



# Verona Pharma



## Breathtaking science

Developing respiratory drugs  
to improve health and quality of life



17th Annual Needham Healthcare Conference  
New York  
March 27, 2018

[www.veronapharma.com](http://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 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 our annual report on Form 20-F filed with the Securities and Exchange Commission (the “SEC”) on February 27, 2018, 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**








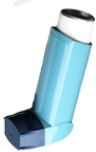

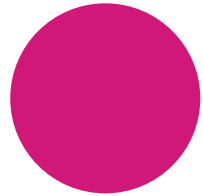


Current Focus:  
COPD and CF

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

# RPL554: Rich Product Pipeline

12 completed Phase 1, 2a & 2b clinical trials with >730 subjects



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

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



# COPD Sufferers Require Maintenance and Acute Treatment



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## Maintenance (Home)



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

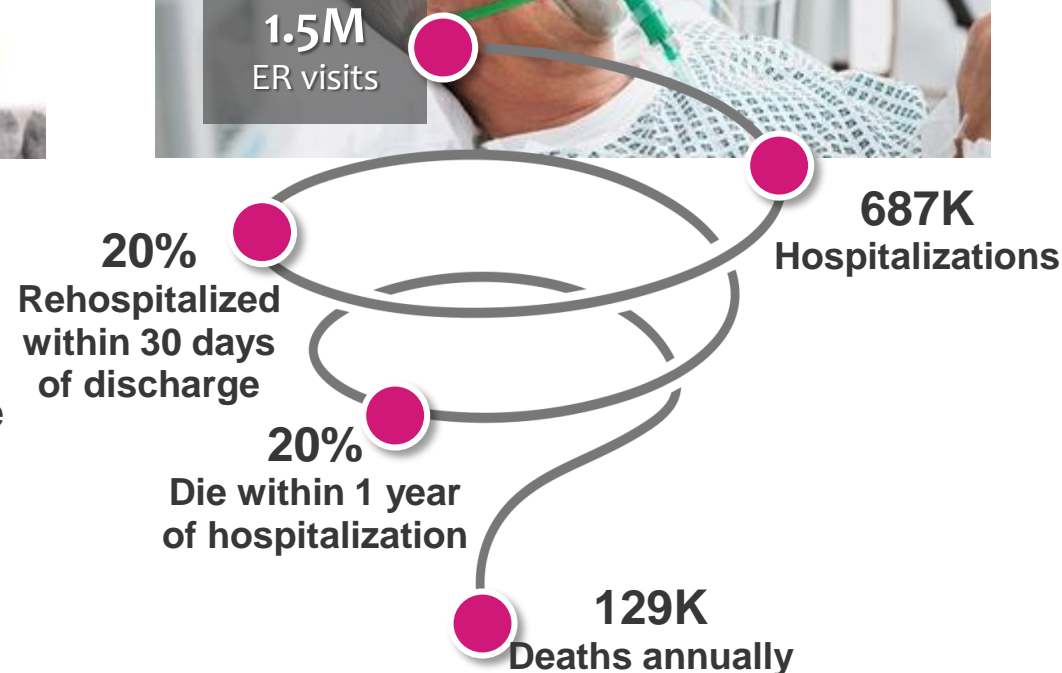
- 15M diagnosed and under treatment
- Approximately 2M severe/very severe

### Treatment goals:

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

**Despite new therapies, the number of COPD patients and hospitalizations remains high**

## Acute (Hospital)



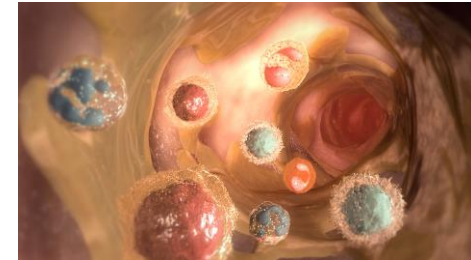
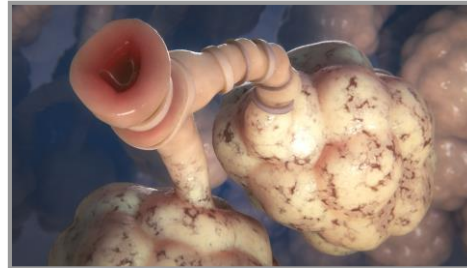
# RPL554 First-in-Class Candidate: Bronchodilator and Anti-inflammatory in a Single Compound



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**RPL554**  
Dual PDE<sub>3</sub> and PDE<sub>4</sub> enzyme inhibitor

Impacts 3 Key Mechanisms in Respiratory Disease:



## Airway Smooth Muscle



PDE<sub>3</sub>, PDE<sub>4</sub>

Relaxation



Increased bronchodilation

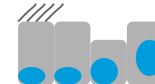
## Inflammatory Cells



Neutrophils  
PDE<sub>4</sub>



Eosinophils  
PDE<sub>4</sub>



Epithelial cells  
PDE<sub>3</sub>, PDE<sub>4</sub>



Lymphocytes  
PDE<sub>3</sub>, PDE<sub>4</sub>



Macrophages  
PDE<sub>3</sub>, PDE<sub>4</sub>



Fibroblasts  
PDE<sub>4</sub>



Increased anti-inflammatory effects

## Epithelial Cells



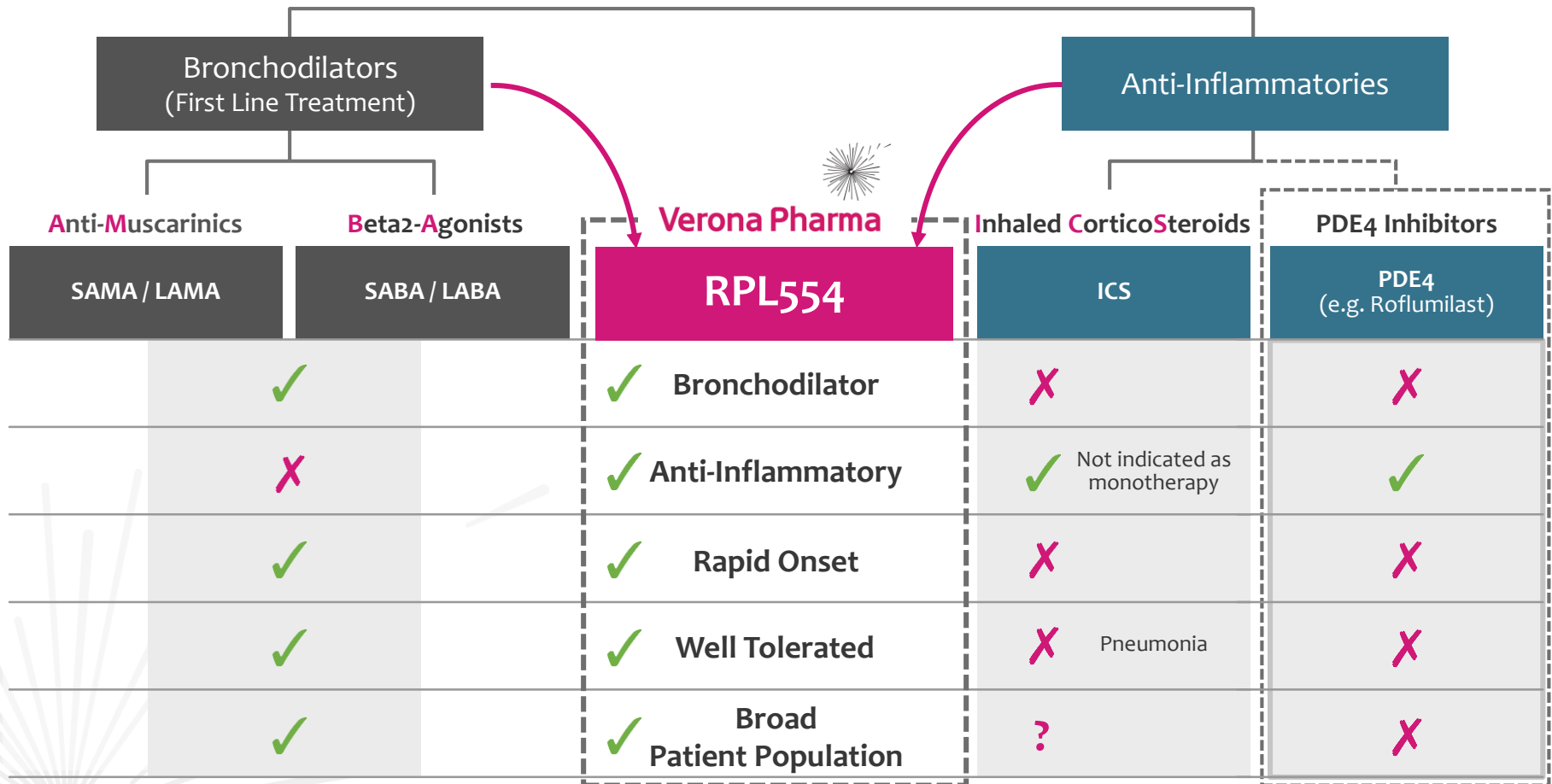
PDE<sub>3</sub>, PDE<sub>4</sub>

CFTR Activation



Increased mucociliary clearance

# RPL554: Potential to Address Limitations of Current Therapies



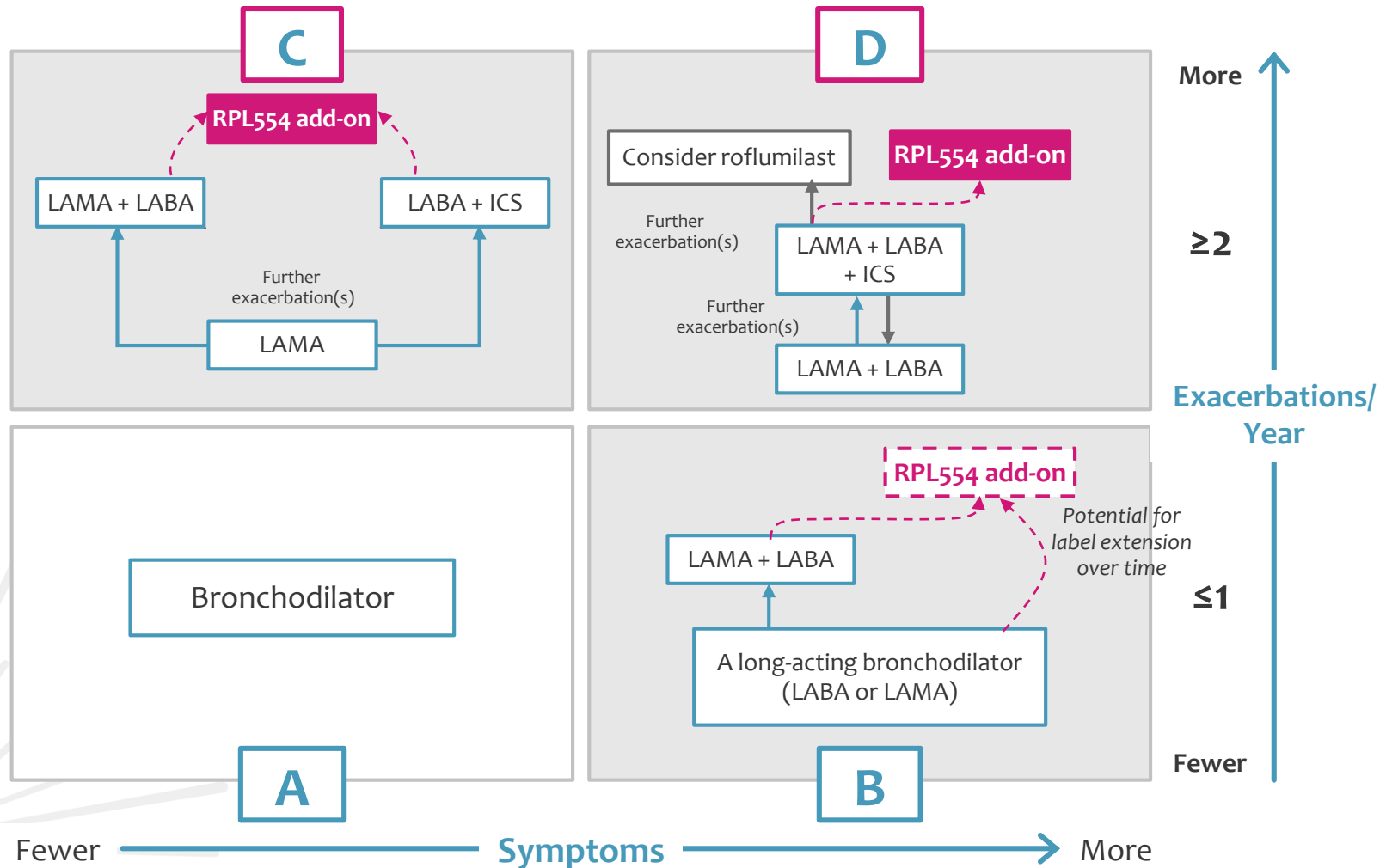
Eventually patients will have “exhausted” all available drug therapies

