

# Verona Pharma



## Breathtaking science

Developing respiratory drugs  
to improve health and quality of life

[www.veronapharma.com](http://www.veronapharma.com)

February 2018



# 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 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 final prospectus filed with the Securities and Exchange Commission (the “SEC”) on April 28, 2017 relating to the Company’s Registration Statement on Form F-1 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.



# Verona Pharma



**Clinical-stage** biopharma focused on developing & commercializing **innovative therapeutics** for treatment of **respiratory diseases** with significant **unmet need**

Inhaled dual inhibitor of  
enzymes PDE3 and PDE4










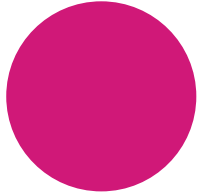


**RPL554**

Current Focus:  
COPD and CF

Potential first novel class of bronchodilator in decades  
Bronchodilator + anti-inflammatory agent in single compound



# RPL554: Rich Product Pipeline

Indication	Delivery	Pre-Clinical	Phase 1	Phase 2	Phase 3	Addressable Market Opportunity
<b>COPD</b> Maintenance (Home)	 Nebulizer					
<b>COPD</b> Acute (Hospital)						
<b>Cystic Fibrosis</b>						
<b>COPD</b> Maintenance (Home)	<b>MDI</b> 					
<b>COPD</b> Maintenance (Home)	<b>DPI</b> 					

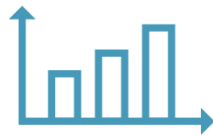
RPL554 also has applications in other significant respiratory diseases such as asthma.



# Clear Success Drivers



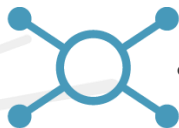
- Large patient population
- Significant unmet medical need
- Little innovation in COPD



- Robust clinical data
- validated endpoints (FEV1)
- 10 P1 and P2a trials, 400+ subjects treated



- Significant KOL interest and support
- Novel Mode of Action



- Multiple respiratory indications
- Global commercialization rights
- Near term Phase 2b data

**Significant  
Market opportunity**

**Clear, efficient  
pathway to  
Approval**

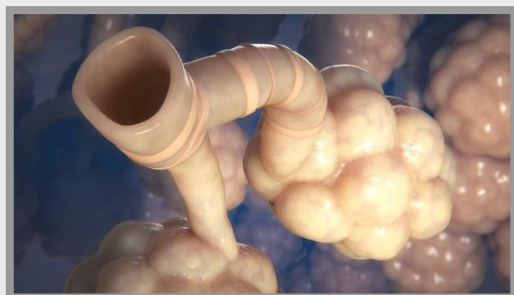
**Strong potential for  
Adoption**

**Significant outlook for  
Growth**

# COPD: Devastating Disease, Affecting Many

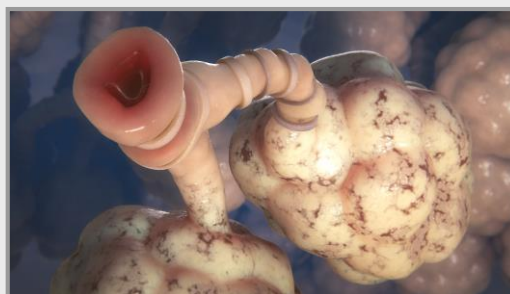


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CAUSES

Smoking  
Air pollution



Inflames and constricts  
airways (bronchioles) and  
can damage alveoli

PROGRESSIVE  
DISEASE

No cure



“Take a deep breath, blow out 20%  
now walk around,  
holding the rest forever.”  
COPD Sufferer



**Affects Many**

**Increasing** prevalence  
**384M** global sufferers  
**3rd** leading cause of death in U.S.

Sources: IMS, CDC



**Very Costly**

**Many** exacerbations and hospitalizations  
**~\$50B** projected annual medical costs by  
2020 (U.S. alone)  
**\$10B+** annual global sales of COPD drugs

# COPD Sufferers Require Maintenance and Acute Treatment



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## Maintenance (Home)



### U.S. alone: 24M living with COPD

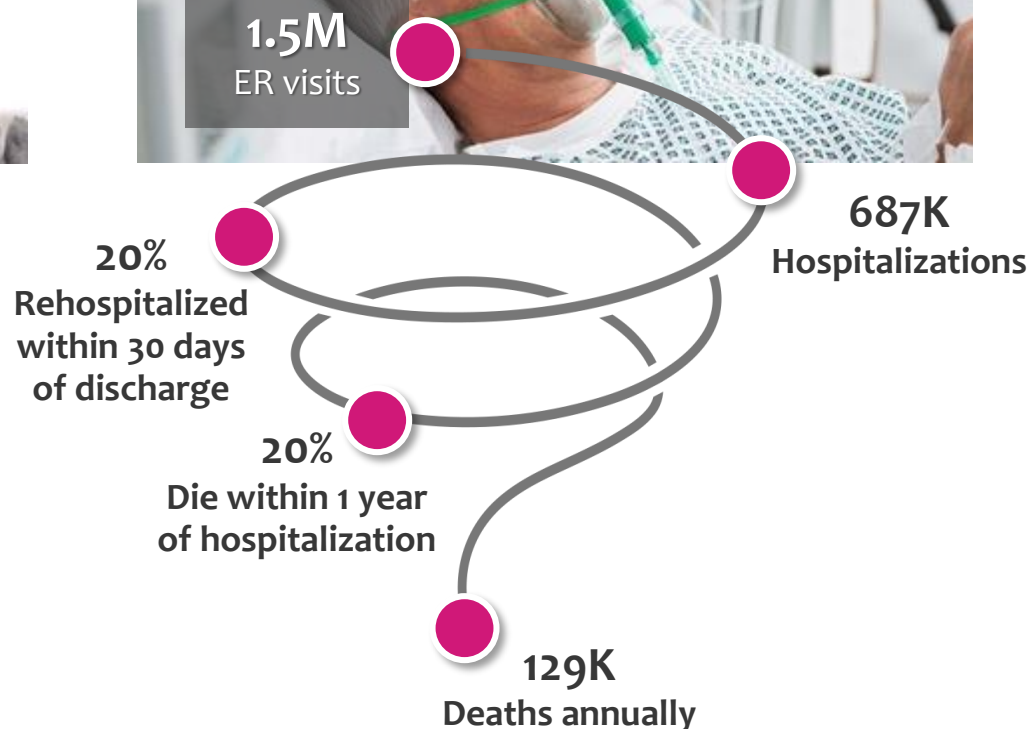
- 15M diagnosed and under treatment
- Approximately 2M severe/very severe

