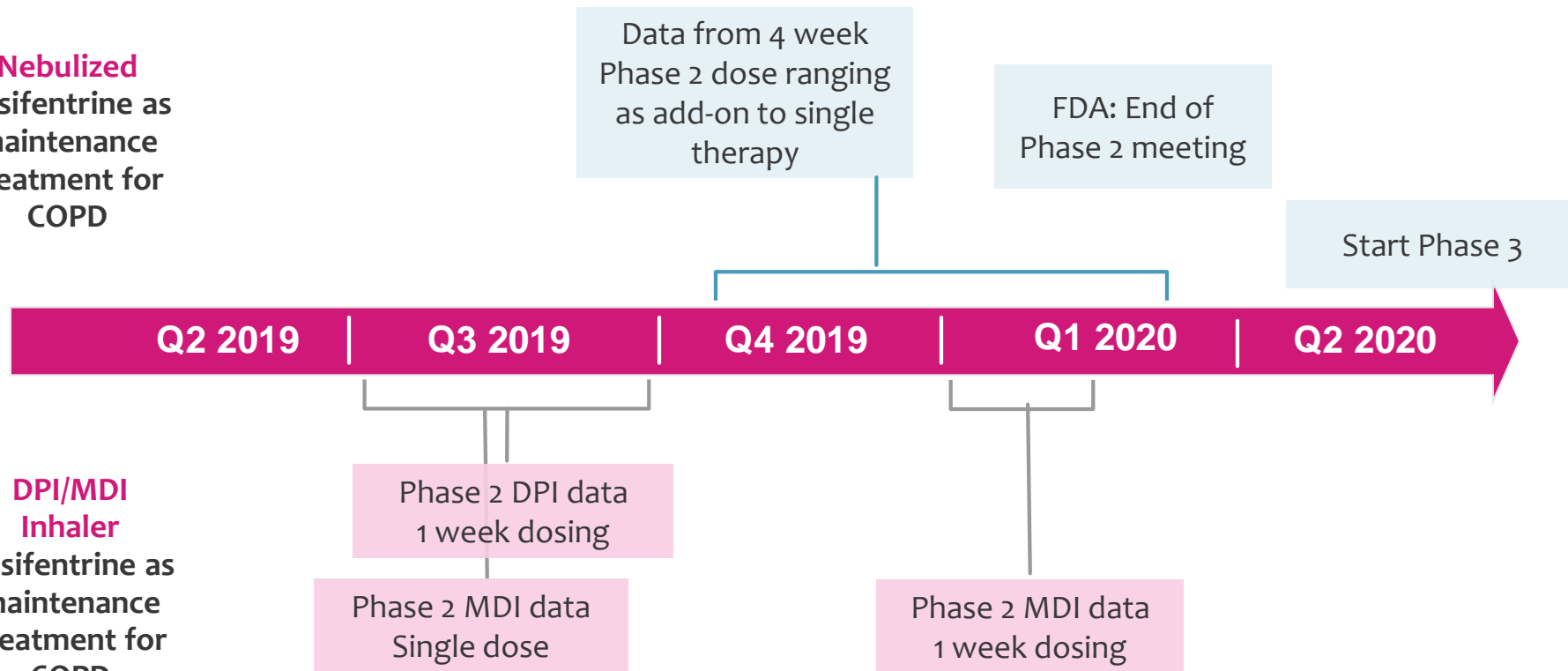
**Upside potential: China, DPI/MDI formulations and additional indications**



# 2019 - multiple significant milestones as ensifentrine advances towards Phase 3 in 2020

**Nebulized ensifentrine as maintenance treatment for COPD**

**DPI/MDI Inhaler ensifentrine as maintenance treatment for COPD**



**Simple Phase 3 trial design, similar to Phase 2b studies, to increase likelihood of regulatory success**



# Ensifentrine: Promising novel treatment for patients with COPD

Data collected to date indicates:

- ✓ First-in-class PDE<sub>3</sub>/4 inhibitor with **bronchodilator and anti-inflammatory effects**, and well tolerated
- ✓ Improves symptoms in **moderate to severe**, symptomatic COPD patients on twice daily dosing
- ✓ Improves lung function in patients taking maximum bronchodilator treatment with dual/triple therapy
- ✓ Targeting FDA End of Phase 2 Meeting **H1 2020**
- ✓ Subsequently, **advancing nebulized ensifentrine** into Phase 3 trials in patients symptomatic despite using standard COPD medications

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# **Patient Perspectives**

## **Symptoms & Disease Progression: How COPD Symptoms Impact Quality of Life**

**Chris Warburton, Patient Advocate**

COPD Patient





# COPD

How COPD symptoms  
impact the  
quality of my life

NB Chris' video is at <https://bit.ly/2rjVH7g>

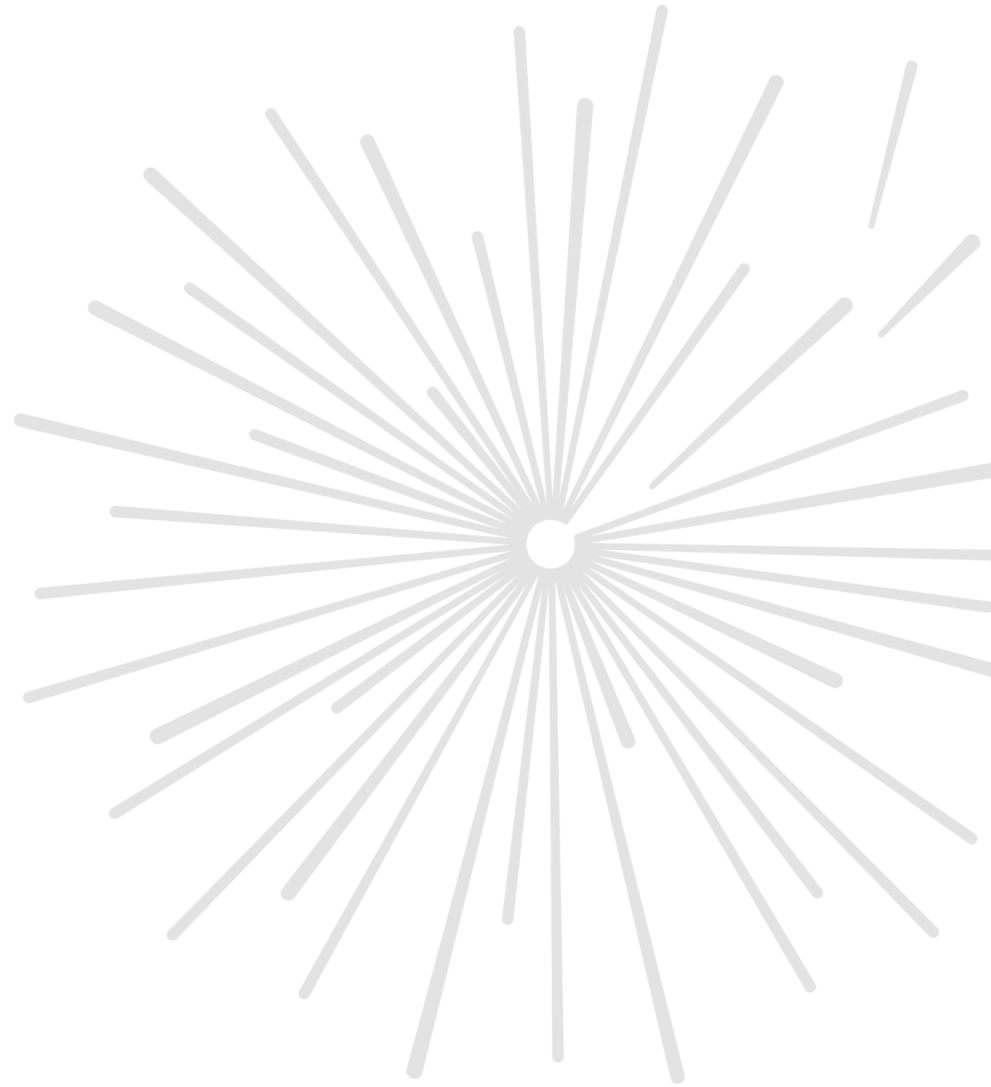




# Clinical Expert Perspective

**Dr Brian Leaker**

Royal Free Hospital



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# Heritage of ensifentrine: Dual targeting in COPD

- Ensifentrine invented by Sir David Jack, former Head of R&D for GlaxoSmithKline and Alexander Oxford, a medicinal chemist
  - Verona Pharma (formerly Rhinopharma Ltd) acquired the rights to intellectual property in 2005
- Sir David Jack recognised for leading a group that developed the following drugs:
  - Beclometasone
  - Salbutamol
  - Salmeterol
  - Fluticasone propionate
- Ensifentrine offers a dual mechanism of action:
  - Bronchodilator and anti-inflammatory properties in one compound
  - Ensifentrine is currently in clinical development for the maintenance treatment of COPD and may also be developed for cystic fibrosis and asthma





# Clinical Expert Perspectives

## COPD treatment challenges/ unmet need

### **Robert Wise**

M.D., Professor of Medicine, Division of Pulmonary and Critical Care Medicine at Johns Hopkins University

# COPD causes considerable clinical and economic burden

- ◆ More than 16 million people diagnosed with COPD in US; millions more may not have been diagnosed<sup>1</sup>
- ◆ In a recent US survey, 83% of patients were classified as symptomatic (GOLD B or D)<sup>2</sup>
- ◆ COPD is the third most common medical cause of death in the USA<sup>3</sup>
- ◆ In 2010, the cost of COPD in the USA was projected to be approximately US\$50 billion<sup>2</sup>
  - \$20 billion in indirect costs
  - \$30 billion in direct health care expenditures
- ◆ These costs can be expected to continue to rise with this progressive disease<sup>3</sup>
- ◆ Hospital stays account for the majority of these costs<sup>3</sup>

<sup>1</sup>NHLBI COPD National Action Plan. Available at: <https://www.nhlbi.nih.gov/health-topics/education-and-awareness/COPD-national-action-plan>

<sup>2</sup>Ding B, et al. Int J COPD 2018;13:927-936.

<sup>3</sup>Guarascio AJ et al. Clinicoecon Outcomes Res 2013;5:235-245.

# Unmet needs in COPD

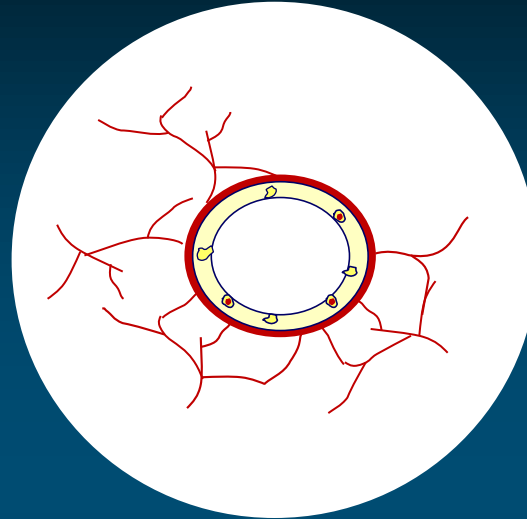
- ◆ Symptoms
- ◆ Impaired physical activity, airflow limitation
- ◆ Recurrent exacerbations
- ◆ Difficulty with handheld inhalers

# Unmet needs in COPD

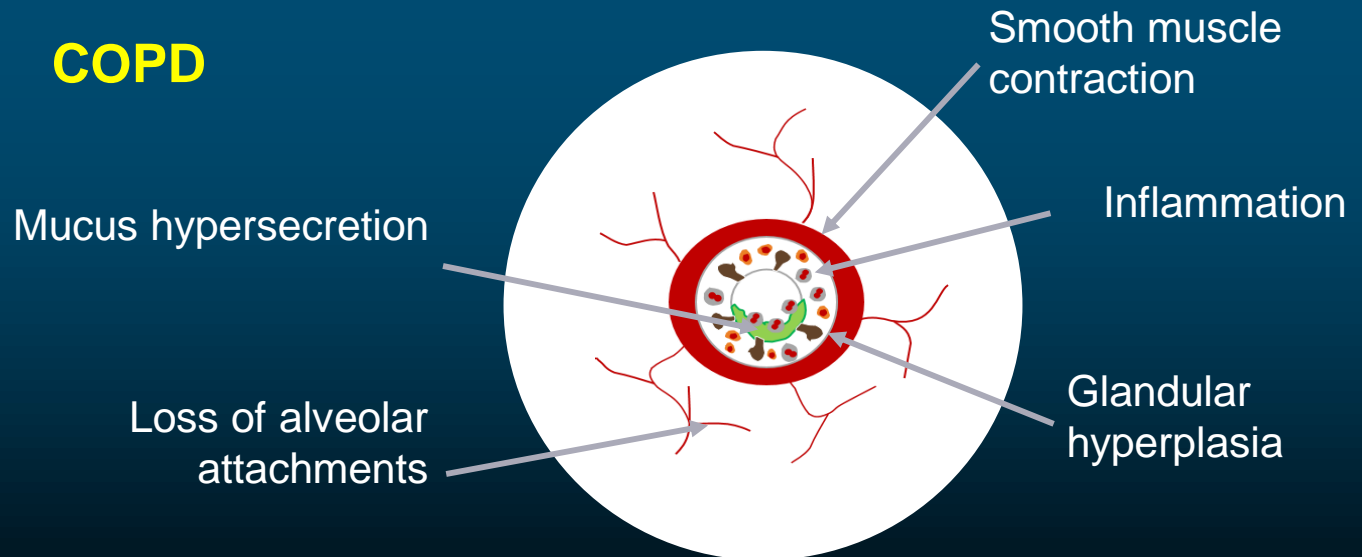
- ◆ Symptoms
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- ◆ Difficulty with handheld inhalers

# Symptoms of COPD: Breathlessness, cough, sputum

**HEALTHY**



**COPD**





# Multiple symptoms of COPD have a real impact on patient well-being

SYMPTOMS <sup>1-4</sup>	IMPACT ON WELL-BEING <sup>1-5</sup>
Shortness of breath	Activity/exercise limitation
Cough	Anxiety and depression
Wheezing	Apprehension about future events
Chest tightness	Lack of confidence about steps to take action
Sputum production	Risk of increasing social isolation
Worse in morning	Loss of independence
Fatigue	

<sup>1</sup>GOLD 2019. Available at <http://www.goldcopd.com/>.