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



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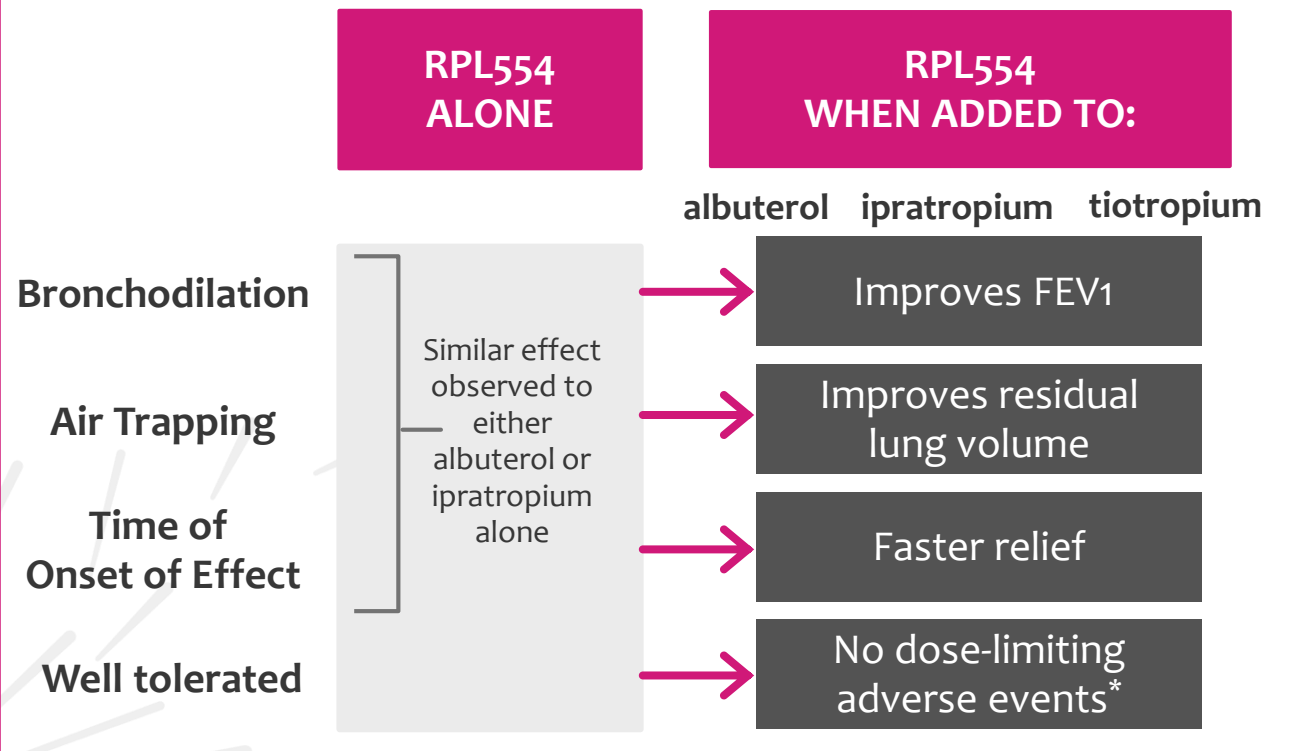
Based on GOLD COPD Guidelines 2017





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

## Key Findings



\*in completed clinical trials

Source: RPL554-009-2015; RPL554-CO-202

# RPL554 – Four Week Phase 2b Study in 403 Patients with Moderate to Severe COPD

## Trial Overview

- **Trial Description:** Phase 2b randomized, double blind, placebo controlled, dose ranging study to assess the effect of nebulized RPL554 in patients with moderate to severe COPD in the outpatient setting
- **Patient Population:** 403 moderate-to-severe COPD patients diagnosed >12 months previously, males and females, age 40-75
- **Location:** approx. 45 centres in Western & Eastern Europe
- **RPL554 Dosage:** Four week, five arm parallel design twice daily dosing with RPL554 at 0.75 mg, 1.5 mg, 3 mg, 6 mg or placebo treatment

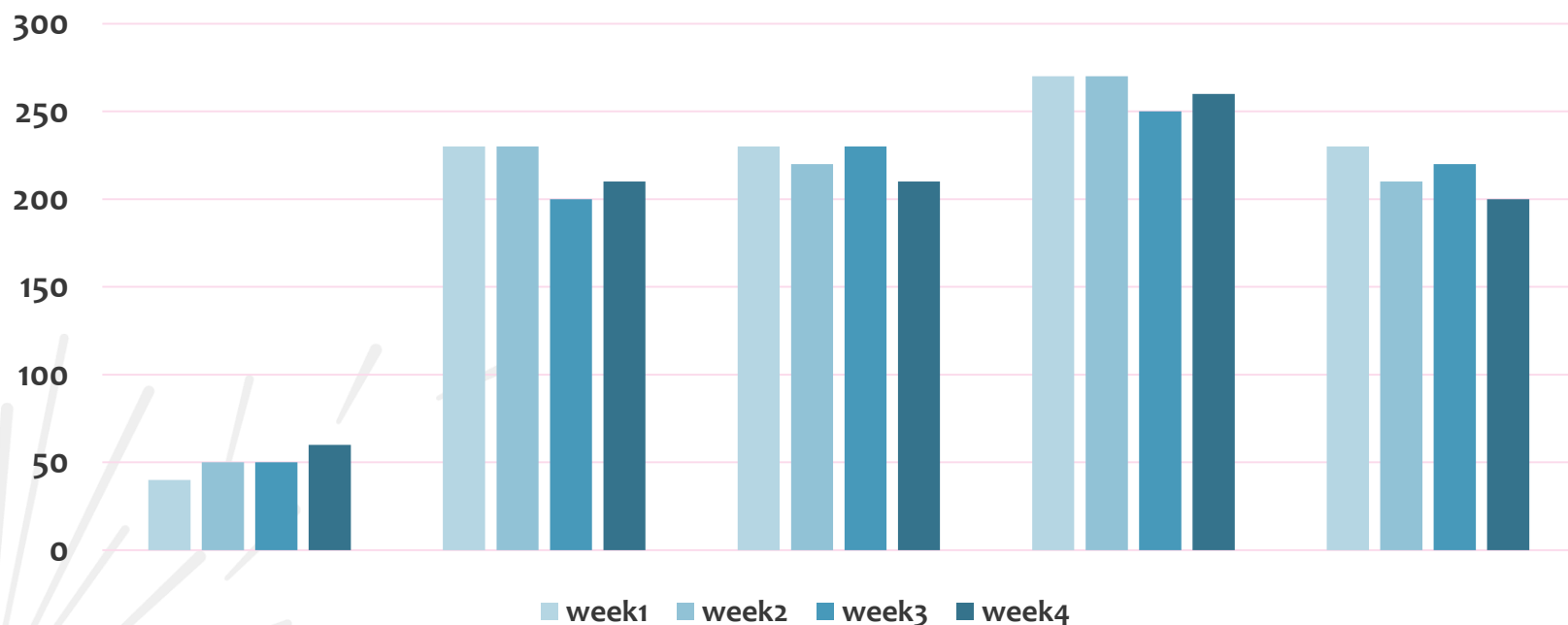
# RPL554 Provides Significant, Clinically Meaningful Bronchodilator Response Maintained over Four Weeks