### Treatment goals:

- Improved lung function
- Improved quality of life
- Prevent exacerbations

Note: U.S. only data

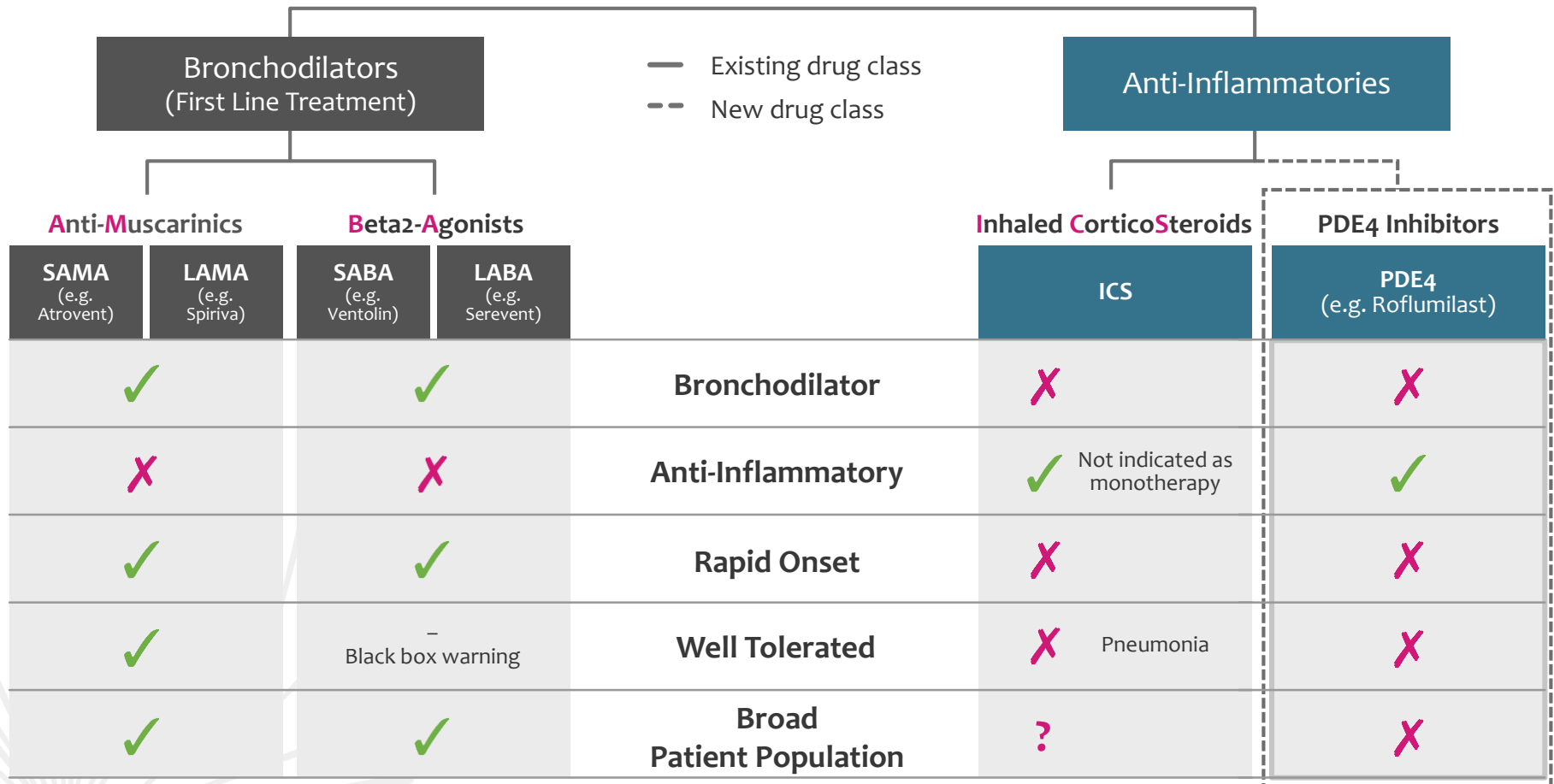
## Acute (Hospital)



# Current Therapies: Little Innovation and Many Limitations

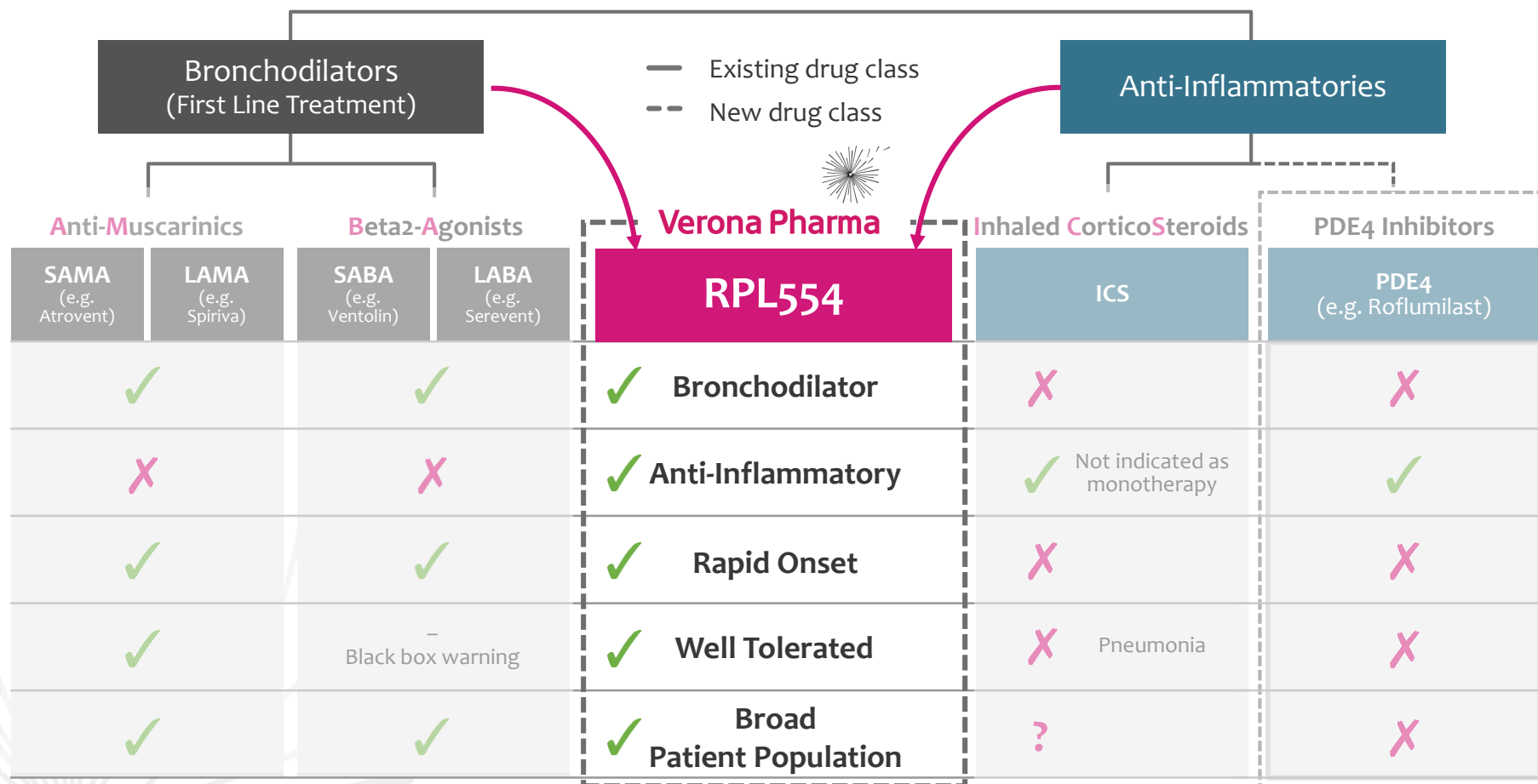


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Many patients treated with approved COPD drugs/combinations do not experience significant improvements in quality of life and continue to suffer from significant symptoms

# RPL554: Potential to Address Limitations of Current Therapies



Many patients treated with approved COPD drugs/combinations do not experience significant improvements in quality of life and continue to suffer from significant symptoms