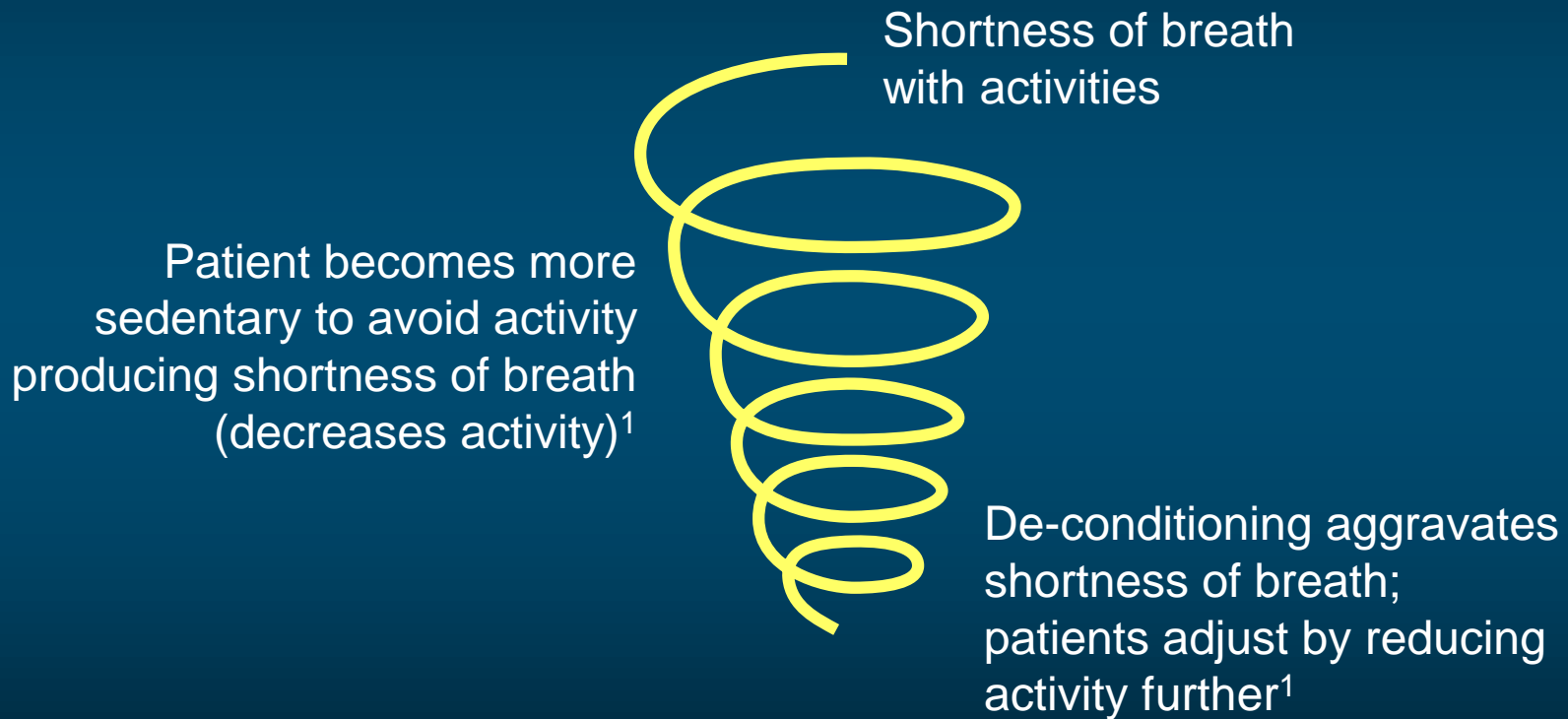
<sup>2</sup>O'Donnell DE. Eur Respir Rev 2006;15:37-41.

<sup>3</sup>Rennard. Eur Respir J 2002;20:799-805.



<sup>4</sup>Barnett M. J Clin Nurs 2005;14:805-12.

<sup>5</sup>Cleland JA. Fam Pract 2007; 24:217-23.

# Patients avoid shortness of breath by becoming less active, leading to de-conditioning/ breathlessness downward spiral



# Case study

- ◆ 67-year-old male; 20 cigarettes a day for 40 years
- ◆ Diagnosed with COPD after complaining of breathlessness during routine activities such as walking; “smokers cough in the mornings”
  
- ◆ Some improvement with BD challenge:
  - Pre-: FEV<sub>1</sub> = 1.60 L, FVC = 2.60 L, FEV<sub>1</sub> % predicted = 60%; CAT score 28
  - Post: FEV<sub>1</sub> = 1.64 L, FVC = 2.65 L, FEV<sub>1</sub> % predicted = 63%
- ◆ Prescribed tiotropium once daily with little benefit
  - FEV<sub>1</sub> increased to 1.68 L; CAT score 24 after 8 weeks
- ◆ Prescribed tiotropium/olodaterol; still uncontrolled
  - FEV<sub>1</sub> increased to 1.71 L; CAT score 22

# COPD maintenance treatments

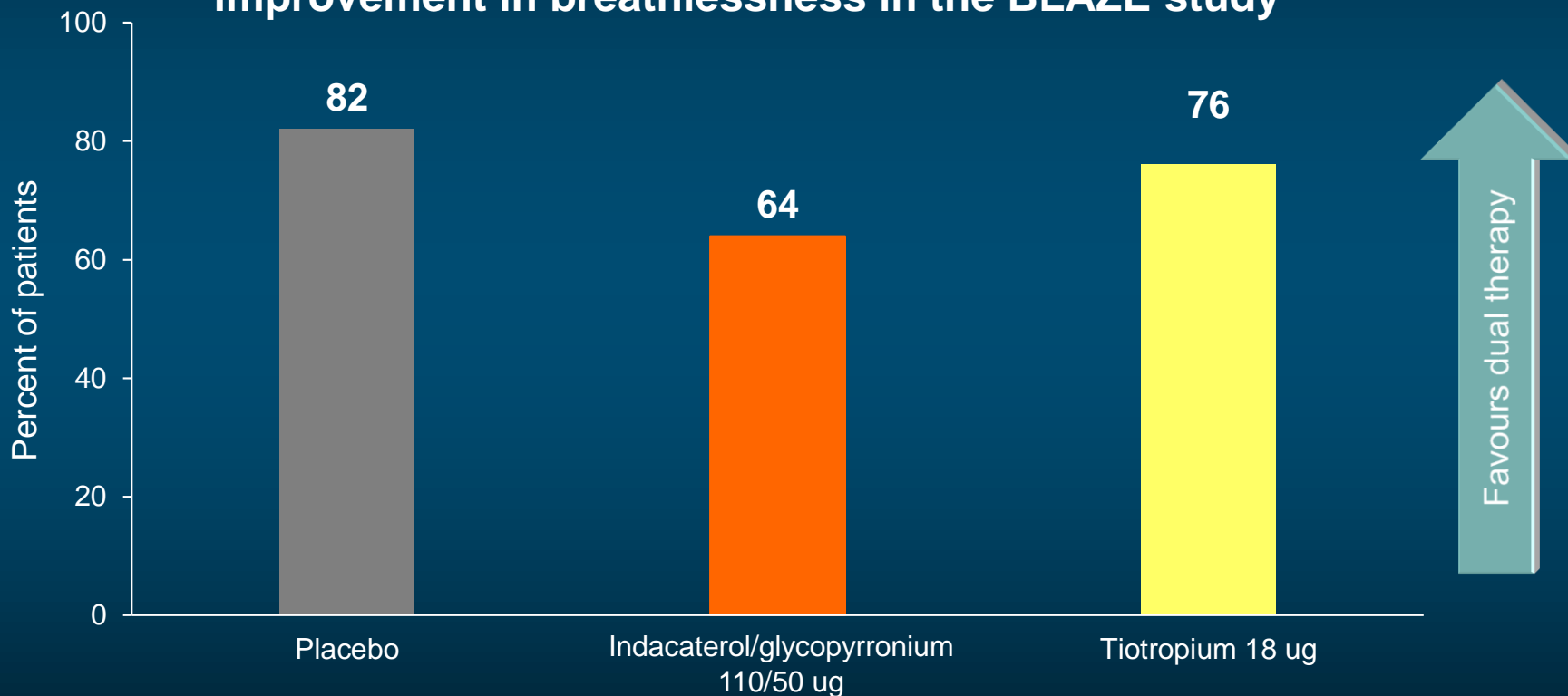
- ◆ Long-acting beta agonists (LABA)
- ◆ Long-acting anti-muscarinics (LAMA)
- ◆ Inhaled corticosteroids (ICS)
- ◆ Oral PDE4 inhibitors

# Guidelines for COPD maintenance therapy in symptomatic patients

- ◆ Symptomatic, low exacerbation risk
  - Long-acting bronchodilator → 2 long-acting bronchodilators
- ◆ Symptomatic, high exacerbation risk
  - 2 long-acting bronchodilators → add anti-inflammatory → add PDE4i, macrolide antibiotic

# A high proportion of patients on single therapy (LAMA) are symptomatic; after moving to dual therapy (LAMA/LABA) many remain symptomatic

Proportion of patients who DID NOT achieve clinically meaningful improvement in breathlessness in the BLAZE study



Patients who did not achieve clinically meaningful improvement in breathlessness were those who did not have a  $\leq 1$ -point improvement in TDI total score (%). A 1-unit change in TDI is considered the minimal clinically important difference or MCID, in breathlessness.

TDI, Transition Dyspnoea Index

# Unmet needs in COPD

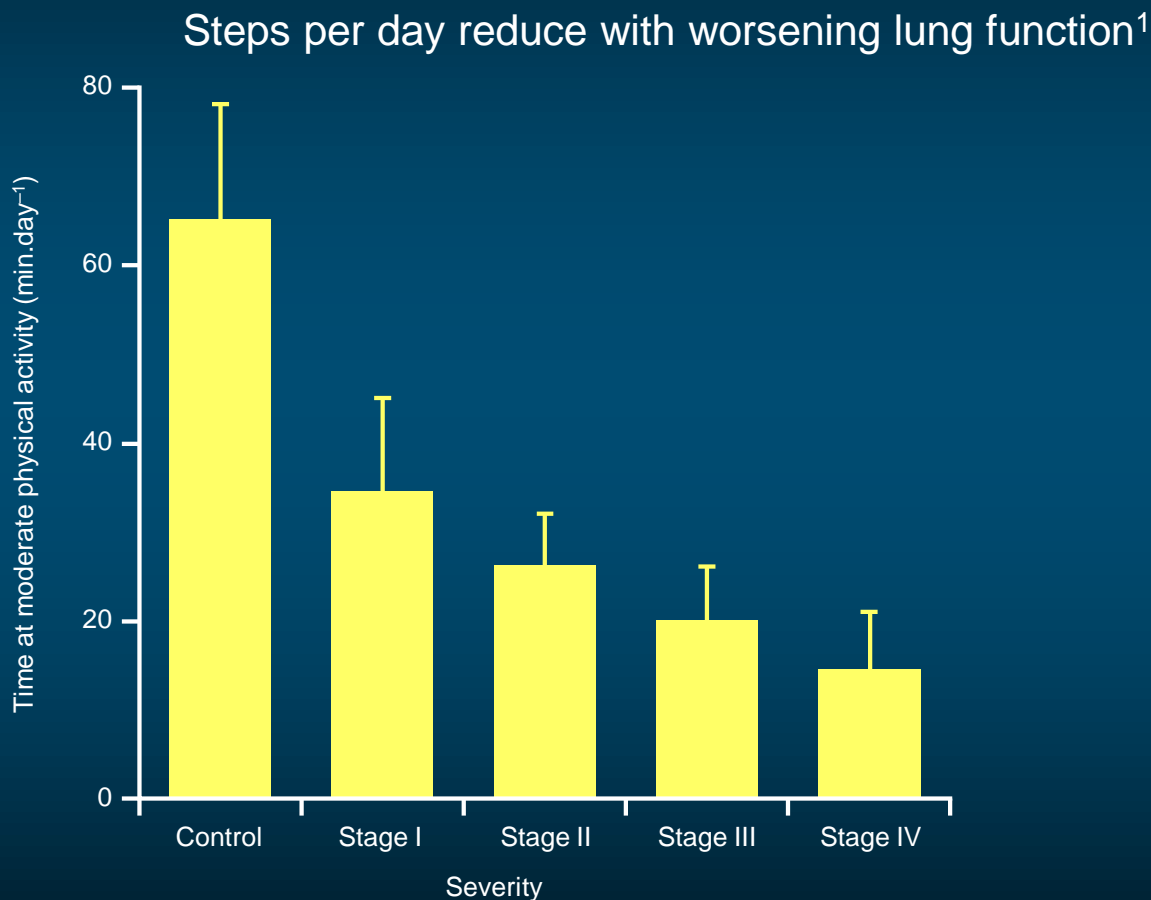
- ◆ Symptoms
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# COPD maintenance treatments

- ◆ Long-acting beta agonists (LABA)
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- ◆ Oral PDE4 inhibitors



# Physical activity reduces with increasing COPD severity, which may lead to hospitalizations or death

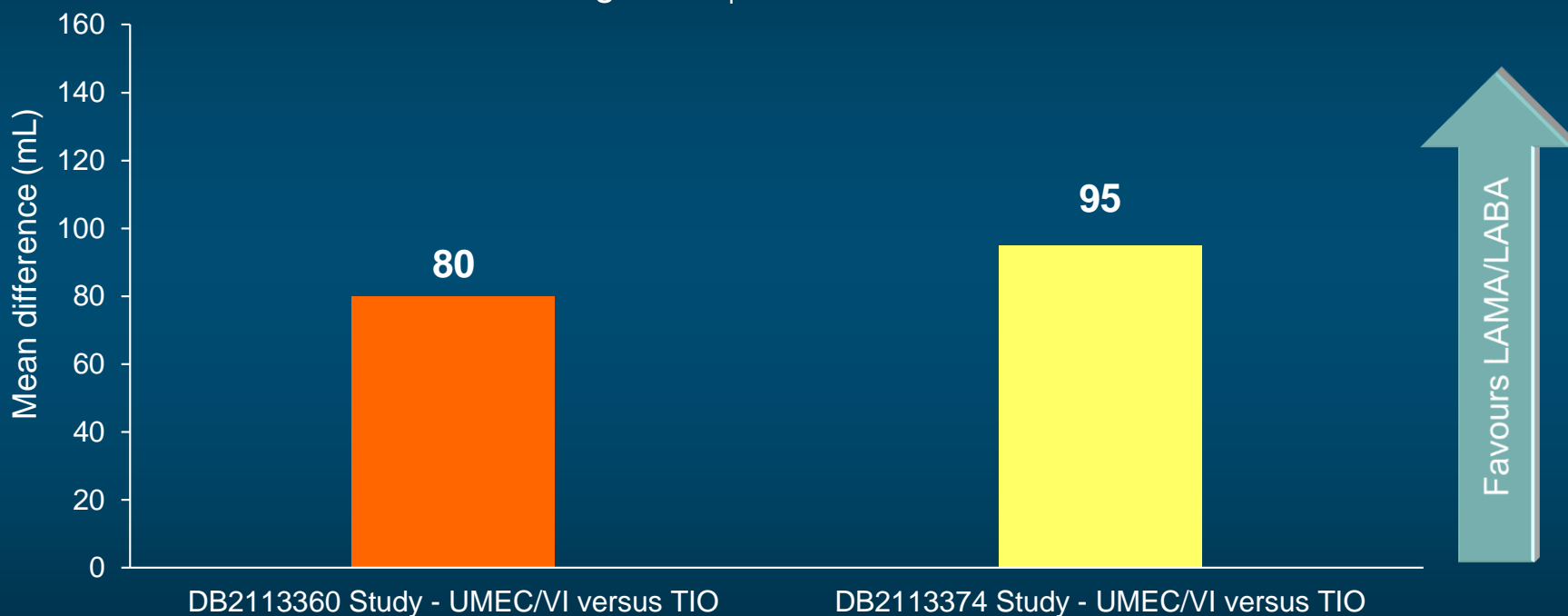


<sup>1</sup>Adapted from Watz H. Eur Respir J 2009;33(2):262-72.