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Peak Change from Day 1 in Baseline in FEV<sub>1</sub> (mL) on week 4  
(p<0.001)

N=403



placebo

0.75 mg

1.5 mg

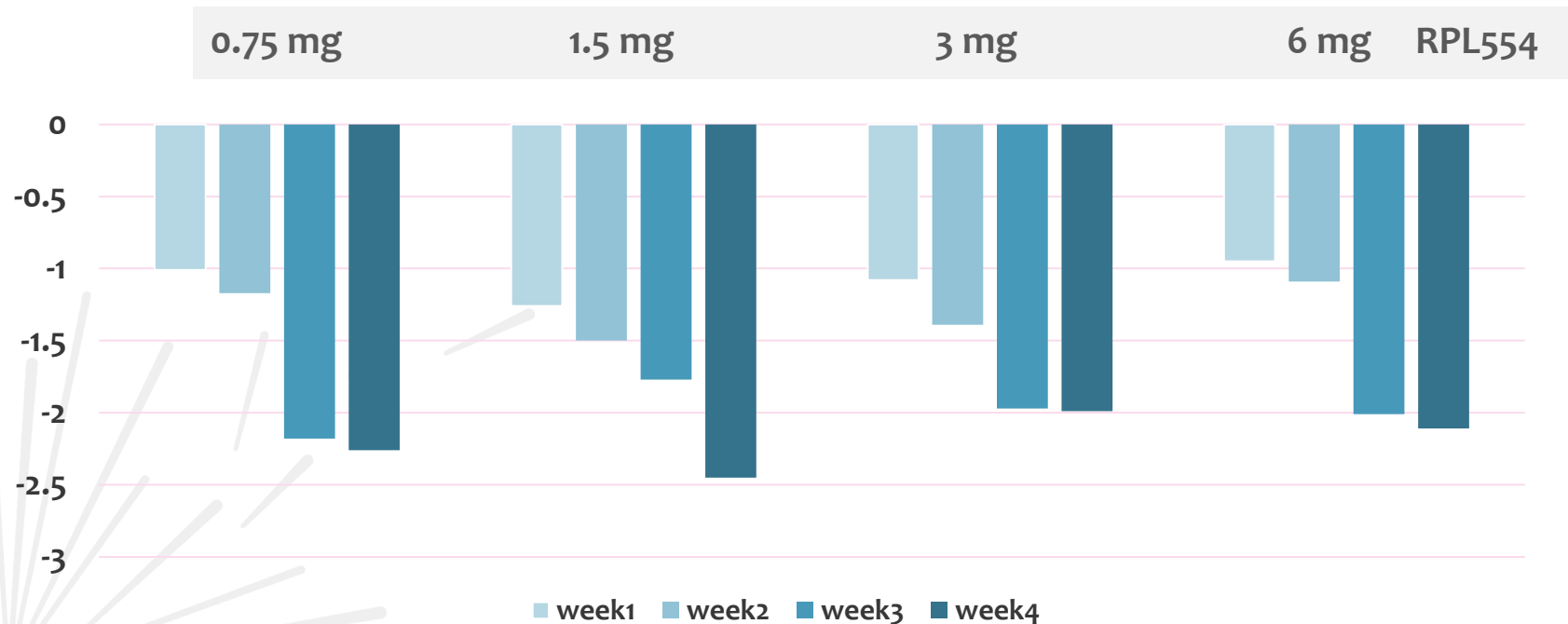
3 mg

6 mg

RPL554

# RPL554 Produced Progressive Improvement of COPD Symptoms with all Doses from Weeks 1 to 4

Total score (0-40) E-RS: COPD by week (placebo corrected,  $p < 0.02$ )  
N=403