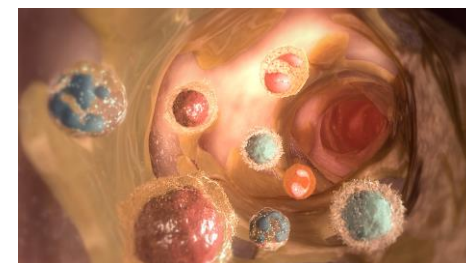
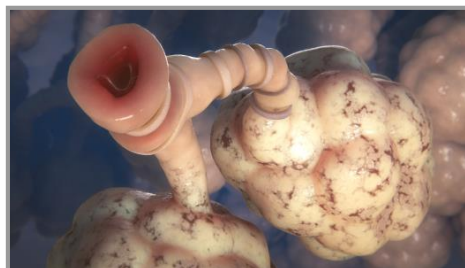
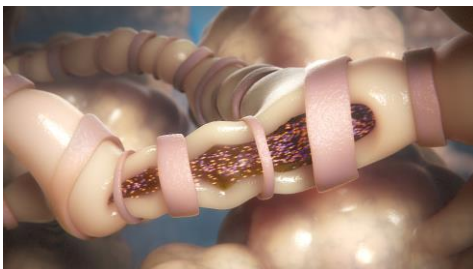
# RPL554 First-in-Class Candidate: Bronchodilator and Anti-inflammatory in a Single Compound



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**RPL554**  
Dual PDE3 and PDE4 enzyme inhibitor

Impacts 3 Key Mechanisms in Respiratory Disease:



## Airway Smooth Muscle



PDE3, PDE4

Relaxation



Increased bronchodilation

## Inflammatory Cells



Neutrophils  
PDE4



Eosinophils  
PDE4



Epithelial cells  
PDE3, PDE4



Lymphocytes  
PDE3, PDE4



Macrophages  
PDE3, PDE4



Fibroblasts  
PDE4



Increased anti-inflammatory effects

## Epithelial Cells



PDE3, PDE4

CFTR Activation

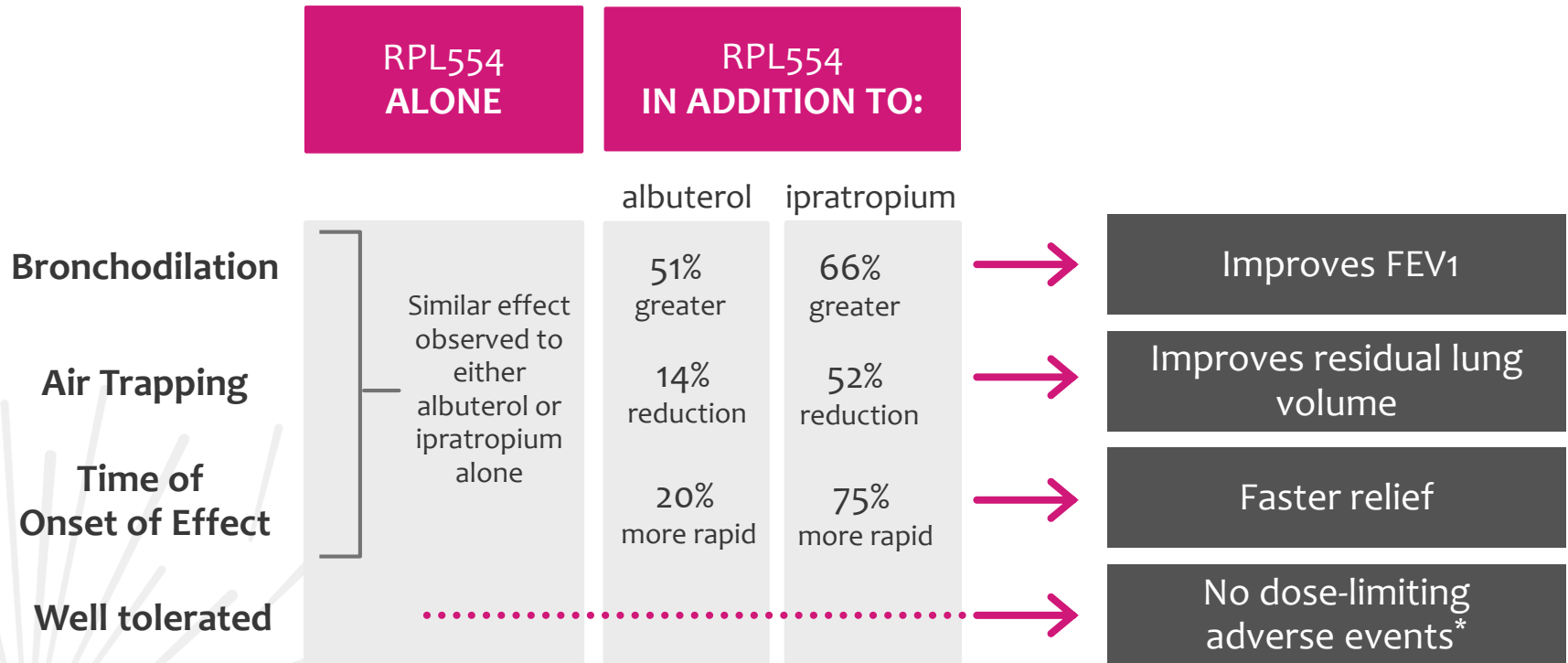


Increased mucociliary clearance



# RPL554: Significantly De-Risked Add-on Effect Reproduced in Independent Study

## Key Findings



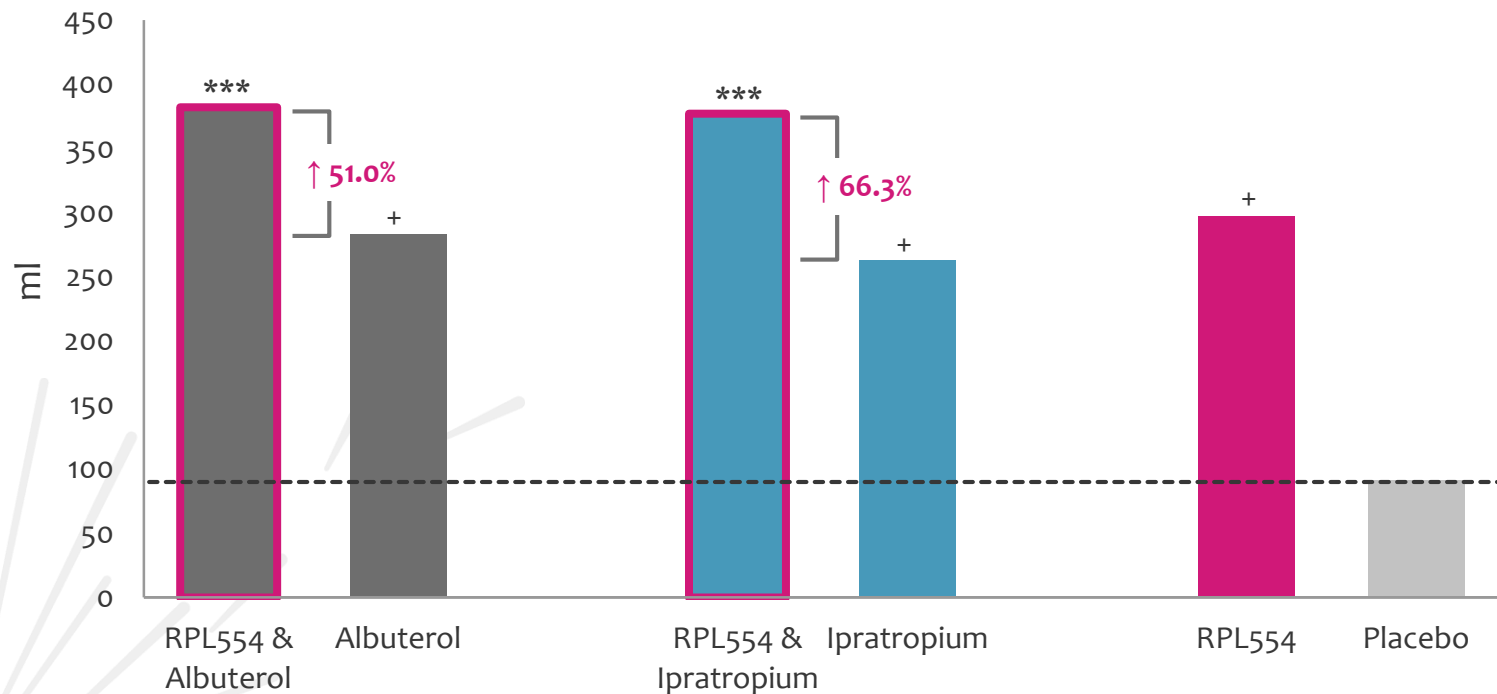
\*in completed clinical trials  
Source: RPL554-009-2015