<sup>2</sup>Garcia-Aymerich J, et al. Thorax. 2006;61:772-778.

# Effect on lung function: Incremental benefit with LAMA/LABA over LAMA

Mean difference (LABA/LAMA vs LAMA) from baseline in  
trough FEV<sub>1</sub> at Week 12<sup>1,2</sup>



LAMA/LABA versus LAMA (TIO) at 12 weeks. Dotted line shows the weighted mean difference in a random effects model across 6 studies included in a meta-analysis. FEV<sub>1</sub> forced expiratory volume in 1 s, TIO tiotropium.

<sup>1</sup>Han MK, et al. npj Primary Care Resp Med. 2018;28:32.

<sup>2</sup>Decramer M, et al. Lancet Resp Med 2014;2(6):472-486.

# Unmet needs in COPD

- ◆ Symptoms
- ◆ Impaired physical activity, airflow limitation
- ◆ Recurrent exacerbations
- ◆ Difficulty with handheld inhalers

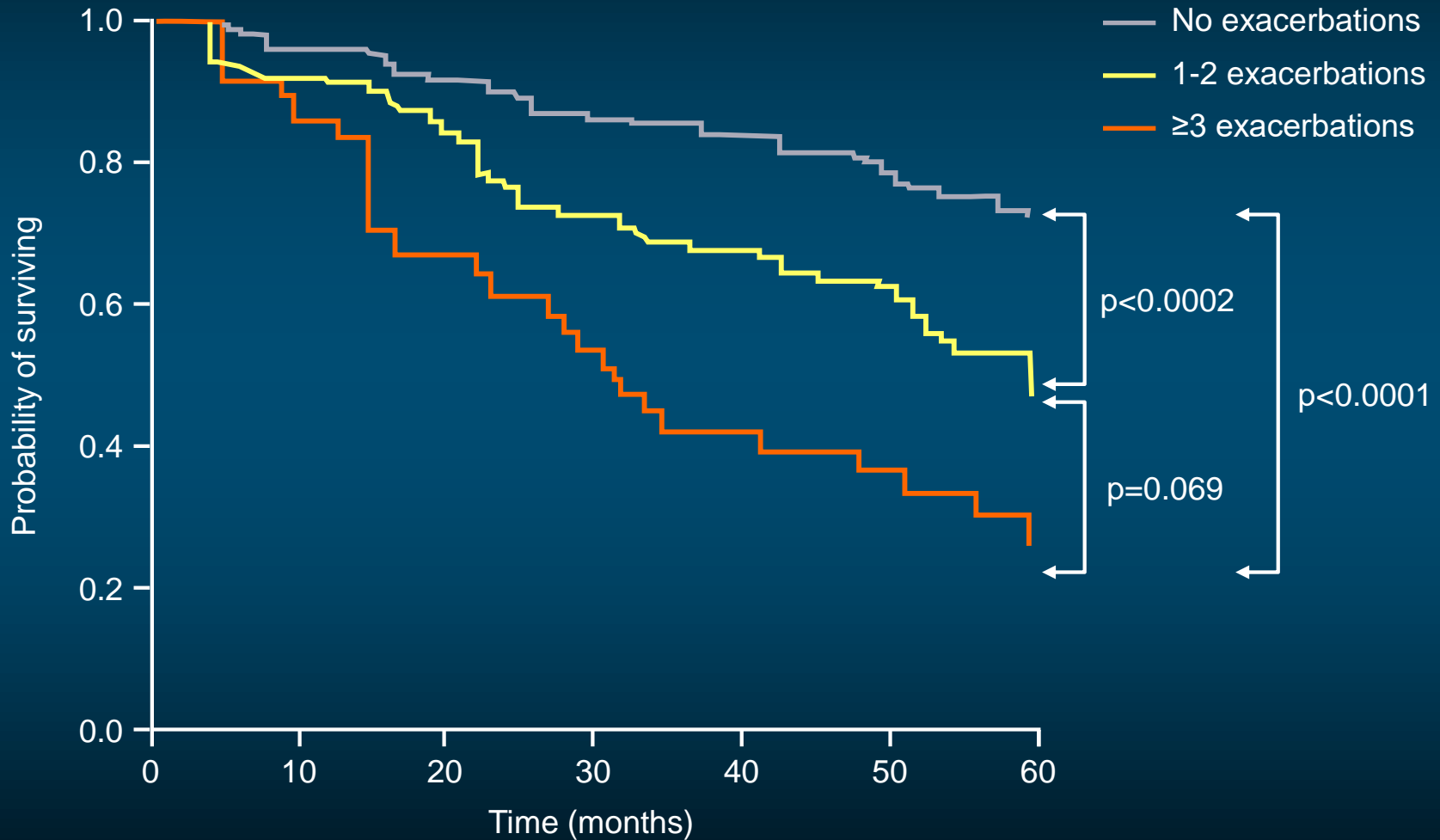
# COPD maintenance treatments

- ◆ Long-acting beta agonists (LABA)
- ◆ Long-acting anti-muscarinics (LAMA)
- ◆ Inhaled corticosteroids (ICS)
- ◆ Oral PDE4 inhibitors

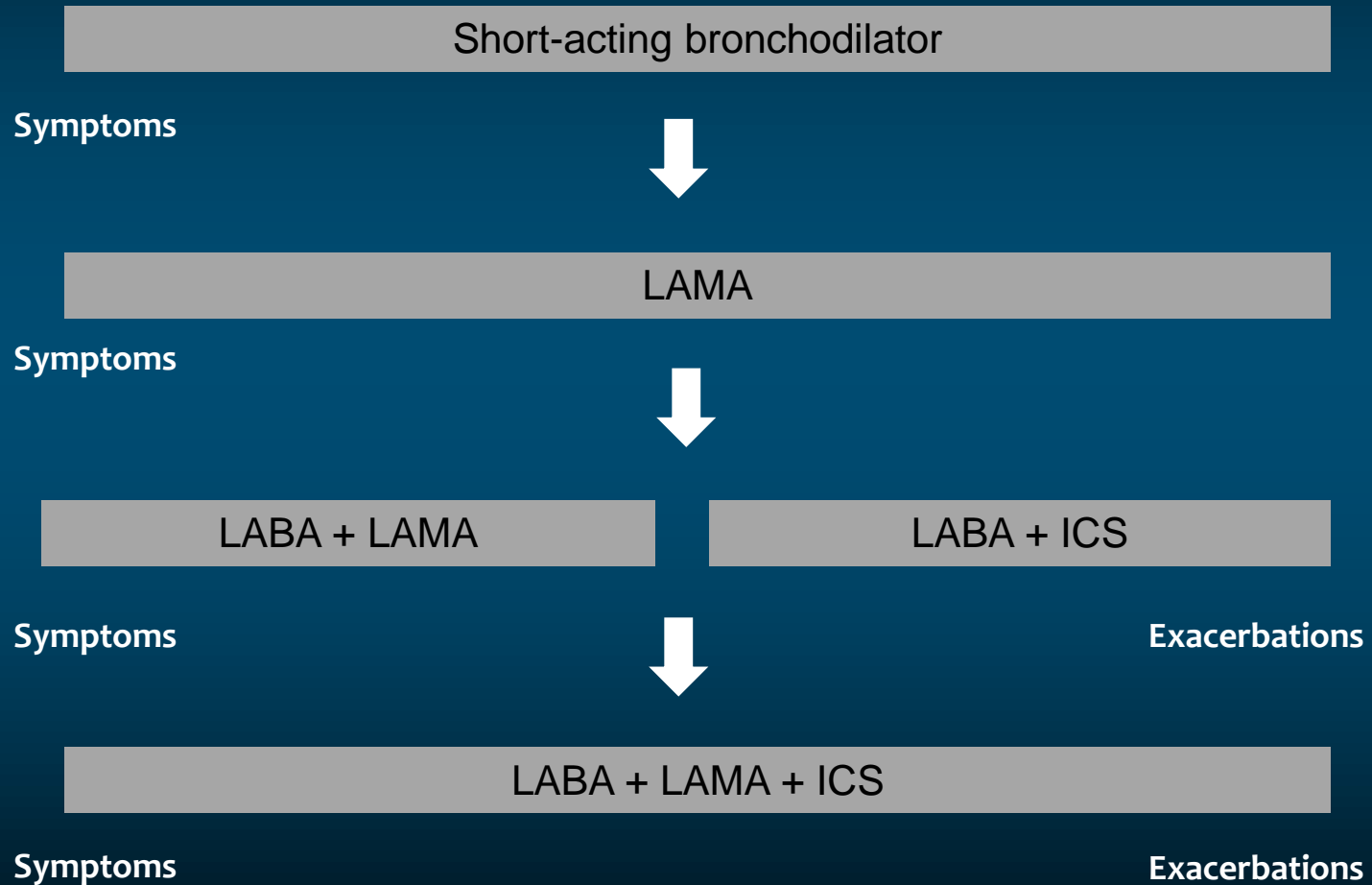
# Burden of exacerbations

- ◆ Mild and moderate exacerbations are common in COPD
- ◆ Severe exacerbations (requiring hospitalization) are associated with:
  - A high mortality rate
  - A decline in lung function that may be prolonged and not recoverable
  - Disease progression
  - High costs – hospitalized exacerbations account for the majority of the costs associated with COPD

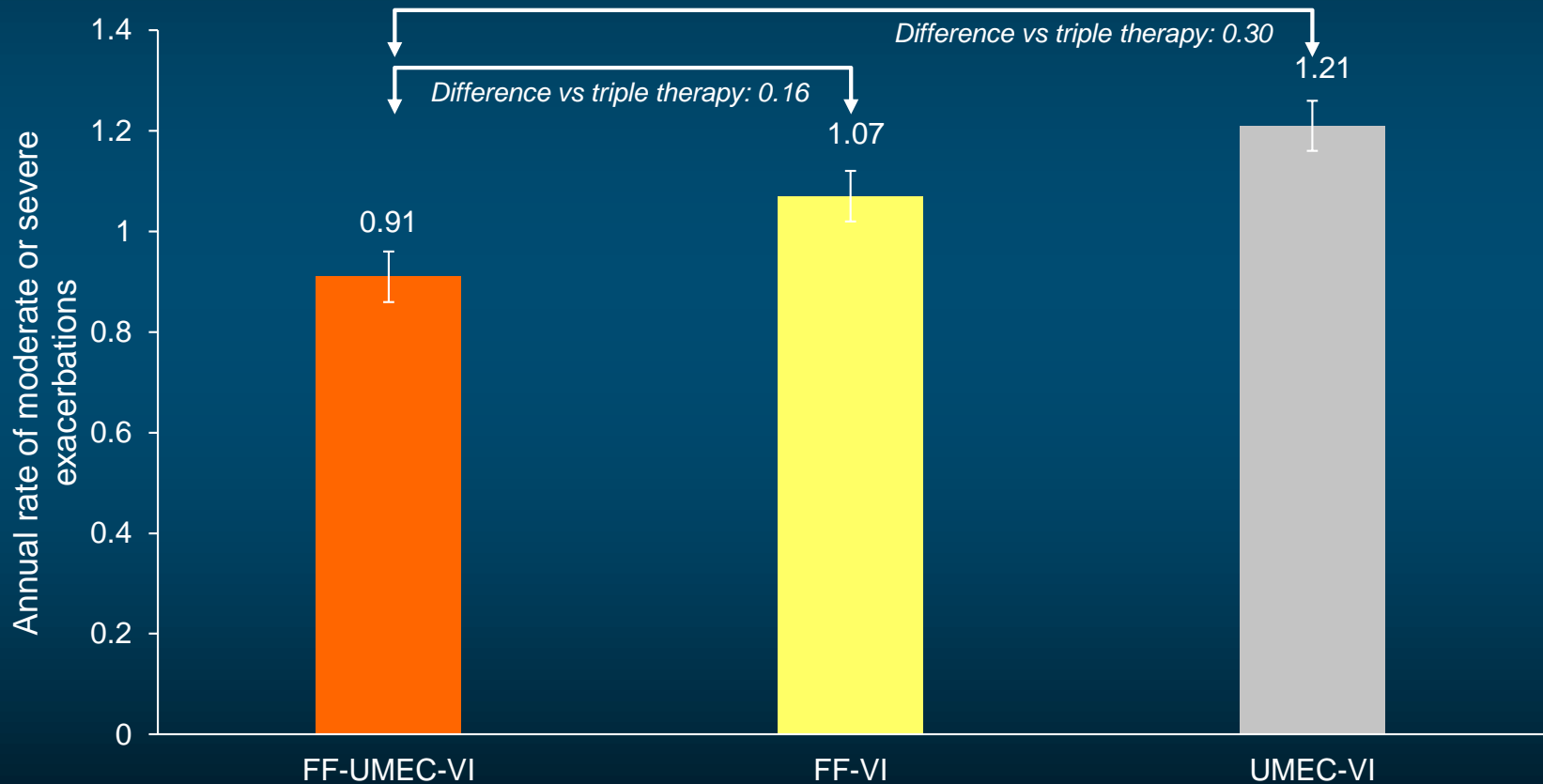
# Mortality increases with the frequency of severe exacerbations



# Therapy flow chart



# Limited incremental benefit of triple vs. dual therapy on the rate of moderate or severe exacerbations





# Effect of PDE-4 inhibitors on COPD management goals

- ◆ Statistically significant improvements in lung function; however, change was below what is usually considered a minimum clinically important difference
- ◆ Effect on COPD symptoms was small, regardless of how measured
- ◆ Individuals were 22% less likely to have an exacerbation; overall rate of exacerbations was reduced by 13%

# Safety of medications for the prevention of COPD exacerbations

- ◆ ICS
  - Pneumonia
  - Bones, Skin, Eyes
- ◆ Roflumilast
  - Nausea, Diarrhea, Weight Loss

# Unmet needs in COPD

- ◆ Symptoms
- ◆ Impaired physical activity, airflow limitation
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- ◆ Difficulty with handheld inhalers

# COPD maintenance treatments

- ◆ Long-acting beta agonists (LABA)
- ◆ Long-acting anti-muscarinics (LAMA)
- ◆ Inhaled corticosteroids (ICS)
- ◆ Oral PDE4 inhibitors

# Potential reasons for using nebulized medications in COPD

- ◆ Inhaler device handling errors are common:
  - ~15-40% among elderly patients in primary care<sup>1</sup>
  - 81-85% in hospitalized patients<sup>2</sup>
- ◆ Critical errors using conventional inhalers in spite of adequate training
  - Inadequate inspiratory flow (ability to breath in)
  - Poor inspiratory timing
  - Inability to activate inhaler (by breath or by hand)
- ◆ Medical conditions limiting inhaler use
  - Mental impairment or cognitive dysfunction
  - Neuromuscular diseases
  - Arthritis
  - Visual impairment

<sup>1</sup>Molimard M, et al. *J Aerosol Med.* 2003;16:249-254.

<sup>2</sup>Press VG, et al. *J Gen Intern Med.* 2011;26(6):635-642.