# RPL554 Shown to be Effective and Well Tolerated over Four Weeks when Treating COPD Patients in Outpatient Setting

## Primary endpoint:

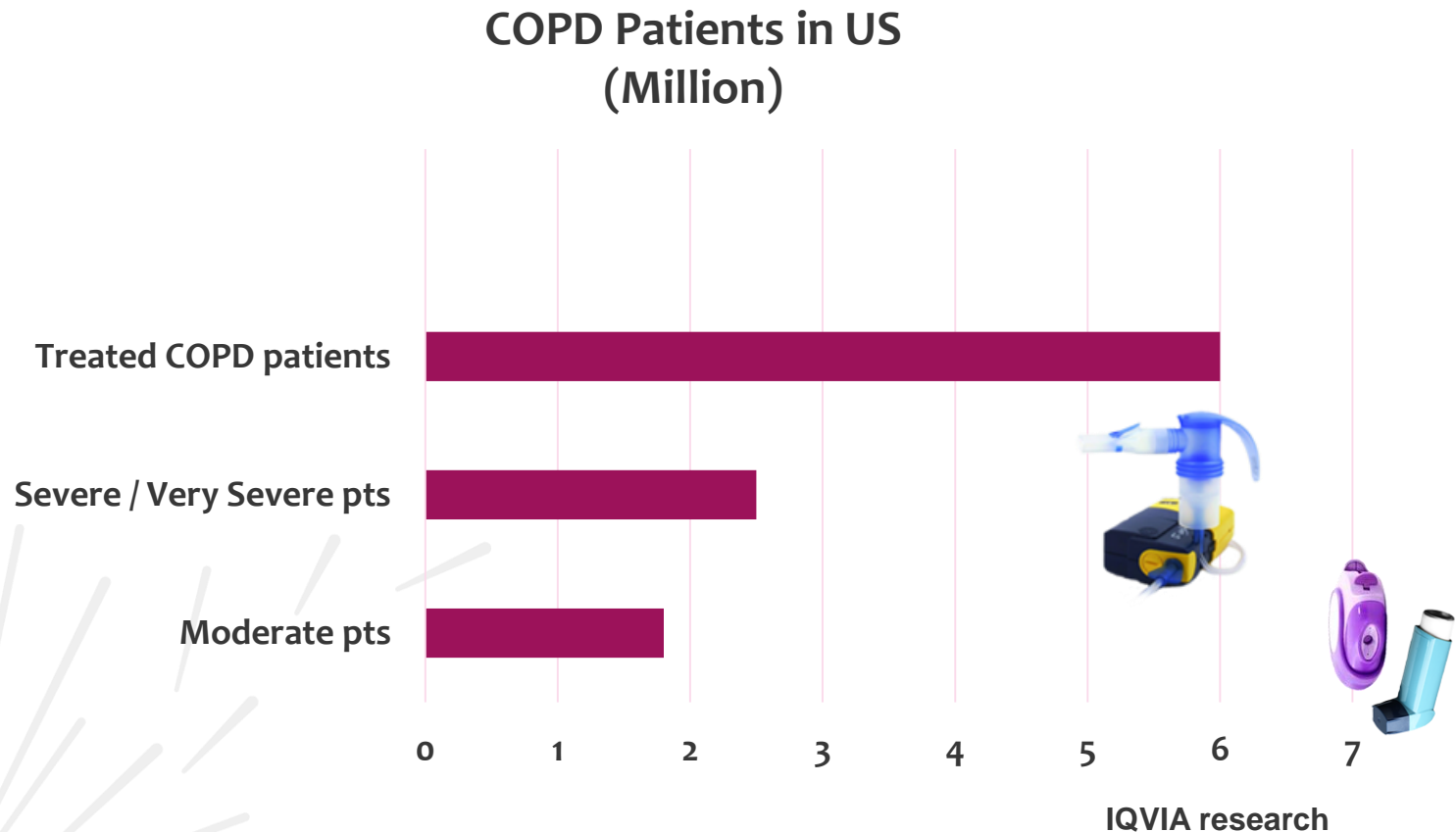
- RPL554 met the primary endpoint, peak FEV1; all doses showed a statistically significant difference vs. placebo ( $p < 0.001$ )
- Peak bronchodilator effect observed at first dose, sustained over four weeks ( $p < 0.001$ )