**Phase 1 and 2a:** 10 Clinical Trials, 324 Subjects

# RPL554: Significantly Improves Lung Function in COPD Patients

## Peak Change from Baseline in FEV<sub>1</sub>(ml)

N=36



Source: RPL554-009-2015

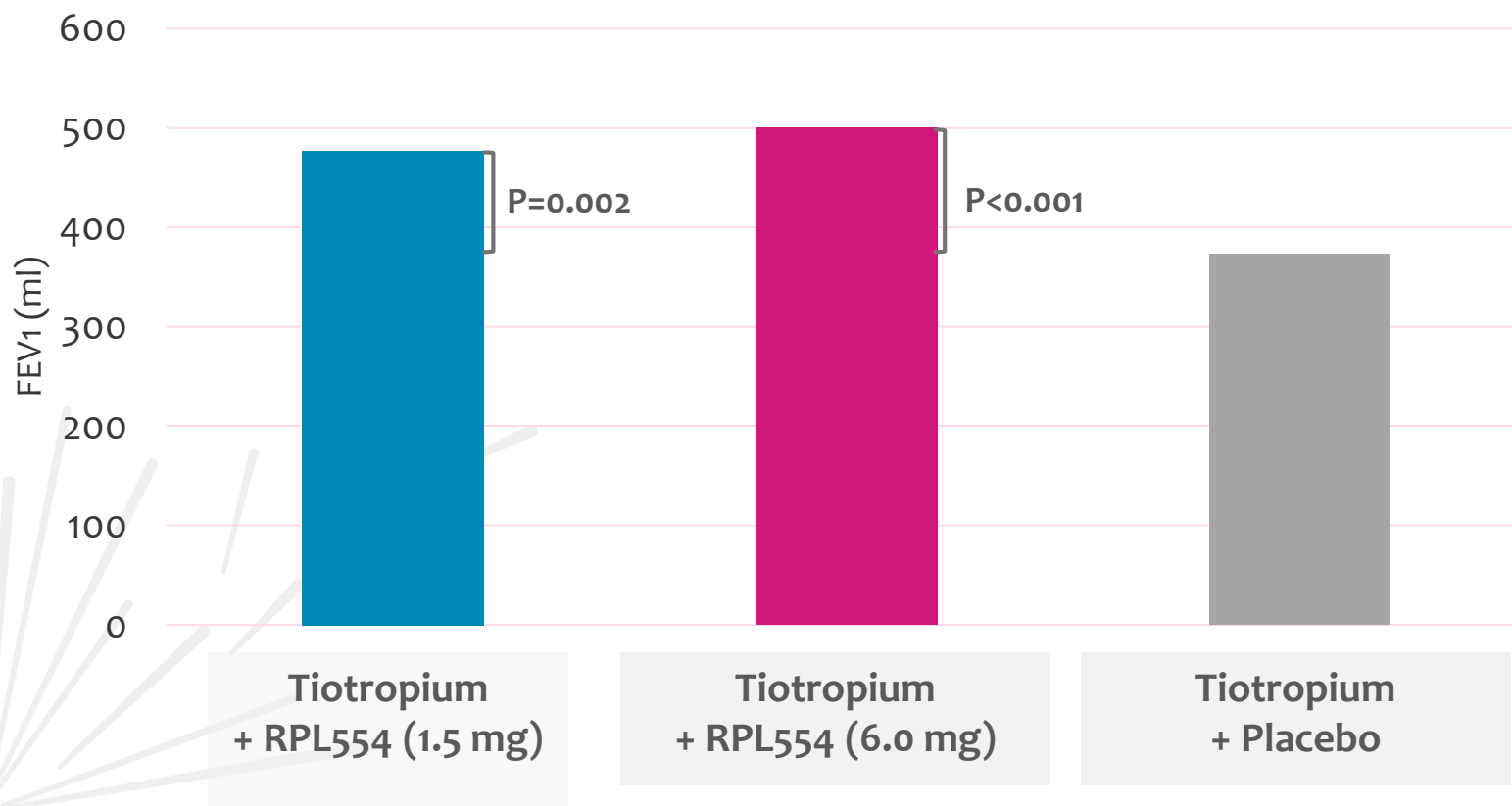
+ p < 0.001 vs placebo

\*\*\* p < 0.001 vs. albuterol or ipratropium alone

# RPL554: Significant Additional Bronchodilator Response when Inhaled on Top of Tiotropium (Spiriva)

## Peak Change from Baseline in FEV<sub>1</sub> (ml) on Day 3

N=27-28



Source: RPL554-CO-202  
P values vs placebo

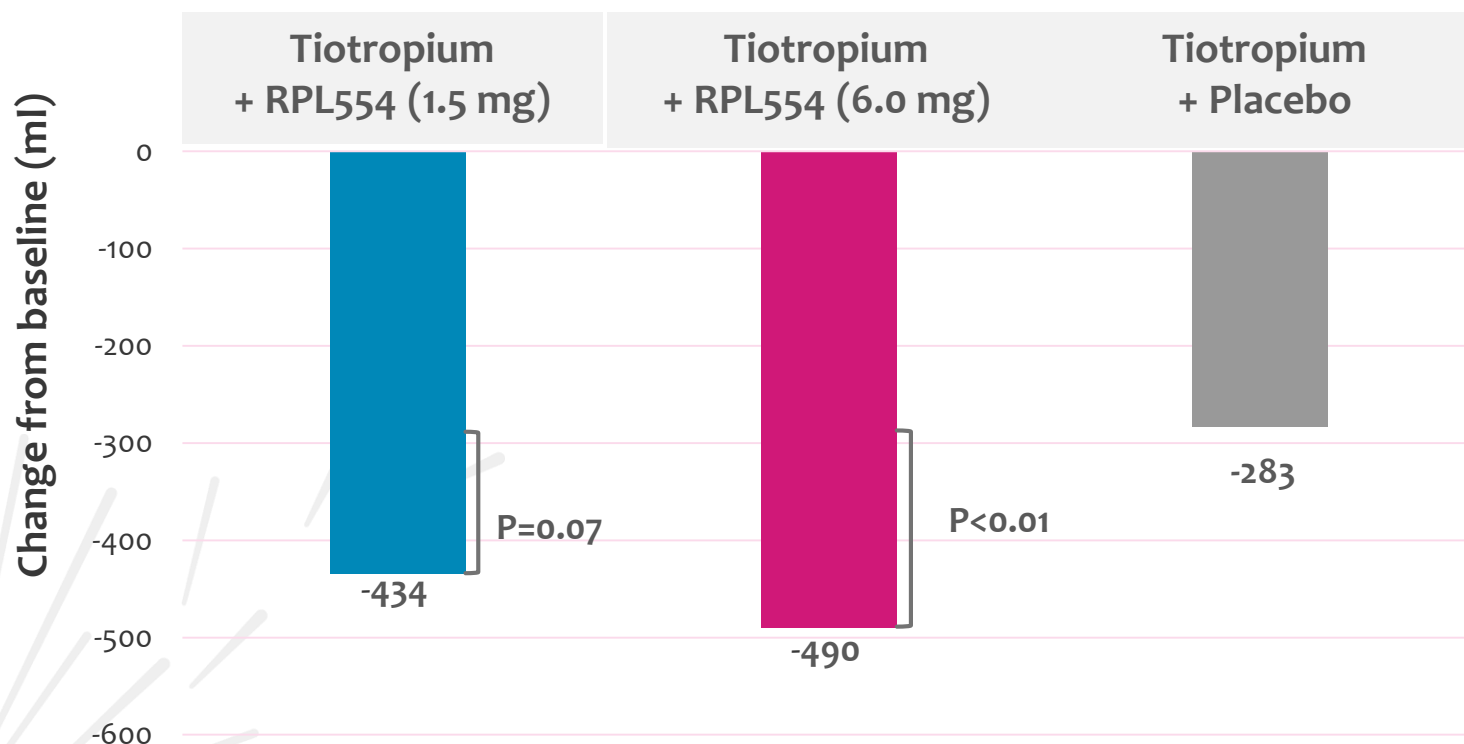
# RPL554: Marked Reduction in Hyperinflation, Residual Volume (RV, air trapping) as Compared to Tiotropium Alone