# Nebulized formulations are often prescribed for US moderate to severe patients

- ◆ Current adoption of nebulized therapy by COPD severity
  - Mild: 14%
  - Moderate: 27%
  - Severe: 37%

- Physicians also indicate a roughly even split between prescription of nebulized treatments for chronic use (54% patients) vs. temporary use post-discharge (46%)

# What do we need?

Maximum bronchodilation is key to improving symptoms and reducing exacerbation frequency

- ◆ Additional options to control symptoms in treated patients
- ◆ An inhaled bronchodilator that has bronchodilating efficacy in COPD patients already on maintenance therapy
- ◆ An inhaled bronchodilator that can be delivered by nebulizer suitable for all COPD patients
- ◆ An anti-inflammatory with an alternative mechanism of action to inhaled corticosteroids



Verona Pharma

# Clinical Expert Perspectives

## COPD treatment pipeline including ensifentrine

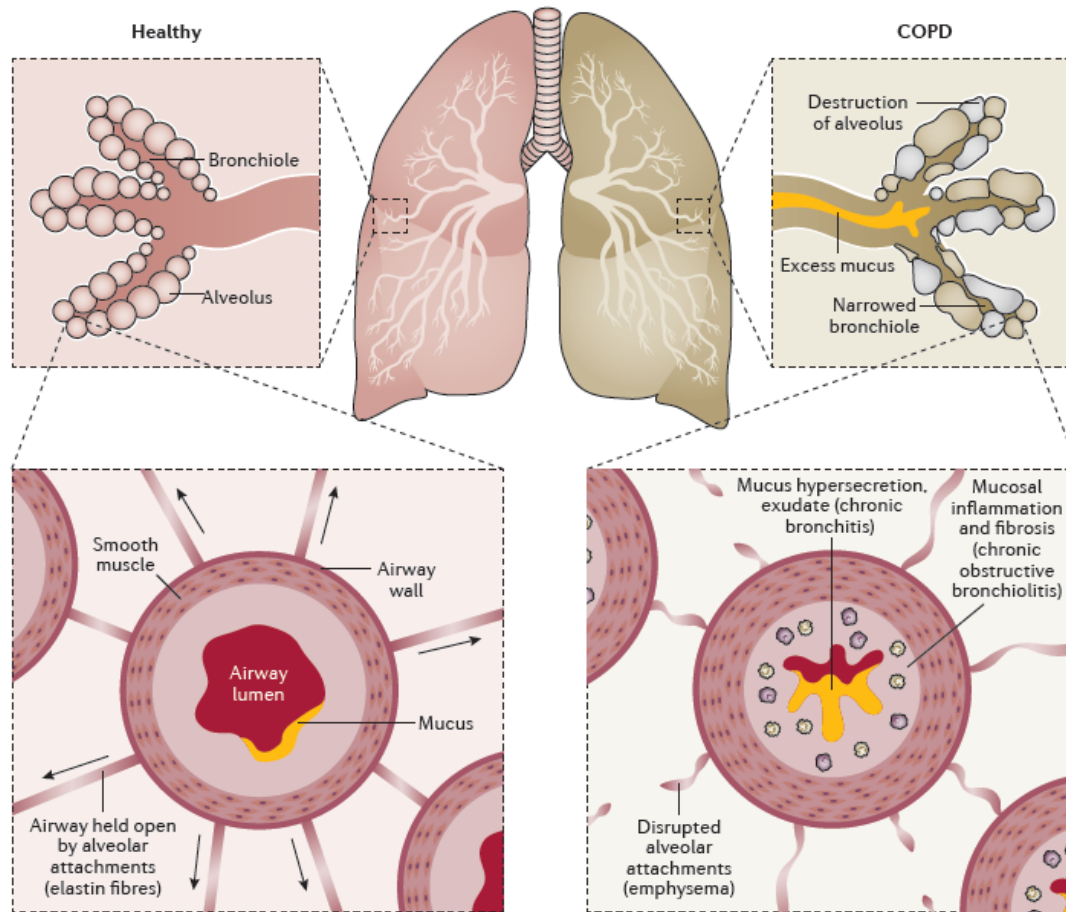
**Gerard J Criner, MD**

Professor and Founding Chair, Department of Thoracic Medicine and Surgery,  
Lewis Katz School of Medicine at Temple University – Philadelphia, Pa



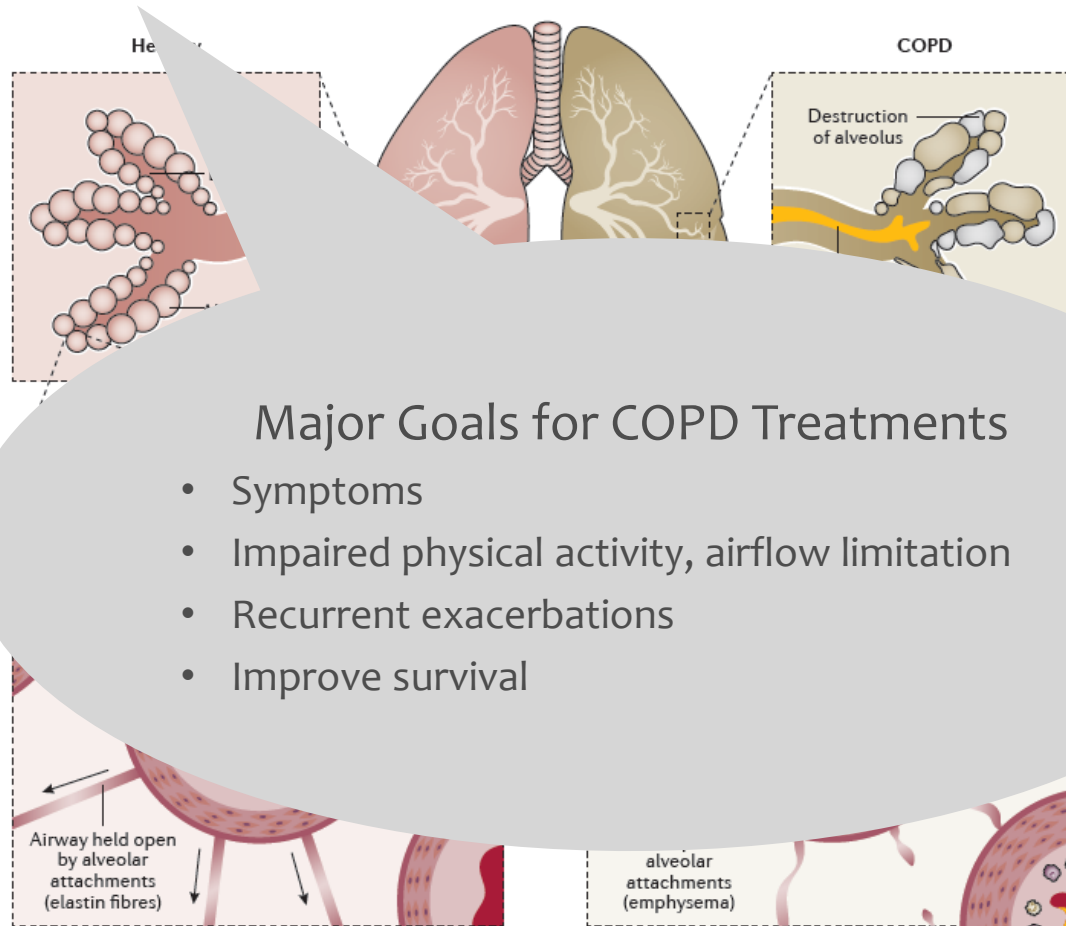


# Airways obstruction in COPD: Targets for treatment





# Airways obstruction in COPD: Targets for treatment

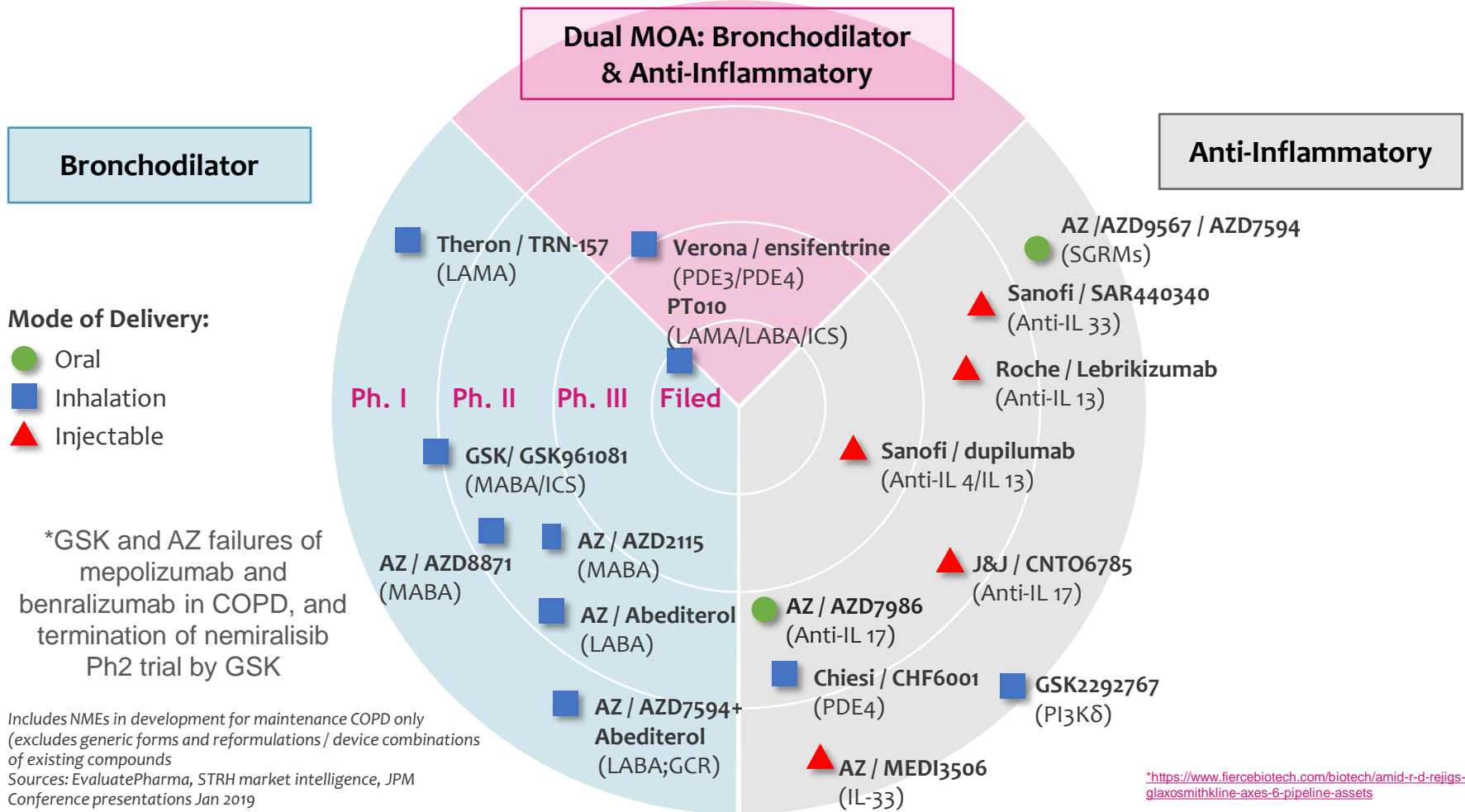


# Overview of maintenance therapy for COPD

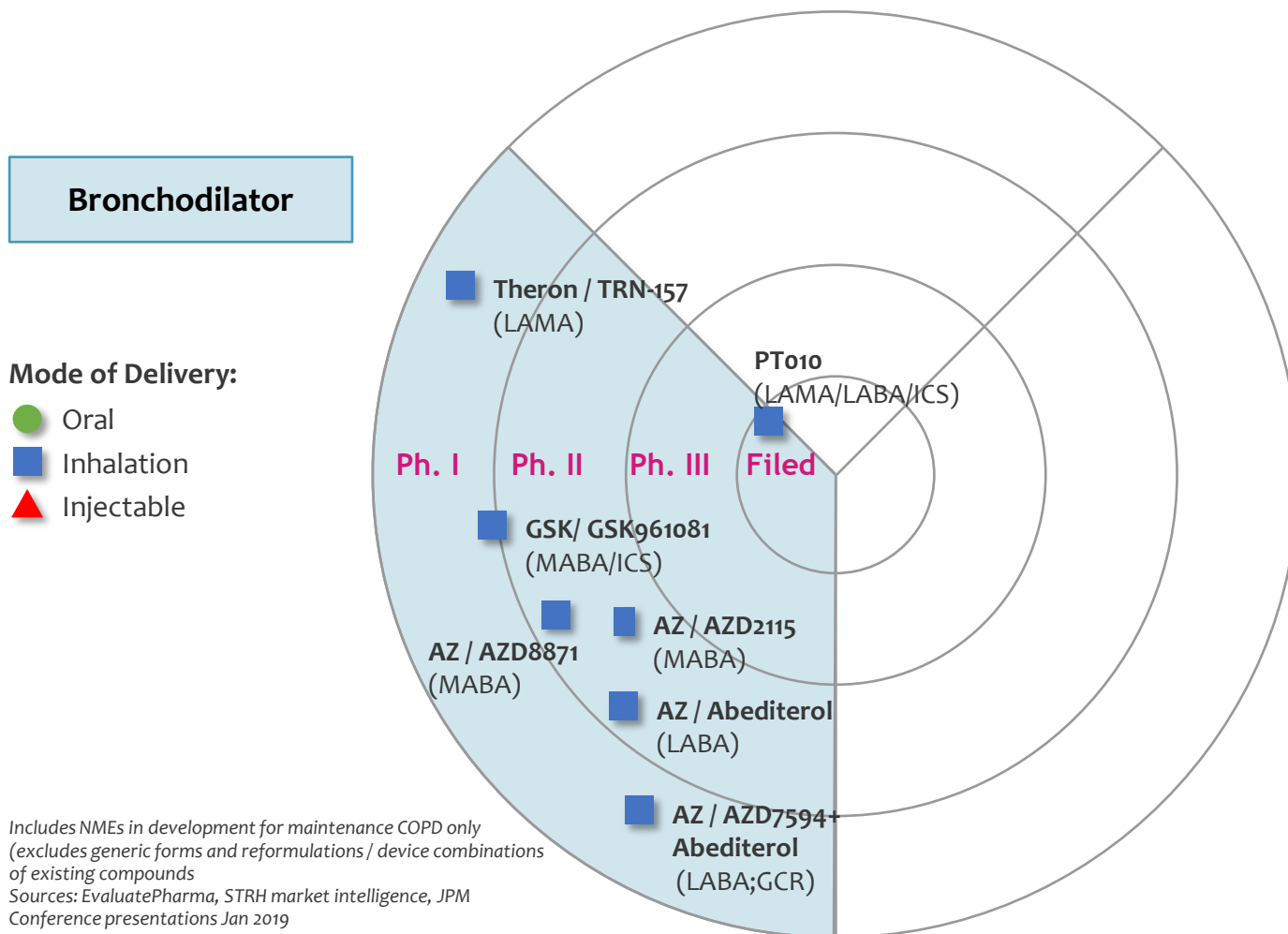
Category	Class	Symptoms	Exacerbation prevention
Bronchodilators	Long-acting $\beta_2$ -agonists (LABAs)	++++	++
	Long-acting muscarinic antagonists (LAMAs)		
	LAMA/LABA		
Bronchodilator/ anti-inflammatory combinations	LABA/inhaled corticosteroids (LABA/ICS)	++++	++++
	LAMA/LABA/ICS		
Anti-inflammatories	ICS alone	++	++++
	PDE-4 inhibitors		
	Targeted anti-inflammatories		
Other	Smoking cessation	++	+++
	Mucolytics	++	+
	Vaccinations	+	+++
	Non-pharmacological devices	NA	NA