## Secondary endpoints include:

- Statistically significant improvement in average FEV1 over 12 hours was observed at all dose levels at the first dose, and the effect was sustained over the four weeks of dosing
- This study did not demonstrate consistent improvements in trough FEV1
- Statistically significant and progressive improvements in daily COPD symptoms, using E-RS ( $p < 0.02$  improvements in all sub domains of EXACT-PRO)
- RPL554 was well tolerated at all doses with an adverse event profile similar to placebo



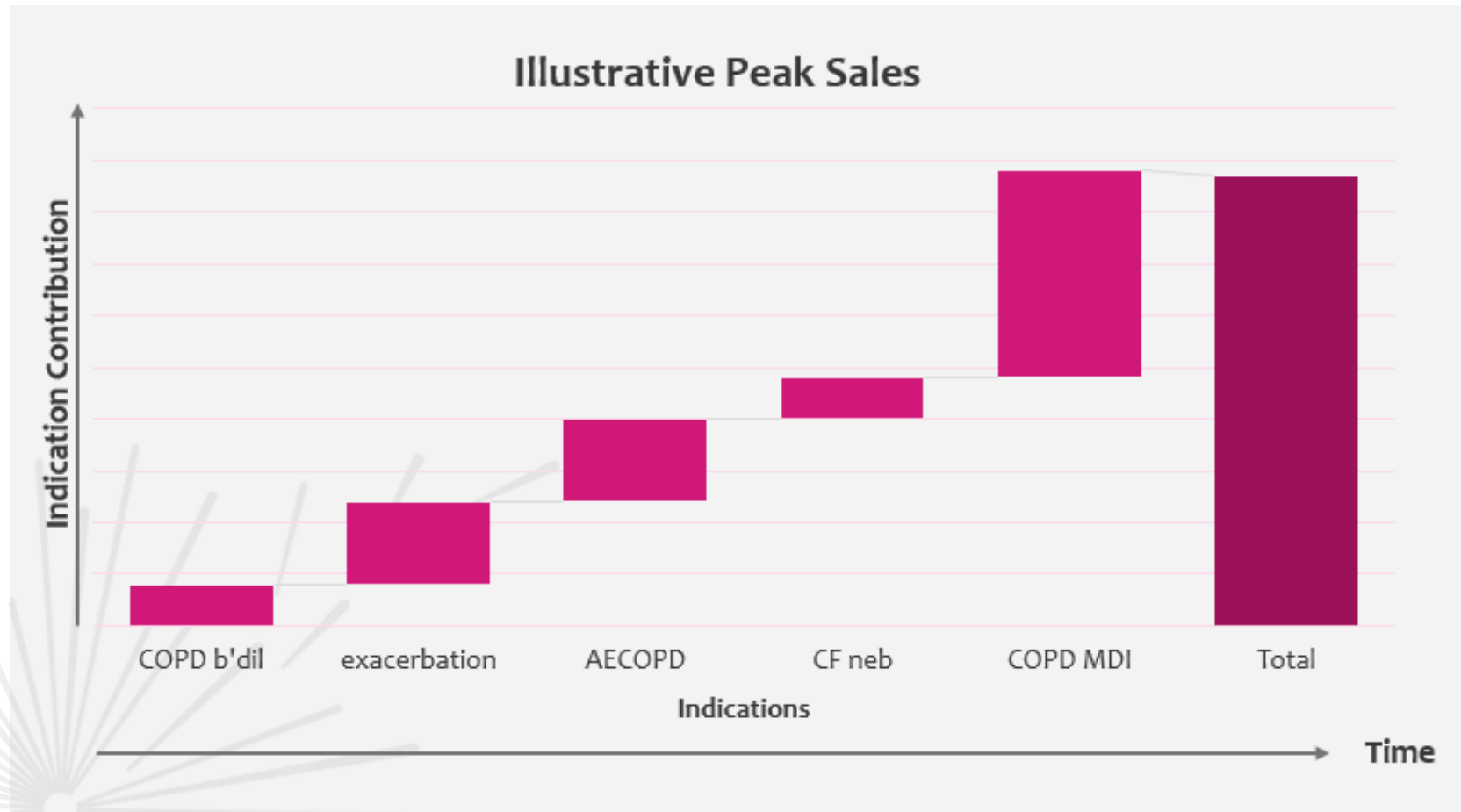
# RPL554: Potential to Improve Standard of Care Treatment for Millions of Patients



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



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# CF: A Devastating Orphan Disease



- Most common fatal inherited disease in U.S.
- Mutations in gene that encodes CFTR protein
- Inability to clear thickened mucus, impaired lung function and persistent lung infection
- Frequent exacerbations and hospitalization
- No cure
- Median age of death – 37 years
- RPL554 has potential to provide treatment independent of CF mutation status
  - Reduce airway obstruction and inhibit inflammation