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## Reduction in Hyperinflation (ml) on Day 3

N=27-28



Reduction of hyperinflation is typically correlated with improvement of shortness of breath

Source: RPL554-CO-202  
P values vs placebo

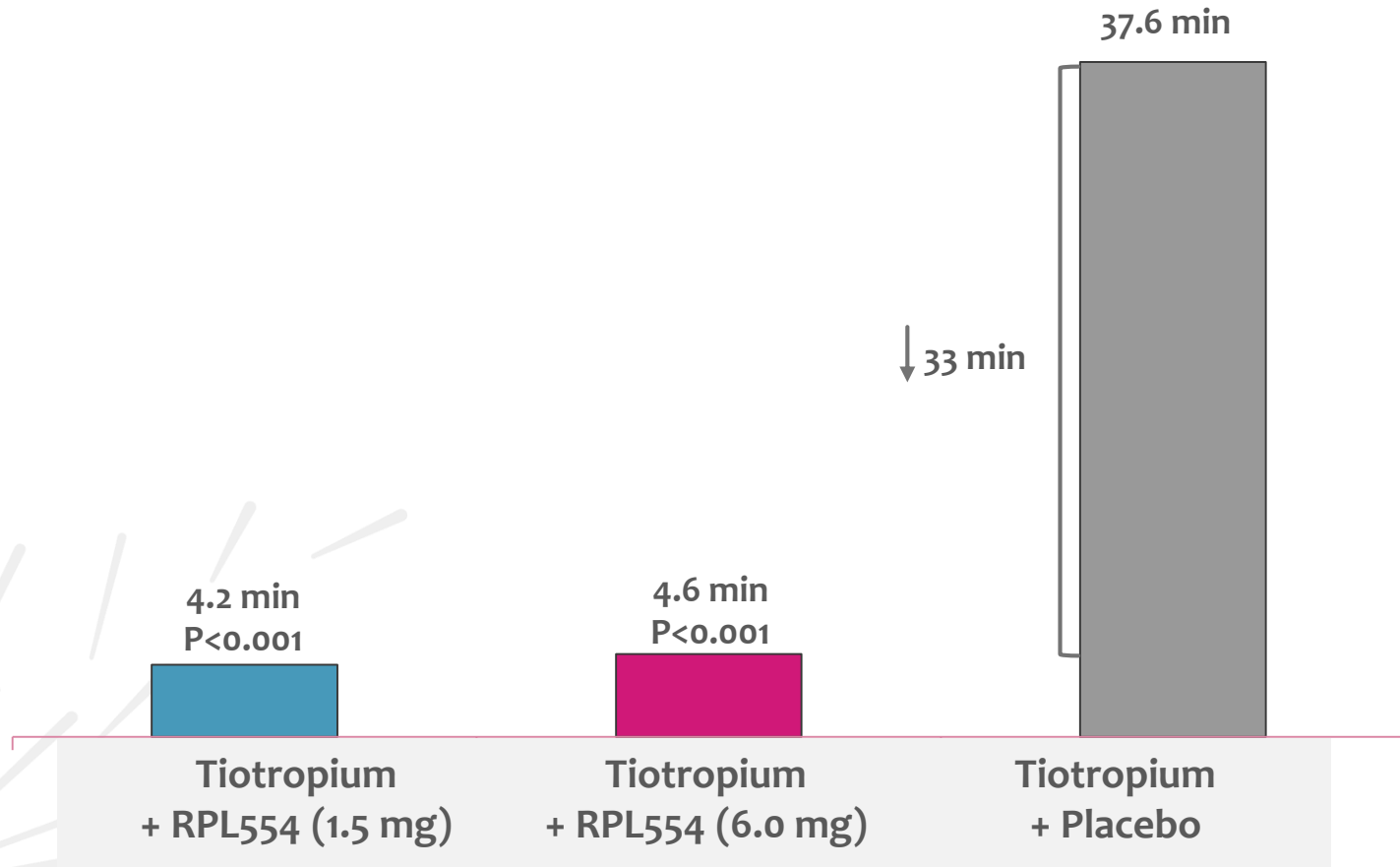
# RPL554: Combination Increases Speed of Onset of Bronchodilator Effect



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Median Time to Onset ( $\geq 10\%$  improvement in FEV<sub>1</sub>; mins) on Day 3

N=27-28



**Reinforces the potential of RPL554 in treating acute exacerbations of COPD**

Source: RPL554-CO-202  
P values vs placebo



# RPL554: Well-Tolerated in Completed Clinical Trials

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	Placebo (n=31)	RPL554 (n=31)	RPL554 + Albuterol (n=31)	Albuterol (n=32)	RPL554 + Ipratropium (n=33)	Ipratropium (n=32)
<b>Any Treatment Related TEAE</b>	8 (25.8%)	5 (16.1%)	8 (25.8%)	11 (34.4%)	10 (30.3%)	6 (18.8%)
Cough	4 (12.9%)	3 (9.7%)	5 (16.1%)	7 (21.9%)	6 (18.2%)	2 (6.3%)
Dizziness	1 (3.2%)			2 (6.3%)	1 (3.0%)	1 (3.1%)
Dyspnea		1 (3.2%)		2 (6.3%)	1 (3.0%)	1 (3.1%)
Headache	1 (3.2%)	1 (3.2%)		1 (3.1%)		
Palpitations	1 (3.2%)					
Rhinorrhea	2 (6.5%)		1 (3.2%)			

Source: RPL554-009-2015, COPD add-on study; number of subjects with adverse reactions following single dosing of RPL554 with the suspension formulation; events with an unlikely, possible or definite relationship are presented.