# Compelling need for therapy with new mode of action for COPD

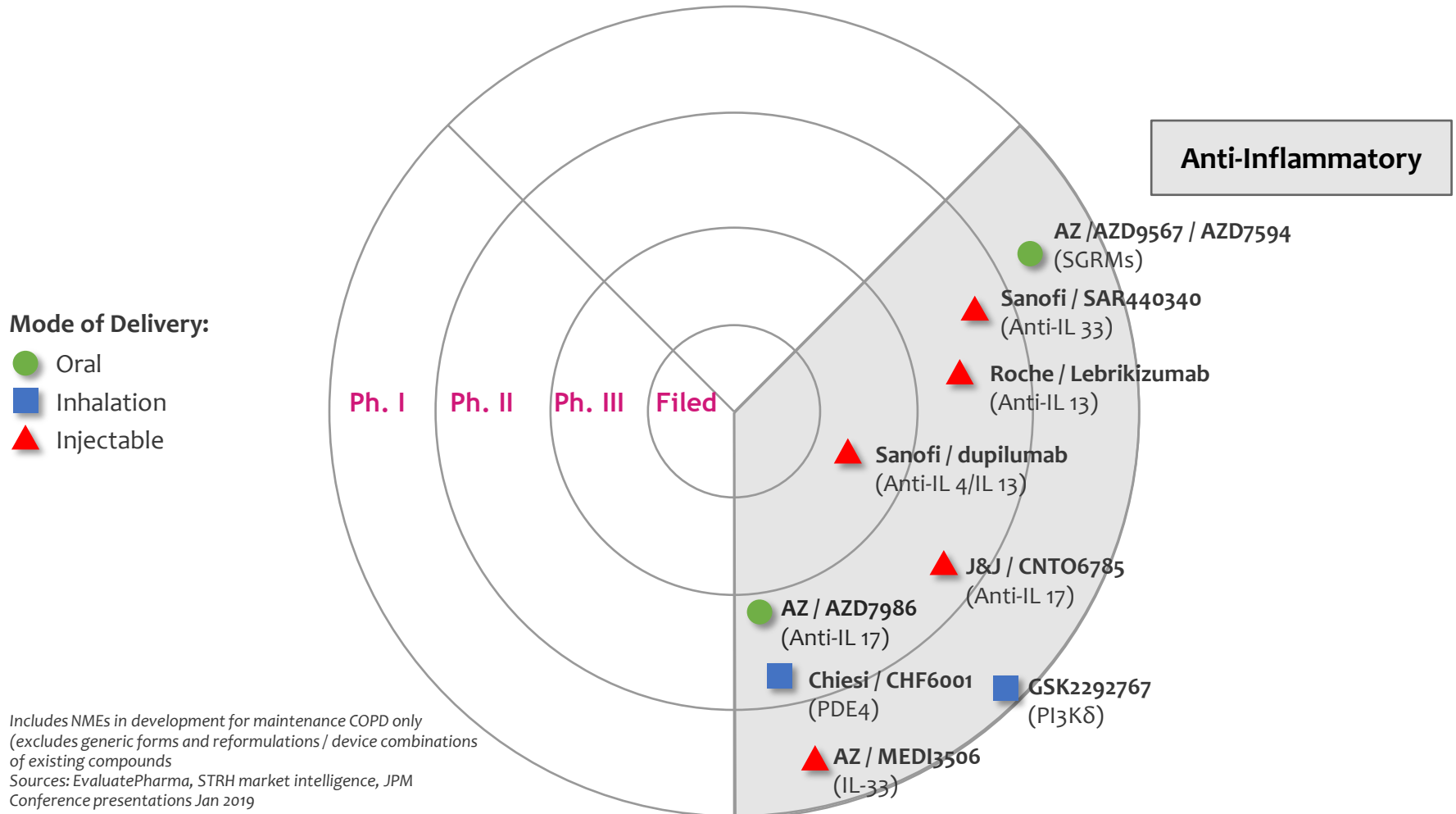
...but few such drugs in development for COPD, and high rate of failure\*



# Bronchodilators in development for COPD

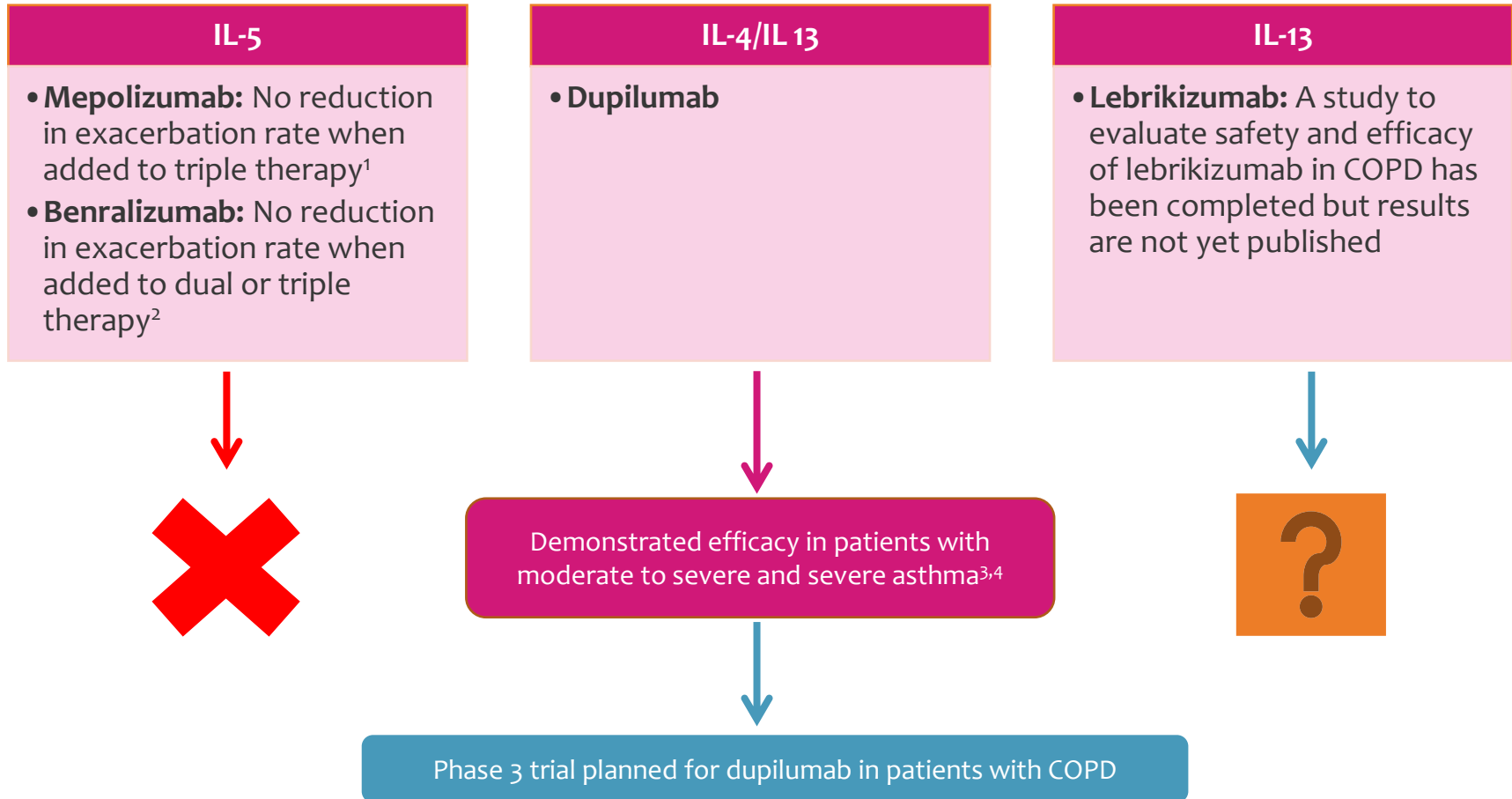


# Anti-inflammatories in development for COPD





# Interleukin-directed therapy in COPD: Still looking to demonstrate proof of concept



1. Pavord I, et al. NEJM 2017;377:1613-1629. 2. Brightling CE, et al. Lancet Respir Med 2014;2:891-901. 3. Castro M, et al. NEJM 2018;378:2486-2496. 4. Rabe KF, et al. NEJM 2018;378:2475-2485.



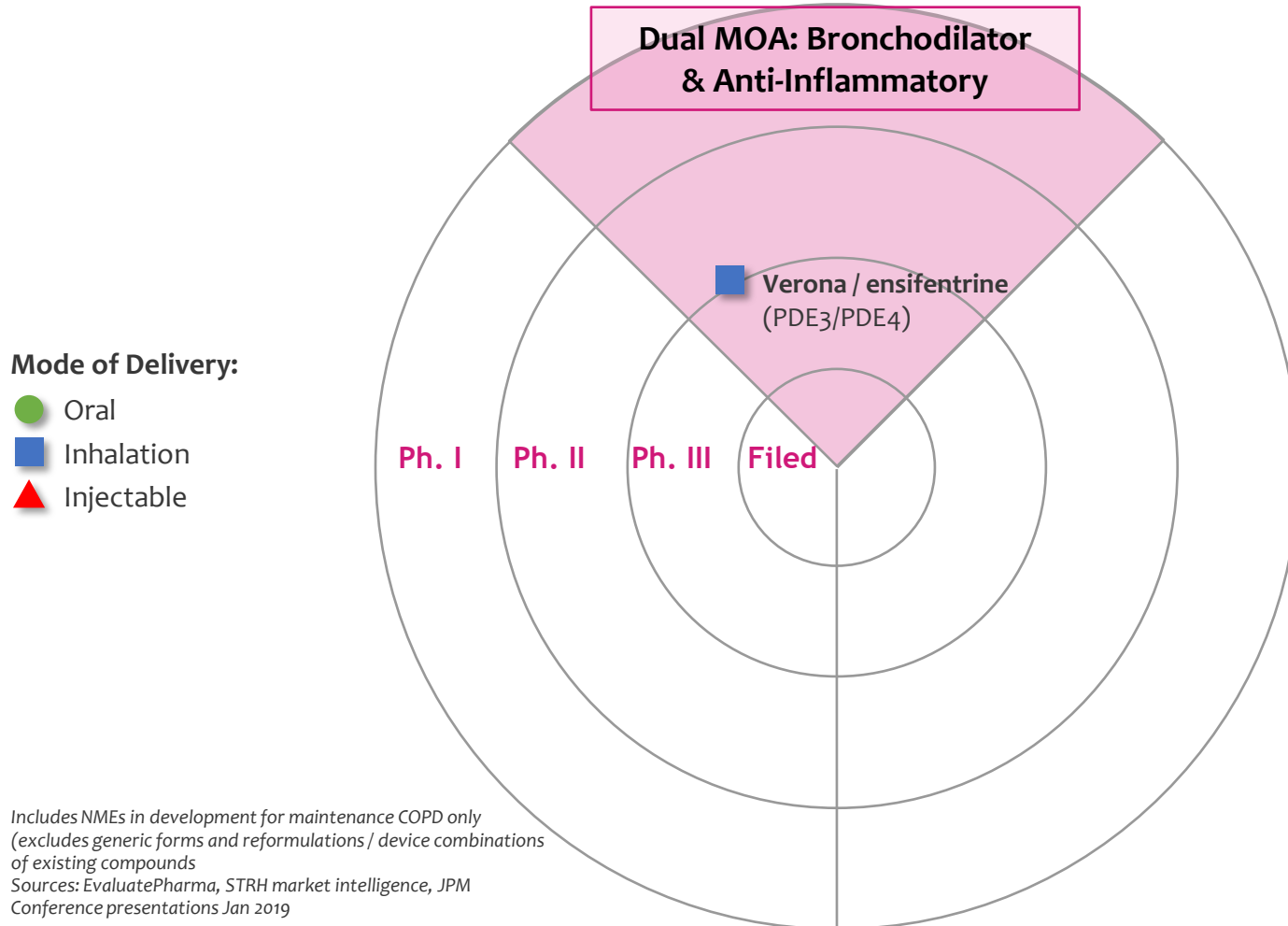
# p38 MAP kinase inhibitor therapy in COPD and other anti-inflammatory therapies

- GSK performed a study of **losmapimod** in 602 patients: No improvement in exercise tolerance or lung function, despite being well tolerated
- AZ recently reported at ERS 2018 that **AZD7624** had a greater effect than budesonide on cytokine production from BECs
- **SK2269557** (PI3K $\delta$  inhibitor): In development for COPD
- **CHF6333** (neutrophil elastase inhibitor): Phase 1 safety, tolerability and pharmacokinetics of single and repeat doses in 72 healthy males (NCT03056326)
- **Emeramide** (antioxidant and metal chelator): Pilot study to explore safety of emeraimide in COPD patients (NCT03123692)





# Only one dual bronchodilator/anti-inflammatory in development for COPD



# Ensifentrine promising clinical trial results

- Verona Pharma announced ensifentrine demonstrated additional bronchodilation in moderate to severe COPD patients already receiving maximum bronchodilator treatment with dual therapy (LAMA/LABA).
- Ensifentrine:
  - First-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4
  - Designed to have bronchodilator as well as anti-inflammatory properties
  - Ensifentrine is in Phase 2b clinical development for the maintenance treatment of COPD and may be developed for cystic fibrosis and asthma