**Phase 2a study data reported March 2, 2018**

# RPL554 Demonstrates Favorable PK and PD Profile in CF Patients



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- Randomized, double blind, cross-over trial comparing 1.5 mg and 6.0 mg doses with RPL554 to placebo in 10 patients with CF
  - Patients displayed a range of CF genotype mutations in the CFTR
- 
- Primary endpoint:
    - PK profile was consistent with that observed in patients with COPD, although with lower peak serum levels of RPL554 in CF patients; and
    - Serum half-life was dose-dependent; 7.5 to 10.1 hours for 1.5 mg and 6 mg, respectively.
  - Secondary endpoints:
    - Statistically significant increase in average FEV1 in treated patients for 1.5 mg (all  $P < 0.01$ ) and 6 mg (all  $P < 0.05$ ) at 4, 6 and 8 hour time points;
    - Drug was well-tolerated in this patient group with an adverse event profile consistent with other studies with RPL554

**Results support further development in CF**



# 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 31 Dec 2017

Cash and Cash  
Equivalents

\$108.6M<sup>1</sup>

Operating  
Expenses

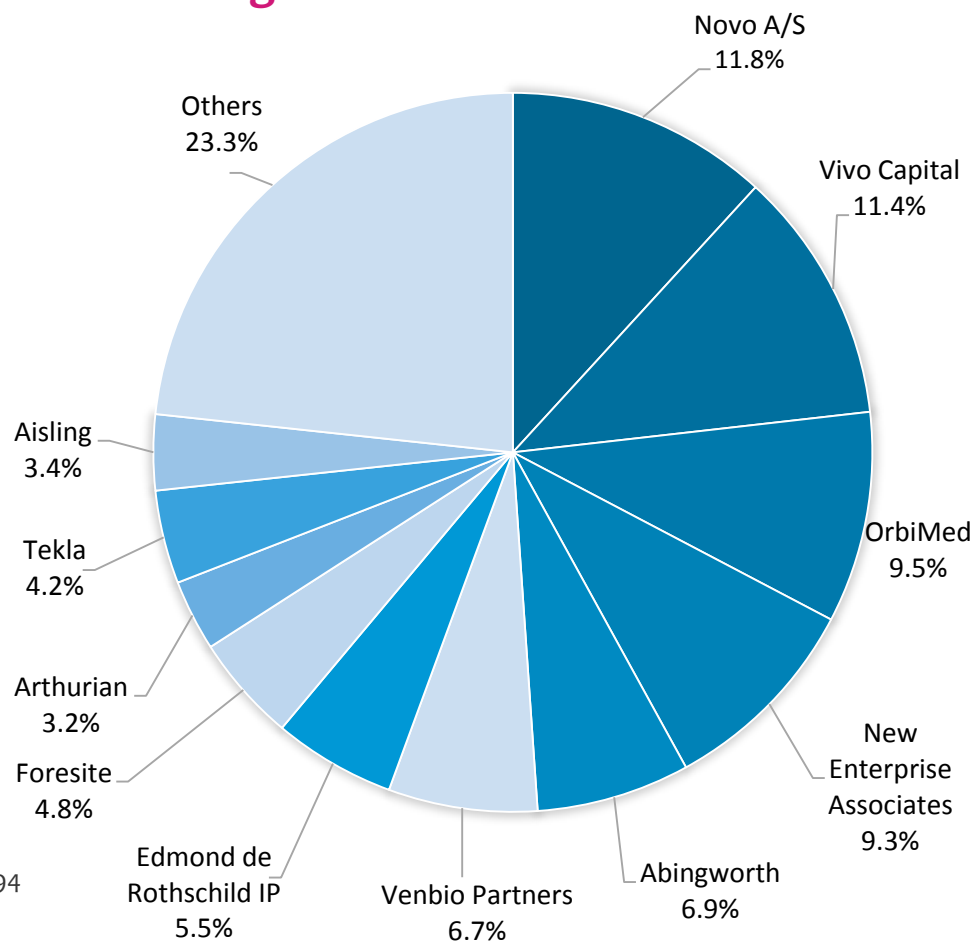
\$40.3M<sup>1</sup>

Total Equity

\$108M<sup>1</sup>

<sup>1</sup>Exchange rate used (US dollars per pound sterling): December 31, 2017 \$1.35294

## Shareholdings



# Next Steps – Focused Development in Attractive Market Segments

## **Key activities leading up to Phase 3 in maintenance treatment in COPD with nebulized RPL554:**

- Positioning study: RPL554 in addition to established combination treatments
- Market research and evaluation of optimal positioning
- “End of Phase 2” meeting to discuss regulatory path
- Pivotal clinical trials in the COPD maintenance setting expected to start in 2019

## **Development of pMDI and DPI formulations of RPL554:**

- Expected start of pre-clinical studies 2H 2018

## **Development as anti-inflammatory treatment in Cystic Fibrosis:**

- Following positive Phase 2a results, KOL and regulatory discussion ahead of clinical proof-of-concept study