## Across All Studies

No SAEs or AEs of concern

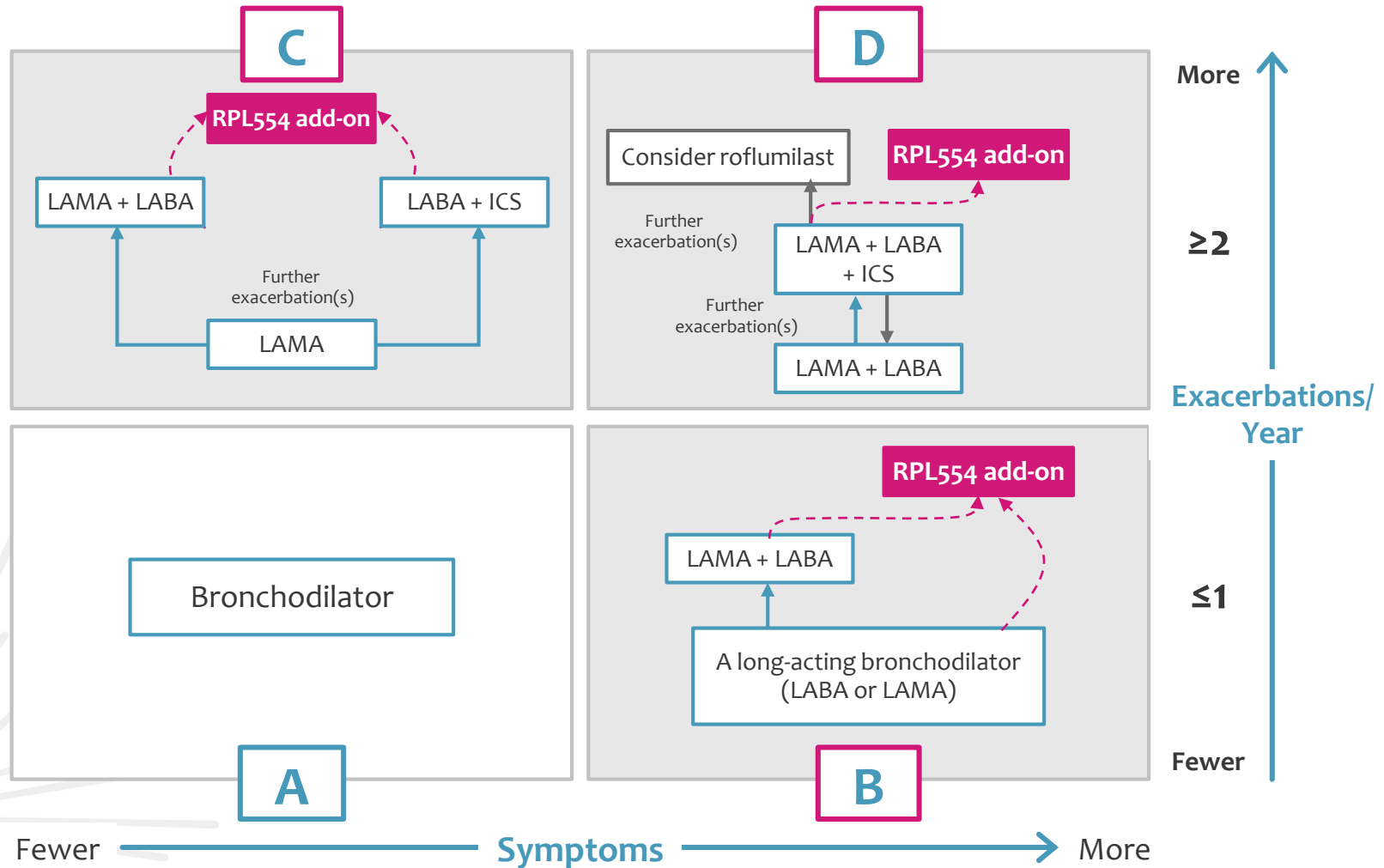
No PDE4 inhibitor-like AEs

# RPL554: Potential to Improve Standard of Care Treatment for More Severe Patients



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Based on GOLD COPD Guidelines 2017





# CF: A Devastating Orphan Disease



## Population:

- Most common fatal inherited disease in U.S.
  - Incidence: ~70K globally; ~30K patients in U.S.

## Cause:

- Mutations in gene that encodes CFTR protein

## Symptoms:

- Inability to clear thickened mucus, impaired lung function and persistent lung infection

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## Consequences:

- Frequent exacerbations and hospitalization
- No cure
- Median age of death – 37 years

**RPL554: Potential to Provide Treatment Independent of CF Mutation Status**



# RPL554: Clinical Trials in U.S. and Europe

## Study

## Study Design

## Data/Milestones

### Studies completed – top line data reported Sept 2017

#### **COPD Phase 2a:** **Add-on Therapy to Tiotropium**

- 30 subjects
- Age: 40-75; moderate-severe COPD
- 2 doses + placebo, 3-way cross-over

- FEV1 improvement of 130mL on top of Spiriva

#### **COPD Phase 1:** **PK Study** (Determine Oral Bioavailability)

- 12 healthy subjects
- Single dose

- Low oral bioavailability

### Ongoing – new guidance: top-line data available sooner

#### **CF Phase 2a:** **PK & PD Trial in Adult CF Patients**

- Up to 10 patients
- Single dose

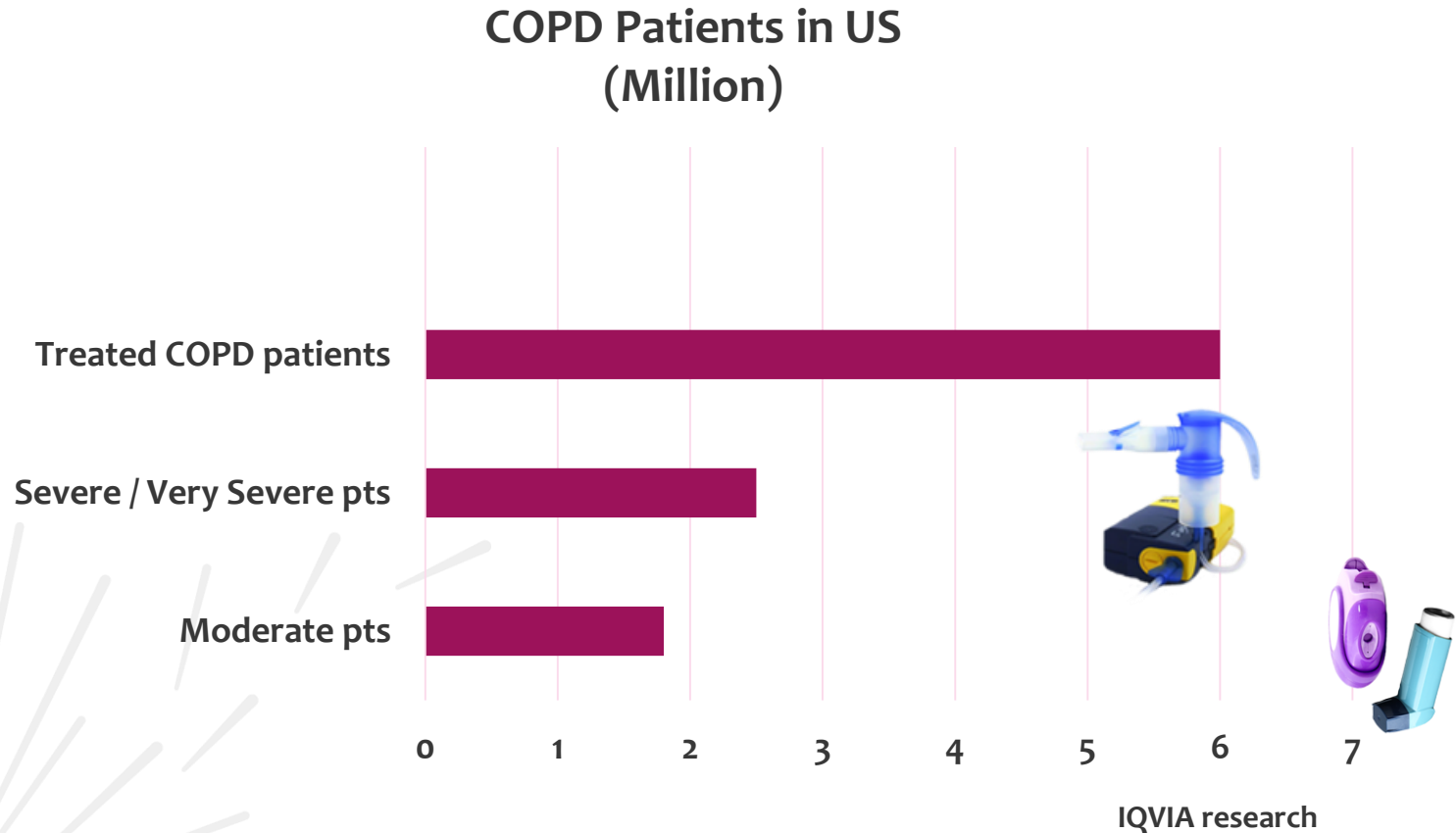
- Fully enrolled
- **Top-line data now in 1Q18** (previously 1H18)