# Ensifentrine clinical progress

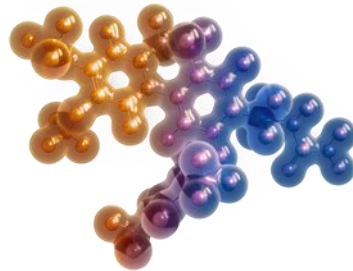
Kathleen Rickard, CMO



## Ensifentrine is a first-in-class candidate for respiratory diseases

*Plan to enter Phase 3 in 2020*

**Inhaled PDE<sub>3</sub> and PDE<sub>4</sub> inhibitor**

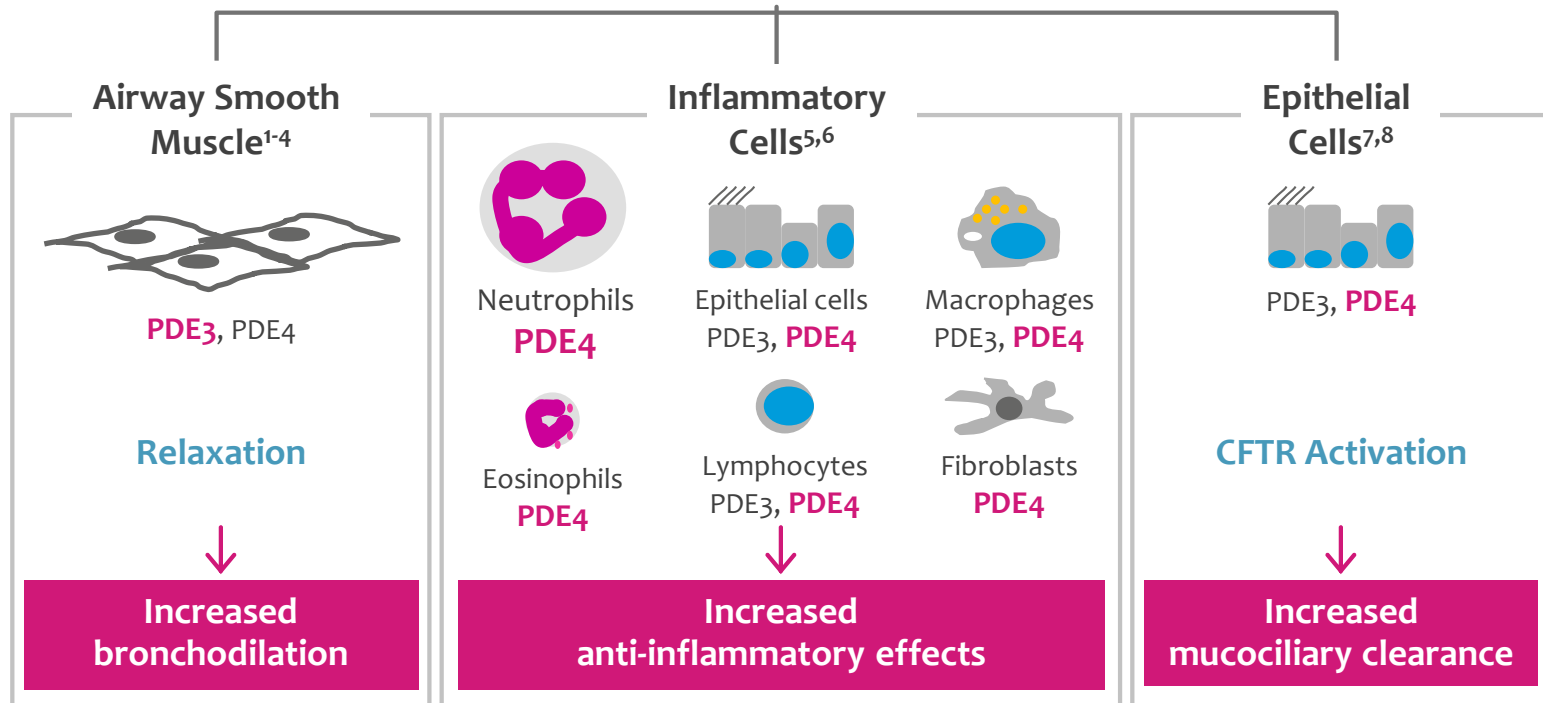


Bronchodilator and anti-inflammatory agent  
in a single compound

# Ensifentrine first-in-class candidate: Bronchodilator and anti-inflammatory in a single compound

**Ensifentrine (RPL554)**  
Dual PDE3 and PDE4 enzyme inhibitor

Impacts 3 Key Mechanisms in Respiratory Disease:



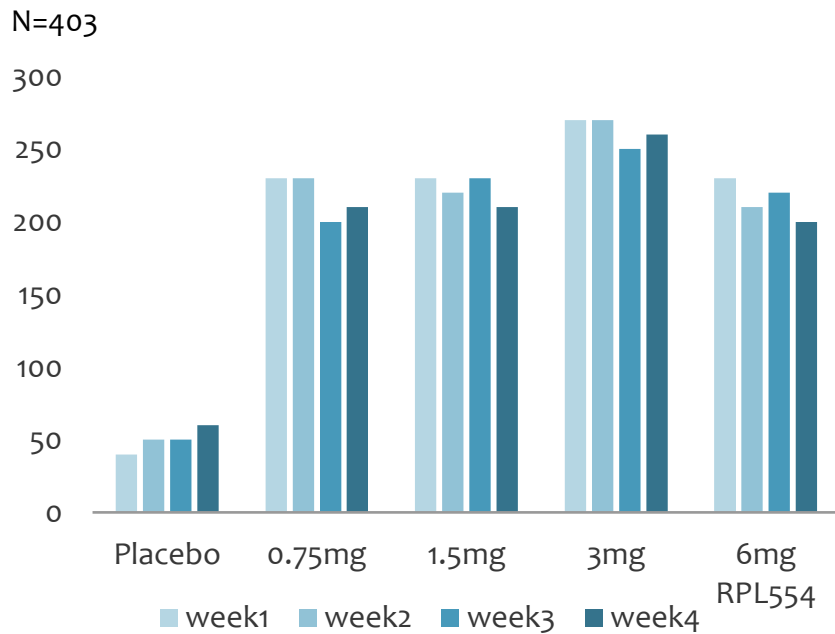
1. Calzetta L, et al. J Pharmacol Exp Ther 2013;346:414-23; 2. Calzetta L, et al. Pulm Pharmacol Ther 2015;32:15-23; 3. Matera MG, et al. Am J Respir Crit Care Med 2013;187:A1495; 4. Venkatasamy R, et al. Br J Pharmacol 2016;173:2335-51; 5. Boswell-Amith V, et al. J Pharmacol Exp Ther 2006;318:840-8; 6. Franciosi LG, et al. Lancet Respir Med 2013;1:714-27; 7. Schmidt D, et al. Br J Pharmacol 2000;131:1607-18; 8. Turner MJ, et al. Am J Physiol Lung Cell Mol Physiol 2016;310:L59-70.



# 4 Week Phase 2b: Rapidly improved lung function and progressive symptom relief as single bronchodilator<sup>1,2</sup>

## Lung function

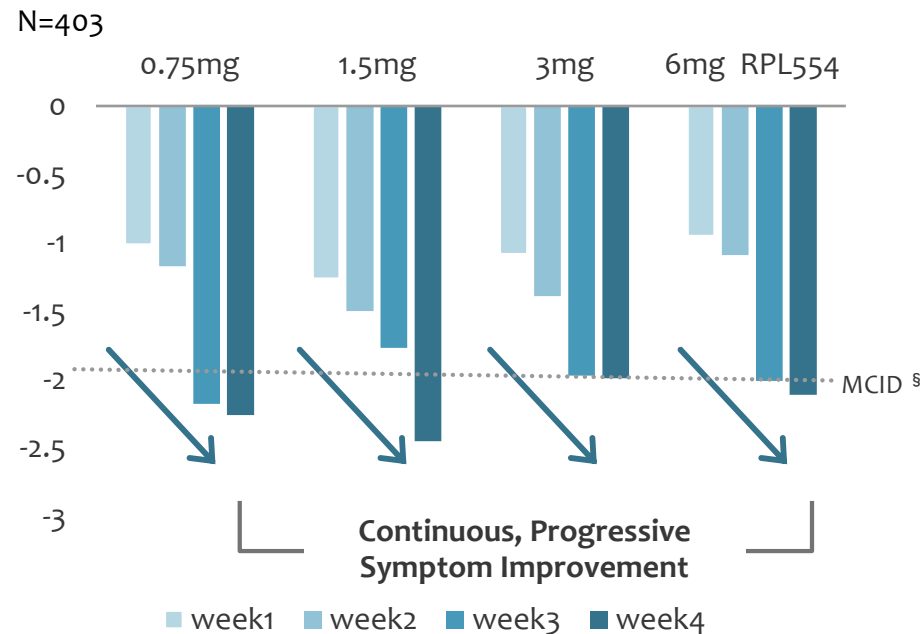
Peak Change FEV<sub>1</sub> (mL) (p<0.001)\*



\*Peak Change from Day 1 in Baseline in FEV<sub>1</sub> (mL) on Day 28, Week 4, Primary endpoint was met

## Symptom relief

Total Score E-RS: COPD by Week, p<0.02\*\*



\*\* Placebo corrected

§ Minimal clinically important difference

Enfisentrine was well tolerated in this and other clinical trials involving > 800 subjects<sup>3-5</sup>

**Bronchodilator + anti-inflammatory = Potential to reduce symptoms and exacerbations<sup>a</sup>**

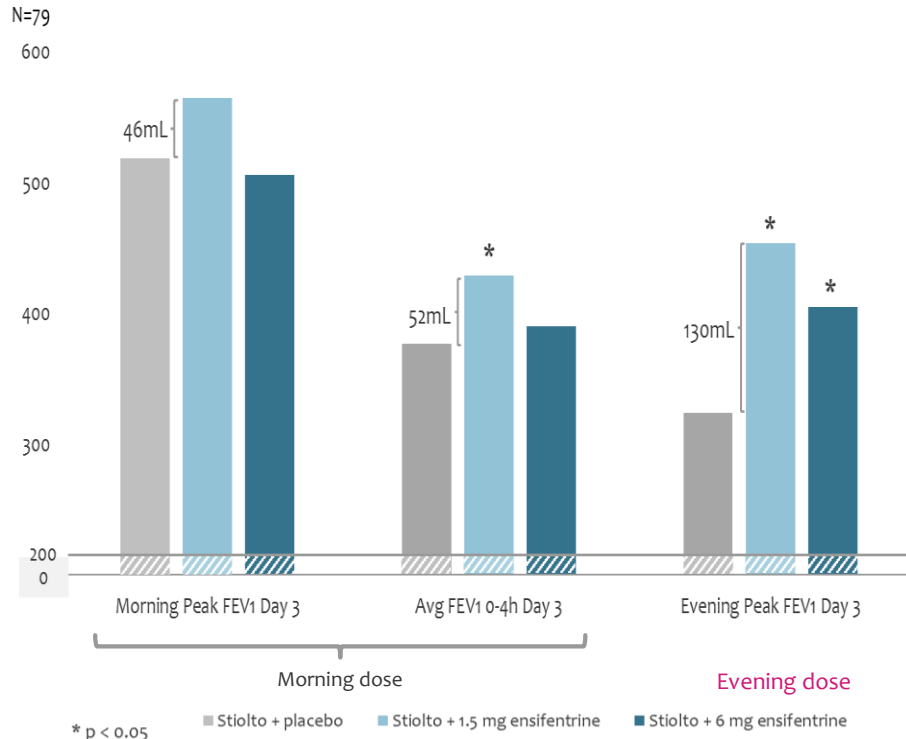
<sup>a</sup>Symptoms are a precursor to exacerbations<sup>6-8</sup>

1. Maurer B, et al. Eur Respir J 2018;52:OA1940; 2. Data on file, Verona Pharma; 3. Franciosi LG, et al. Lancet Respir Med 2013;1:714-27; 4. Singh D, et al. Eur Respir J 2018;52:1801074; 5. Verona Pharma Press Release, January 14, 2019; 6. Donaldson GC, et al. Respir Res 2013;14:79; 7. Ke X, et al. Int J Chron Obstruct Pulmon Dis 2016;11:1689-703; 8. Müllerová H, et al. PLoS One 2014;9:e85540.



# Phase 2: Improvement in both FEV1 and residual volume when inhaled on top of two bronchodilators

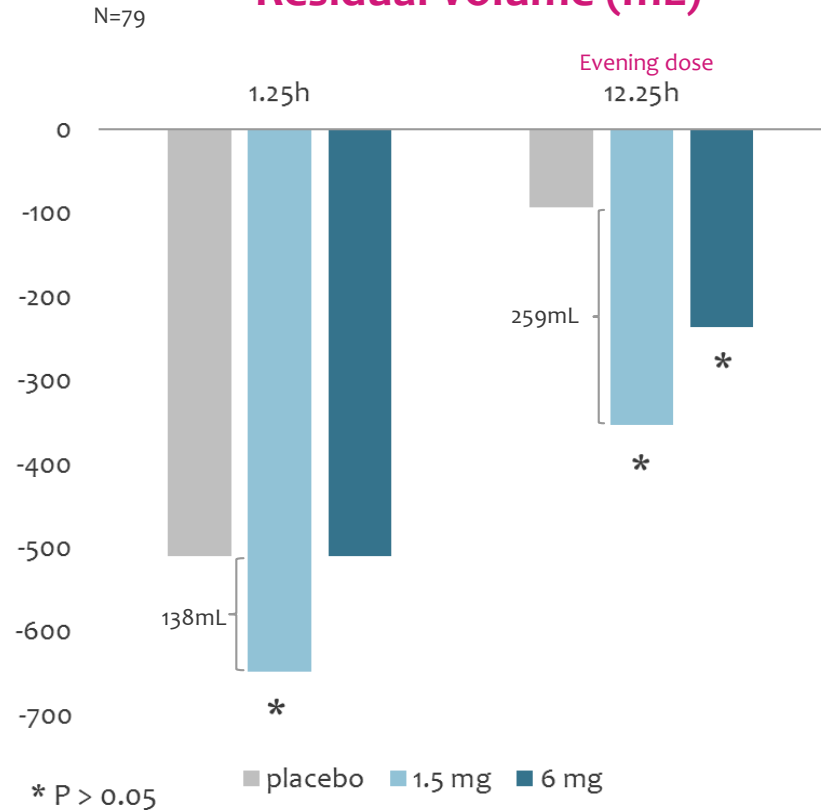
## Lung function FEV1 (mL)<sup>#</sup>



<sup>#</sup> FEV1 (mL) Change from Baseline on Day 3  
 Day 3 morning Peak FEV1, primary endpoint (not statistically significant)

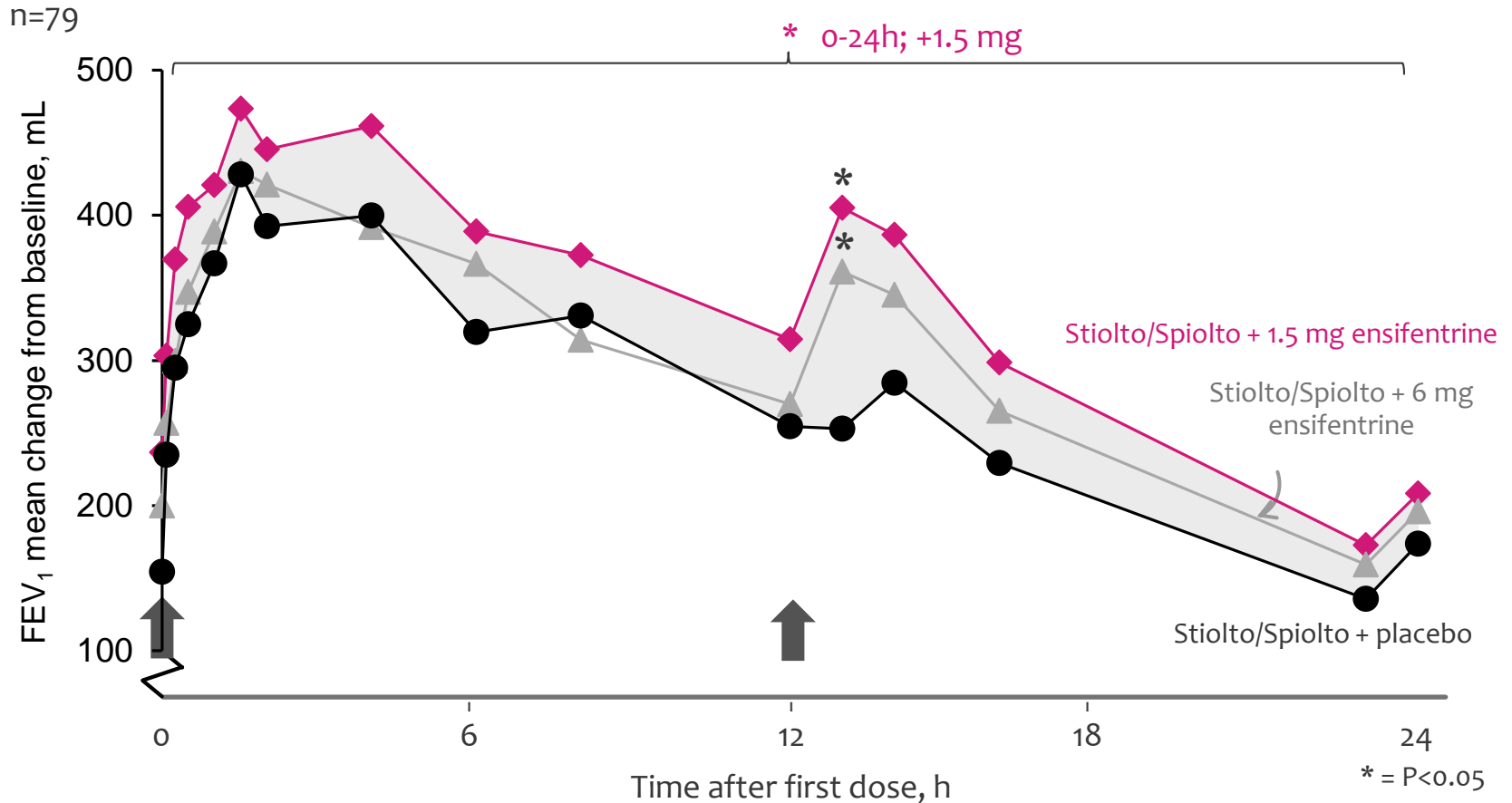
28% of patients used triple therapy (LAMA, LABA, ICS)

## Residual Volume (mL)



Potential to improve symptoms in patients with no further maintenance options

# Phase 2, Day 3: Significant additional lung function improvement over 24 hours on top of dual/triple COPD therapy

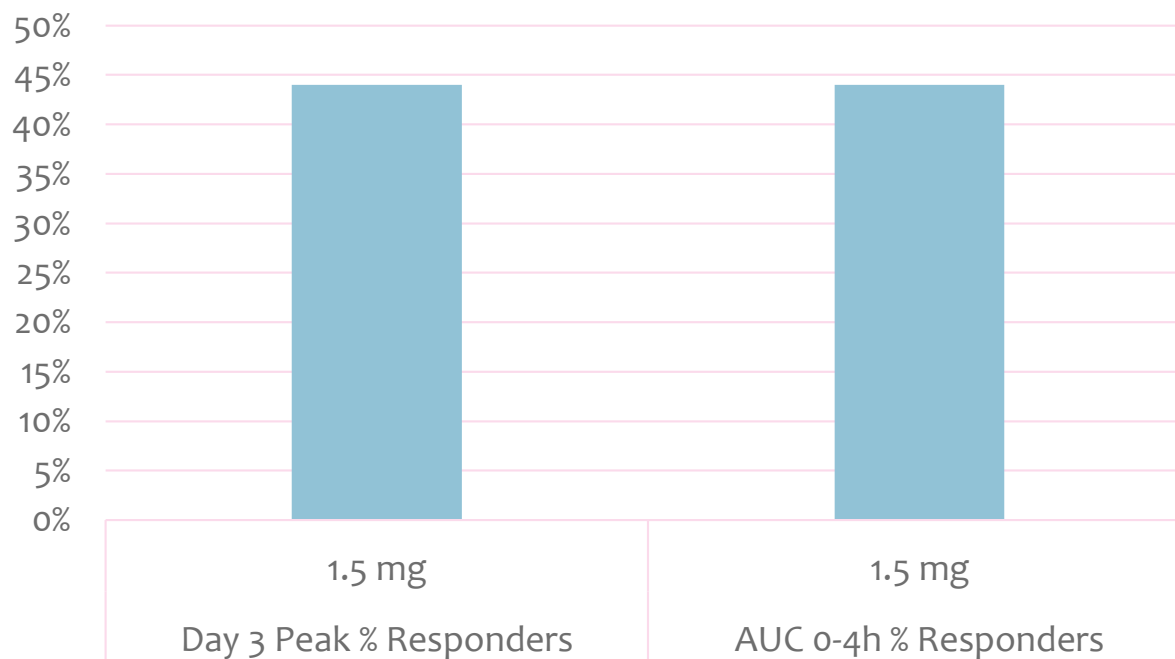


**Significant ~50 to 130 mL additional improvement in FEV<sub>1</sub> through 24 hours when 1.5 mg dose is added on to dual/triple therapy**

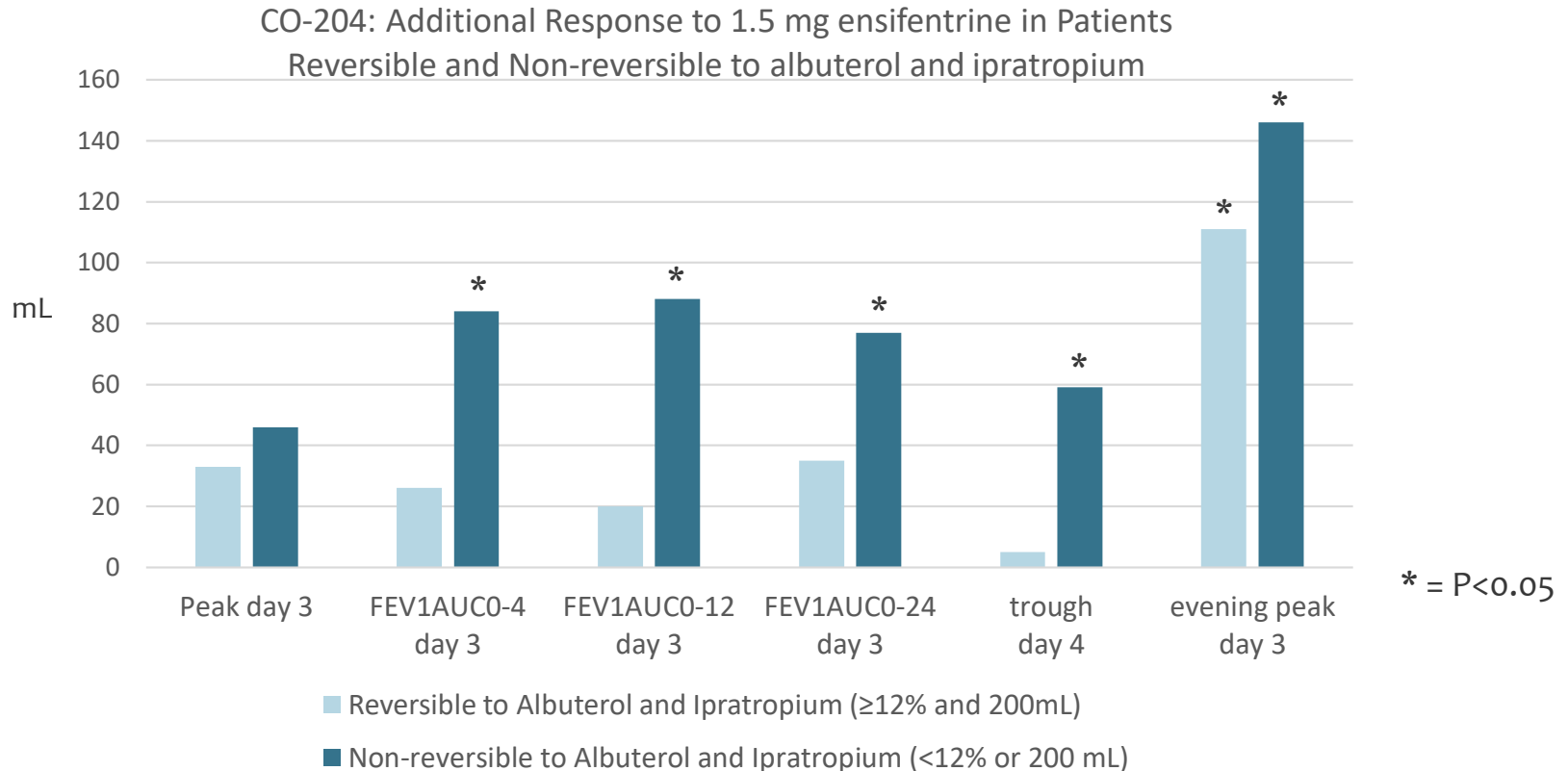


# More than 40% of patients showed >100 ml improvements in FEV1 when added-on to dual/triple therapy

CO-204: % of Patients with  $\geq 100$  mL Increase in FEV1 vs Placebo



# Patients poorly responsive to standard $\beta_2$ -agonist and muscarinic antagonists showed increased response to ensifentrine

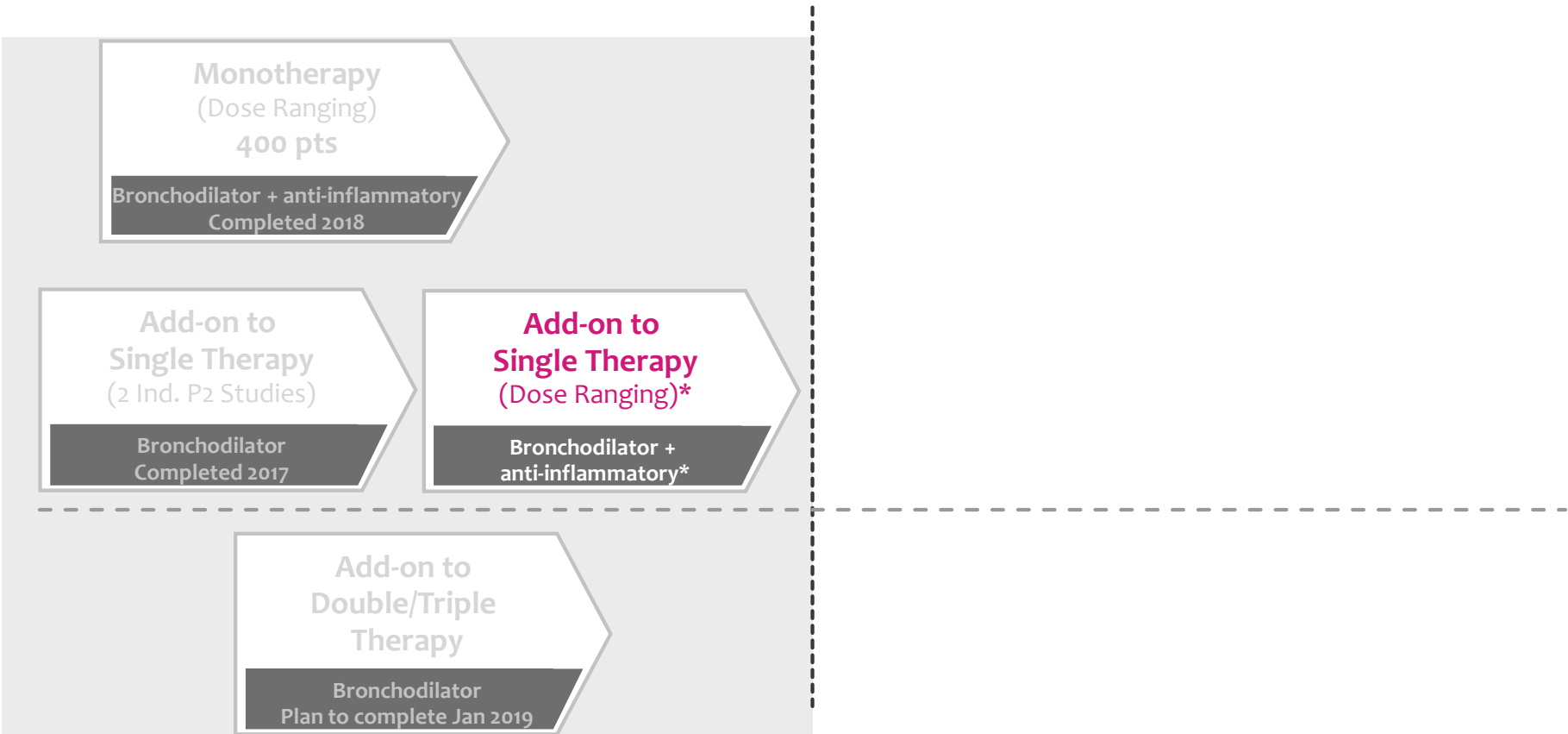


**Potential to include symptomatic COPD patients on dual/triple therapy in Phase 3 program**



# Nebulized ensifentrine: Advancing towards Phase 3

## Phase 2: Establish activity + profile



\* Results expected in 4Q 2019

↑  
End of Phase 2 Meeting  
with FDA, target H1 2020

# Phase 2b 4 week study as add-on to tiotropium to inform EOP2, Ph3 and commercial positioning

## Assumptions

- **Purpose:** Investigate dose response of ensifentrine in moderate to severe COPD patients who are symptomatic despite treatment with tiotropium
  - **Facilitate dose selection for Phase 3** (0.375, 0.75, 1.5 and 3 mg vs placebo)
- **Population:** Moderate to severe COPD
  - **Patients will be required to be symptomatic** at randomization; mMRC  $\geq 2$
  - Stable tiotropium as required background therapy (2-week run-in on tiotropium Respimat)
- **Key Endpoints:** FEV1 (peak, AUC, trough), E-RS symptoms

# Nebulized ensifentrine: Advancing towards Phase 3

**Phase 2:** Establish activity + profile  $\longrightarrow$  **Phase 3:** Regulatory and positioning

## A. Potential pivotal studies: Design and endpoints based on Ph2

2 trials of 6 month duration,  
one with 6 month safety  
extension

-  
None or single bronchodilator  
background

-  
Lung function (FEV<sub>1</sub>),  
symptom improvement,  
explore exacerbations in  
pooled data

## B. Planned positioning study for physicians and payors

Add-on treatment to  
single and dual  
bronchodilators in COPD

Monotherapy  
(Dose Ranging)  
400 pts

Bronchodilator + anti-inflammatory  
Completed 2018

Add-on to  
Single Therapy  
(2 Ind. P2 Studies)