#### **COPD Phase 2b, 4 week:** **Maintenance Treatment;** **No background therapy**

- Approximately 400 subjects
- Age: 40-75; moderate-severe COPD
- 4 doses + placebo, double-blind

- Fully enrolled
- **Top-line data now early 2Q18** (previously mid-2018)

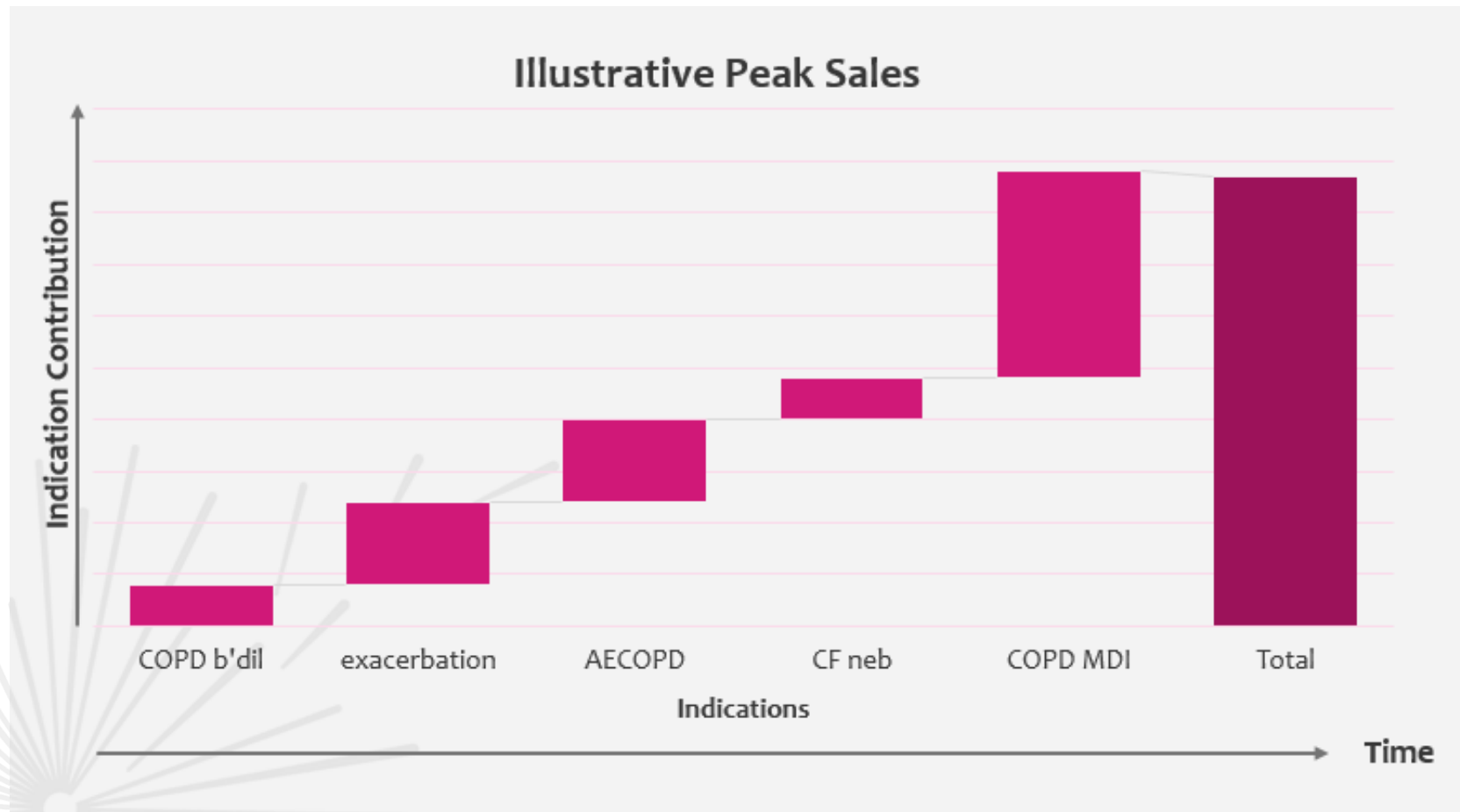
# RPL554: Potential to Improve Standard of Care Treatment for Millions of Patients



# RPL554: Targeting Multiple Indications Allows Earlier Access to Large Markets



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# RPL554 IP Summary

## Patent Portfolio:

- Composition of Matter – granted US, EU, Japan, other; expires 2020
- Polymorphs – granted US, EU, Japan, other; expires 2031
- Formulations, combinations, salt forms, use, manufacturing: granted and pending in US, EU, and other territories; expires 2031 – 2037
- Additional IP opportunities being explored