Bronchodilator  
Completed 2017

Add-on to  
Single Therapy  
(Dose Ranging)\*

Bronchodilator +  
anti-inflammatory\*

Add-on to  
Double/Triple  
Therapy

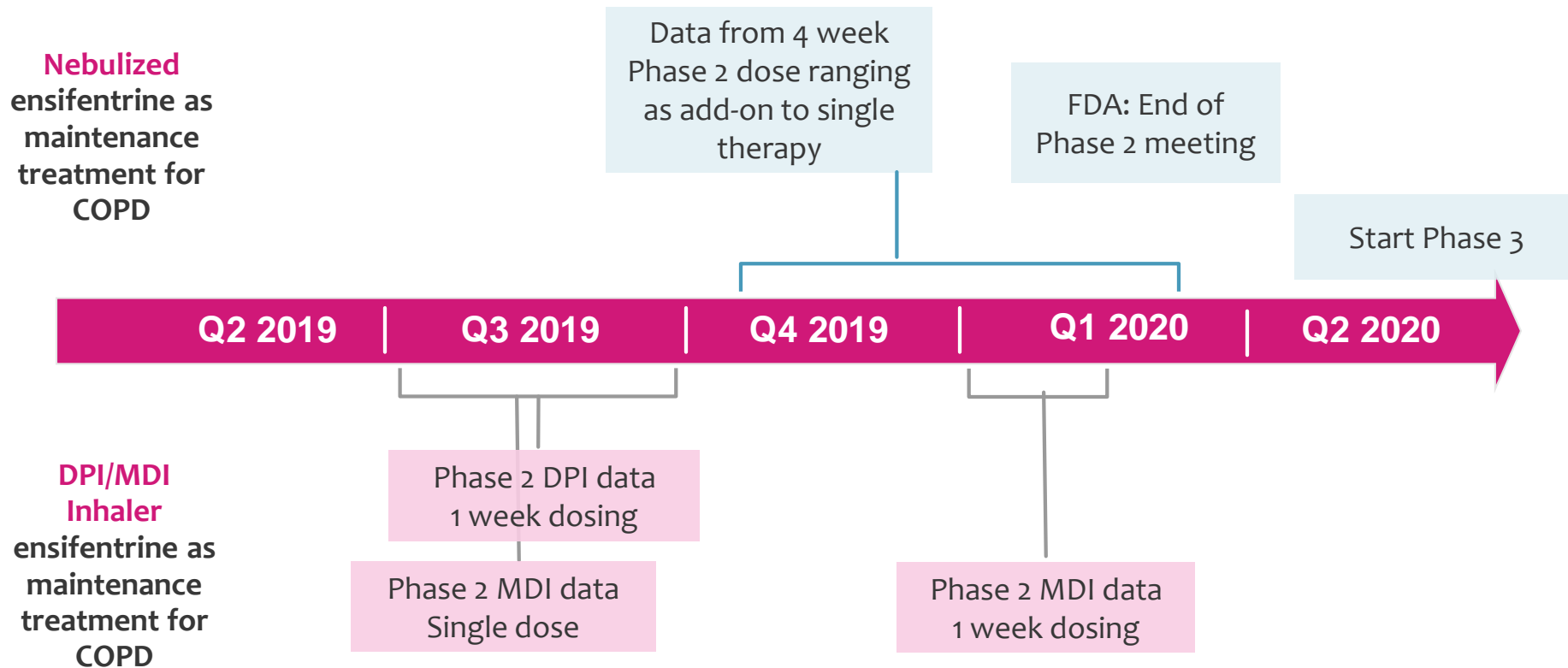
Bronchodilator  
Plan to complete Jan 2019

End of Phase 2 Meeting  
with FDA, target H1 2020

\* Results expected in 4Q 2019



# 2019 - multiple significant milestones as ensifentrine advances towards Phase 3 in 2020



Simple Phase 3 trial design, similar to Phase 2b studies,  
to increase likelihood of regulatory success

## Safety:

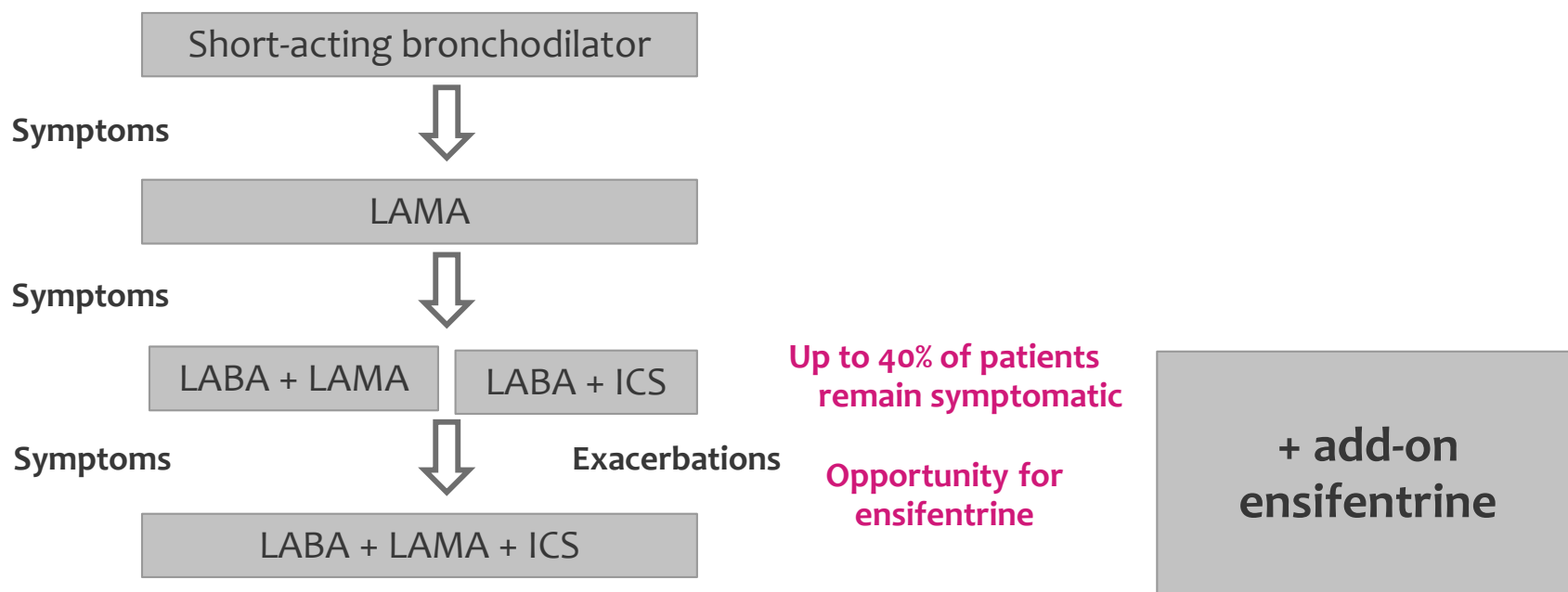
- Ensifentrine well-tolerated at all dose levels
- AEs generally balanced between ensifentrine and placebo
- No GI disturbance observed

## Cardiac Safety:

- No consistent change in systolic or diastolic blood pressure
- Small, not clinically relevant increase in heart rate at higher doses:
  - Approx. 3 bpm with 6 mg dose
  - 6 bpm at ensifentrine 24 mg dose (4x over highest dose in Phase 2b study)
- No QTc prolongation
- No changes in 24 hour Holter Monitors (450 COPD patients, repeat dose studies)
- No changes in ECG parameters
- No consistent or dose-related increase in cardiac AEs in completed clinical trials

# A new class of treatment in COPD: how could ensifentrine alter the treatment paradigm?

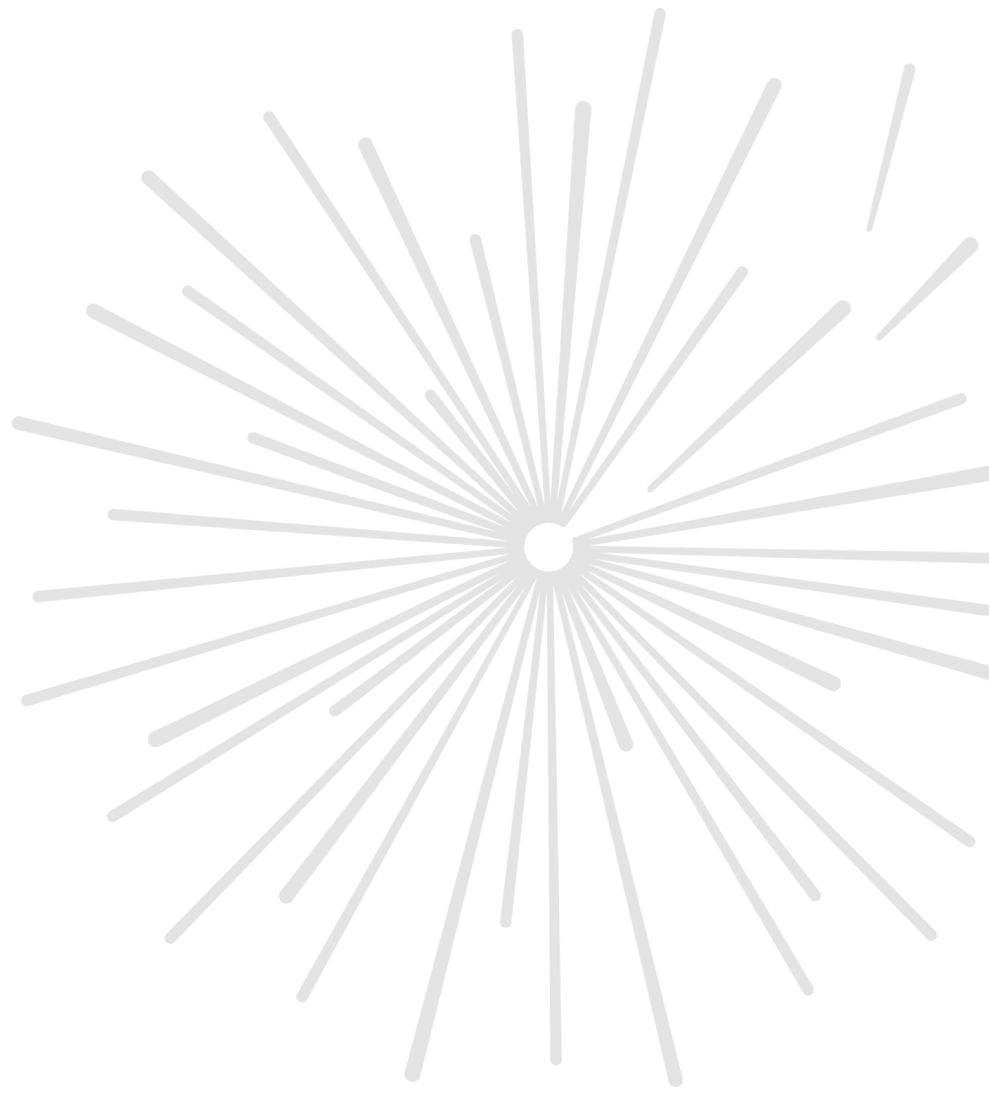
- Many treated patients still require symptomatic improvement – there is room to do more
- Ensifentrine may provide a new anti-inflammatory option
- Ensifentrine offers bronchodilator and anti-inflammatory properties in one compound







# Speaker Panel Q&A



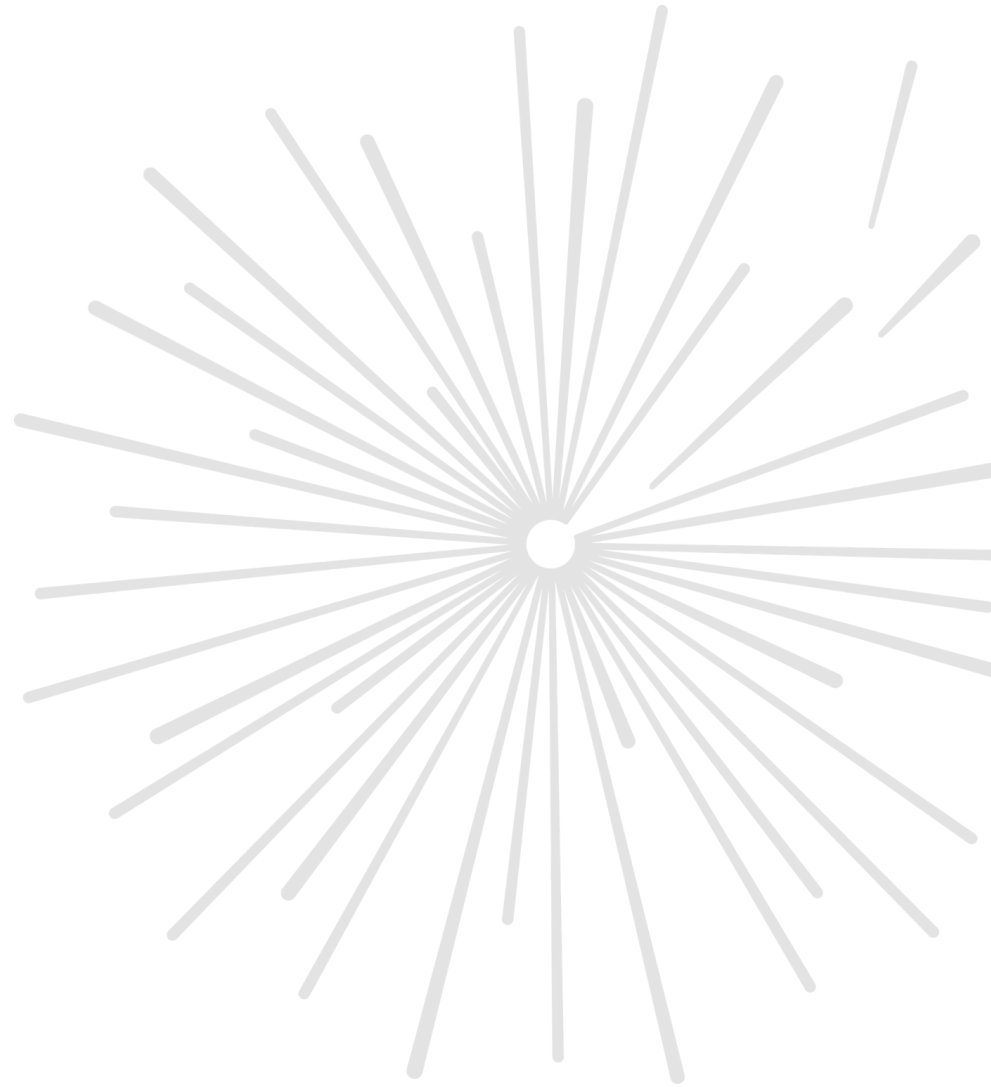
# Agenda

Time	Details
09:00 – 09:15 am	<b>Welcome</b> ( <i>Jan-Anders Karlsson, CEO, Verona Pharma</i> )
09:15 – 09:30 am	<b>The Patient Perspective, British Lung Foundation</b> ( <i>Chris Warburton, Patient Advocate</i> )
09:30 – 10:30 am	<b>Clinical Expert Perspective</b> ( <i>chaired by Brian Leaker, Royal Free Hospital</i> ) <ul style="list-style-type: none"><li>• COPD treatment challenges/unmet need (<i>Robert Wise, M.D. 15 min</i>)</li><li>• US payer landscape (<i>15 min</i>)</li><li>• Treatment pipeline (<i>Gerard Criner, M.D. 15 min</i>)</li><li>• Ensifentrine clinical progress (<i>Kathleen Rickard, CMO 15 min</i>)</li></ul>
10:30 – 11:15 am	<b>Speaker Panel Q&amp;A</b>
11:15 – 11:30 am	<b>Close</b> ( <i>Jan-Anders Karlsson</i> )



## Summary & close

**Jan-Anders Karlsson**  
CEO, Verona Pharma





# Ensifentrine: A promising novel treatment for patients with COPD

Data collected to date indicates:

- ✓ First-in-class PDE<sub>3</sub>/4 inhibitor with **bronchodilator and anti-inflammatory effects**, and well tolerated
- ✓ Improves symptoms in **moderate to severe**, symptomatic COPD patients on twice daily dosing
- ✓ Improves lung function in patients taking maximum bronchodilator treatment with dual/triple therapy
- ✓ Targeting FDA End of Phase 2 Meeting **H1 2020**
- ✓ Subsequently, **advancing nebulized ensifentrine** into Phase 3 trials in patients symptomatic despite using standard COPD medications