**Verona Pharma has global rights**

# Financial Overview and Shareholder Register

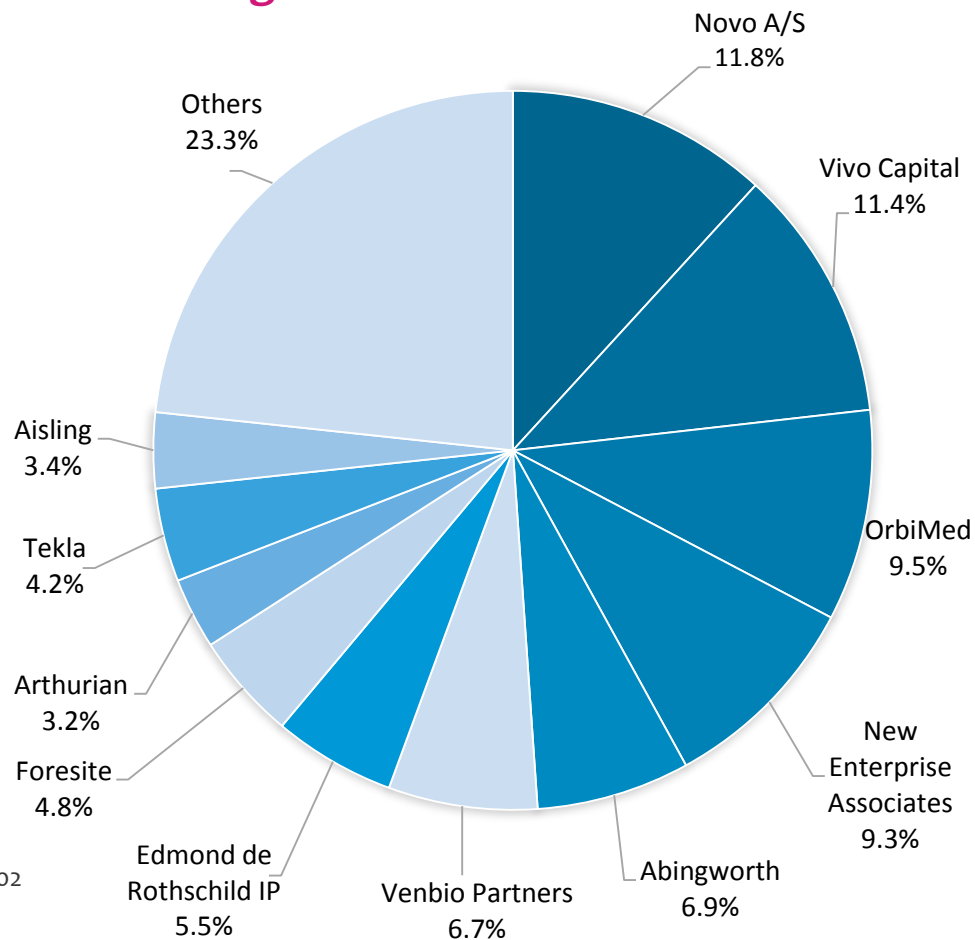
## Financial Overview

Cash and Cash Equivalents	\$114.5M <sup>1</sup> (as of 09/30/2017)
Operating Expenses	\$25.6M <sup>1</sup> (9 Months Ended 09/30/2017)
Total Equity	\$114M <sup>1</sup> (as of 09/30/2017)

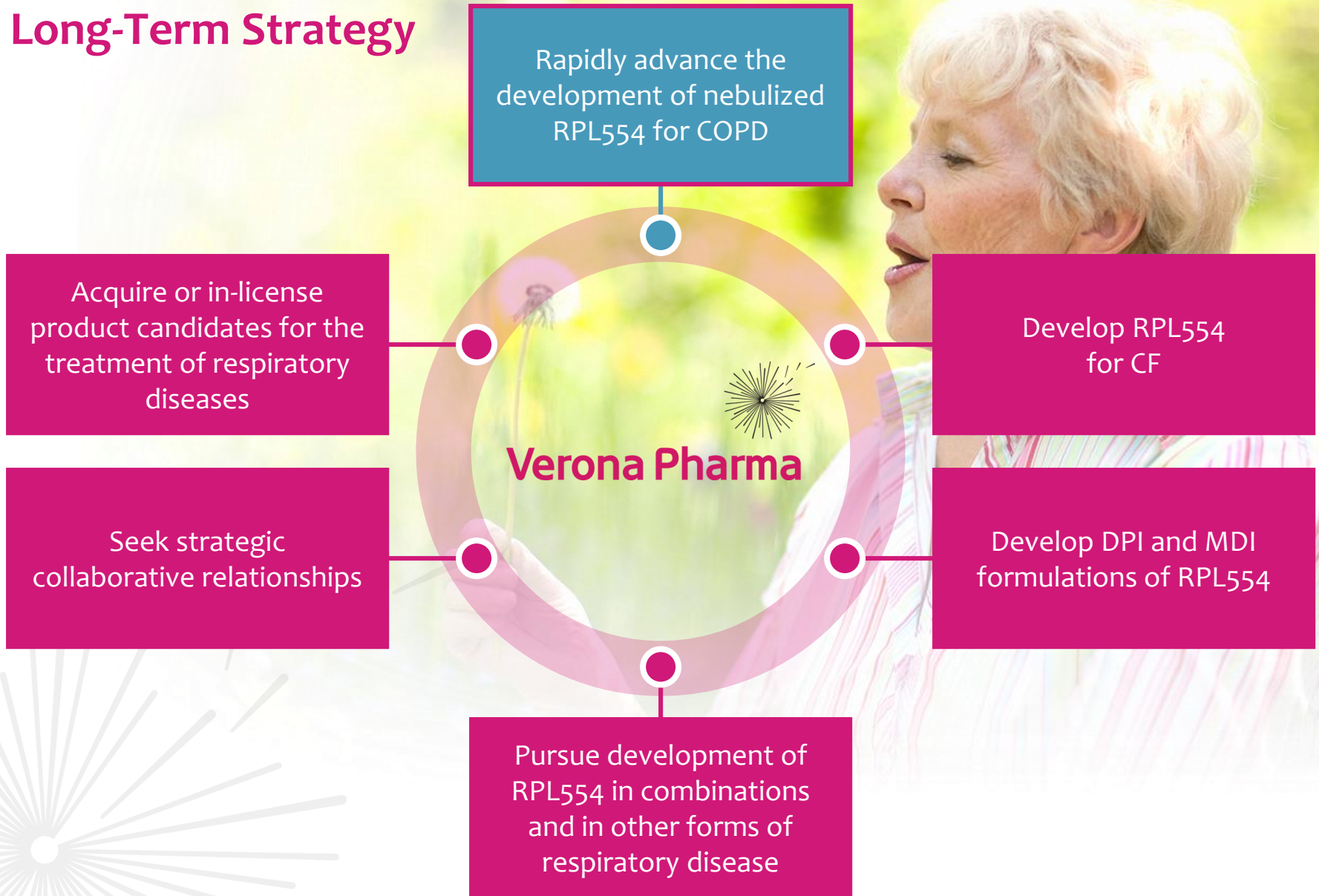
<sup>1</sup>Exchange rate used (US dollars per pound sterling): September 30, 2017 \$1.3402

<sup>2</sup>Based on 126m fully diluted shares, \$15.35 ADS price on September 29, 2017

## Shareholdings



# Long-Term Strategy





# Experienced Management Team and Board

## Management

**Jan-Anders Karlsson, PhD**  
Chief Executive Officer

**Piers Morgan, MA, ACA**  
Chief Financial Officer

**Kenneth Newman, MD, MBA**  
Chief Medical Officer

**Richard Hennings, BSc**  
Commercial Director

**Peter Spargo, PhD**  
SVP CMC

**Claire Poll, LLB**  
Legal Counsel

**Desiree Luthman, DDS**  
VP Regulatory Affairs



## Board

**David Ebsworth, PhD**  
• Ex CEO Vifor Pharma; CEO Galenica

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

**Ken Cunningham, MD**  
• Chair Abzena plc  
• Ex Chair Prosonix; CEO SkyePharma

**Rishi Gupta, JD**  
• Private Equity Partner, OrbiMed

**Mahendra G. Shah, PhD**  
• Managing Director, Vivo Capital  
• Ex Chair CEO, NextWave Pharmaceuticals, First Horizon Pharma

**Andrew Sinclair, PhD**  
• Partner and Portfolio Manager, Abingworth

**Vikas Sinha, CPA**  
• Ex EVP, CFO, Alexion

**Anders Ullman, PhD, MD**  
• Ex Head R&D, Baxter Biosciences; EVP R&D, Nycomed Pharma

## In team's prior lives ...

involved in successful development / commercialization of many of the drugs used to treat COPD

including





# Large Growing COPD Drug Market

## Top U.S. COPD Drug Sales, 2016\*

Drug	Type	Launch	Expiry	Sales (2016)*
Spiriva	LAMA	2002	2018	\$1,900M
Advair	LABA / ICS	1998	2016	\$1,300M
Symbicort	LABA / ICS	2000	2014	\$700M
Atrovent / Ipratropium	SAMA	2005	2007	\$200M
Breo Ellipta	LABA	2013	2021	\$100M
Daliresp	PDE4	2011	2020	\$131M
Brovana** (neb only)	LABA	2006	2021	\$423M
Perforomist** (neb only)	LABA	2007	2021	\$178M

Source IMS

\*Year from Q2 2016

\*\*Only approved in COPD, any off-label use in asthma expected to be limited

## WW COPD Sales

