



# Verona Pharma



## Breathtaking science

Developing respiratory drugs  
to improve health and quality of life



JMP Securities Life Science Conference  
New York City, June 2018

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



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**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



# COPD: Substantial Unmet Need For New Maintenance and Acute Treatments



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## Maintenance (Home)



### 24M living with COPD in U.S.

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

### Treatment goals:

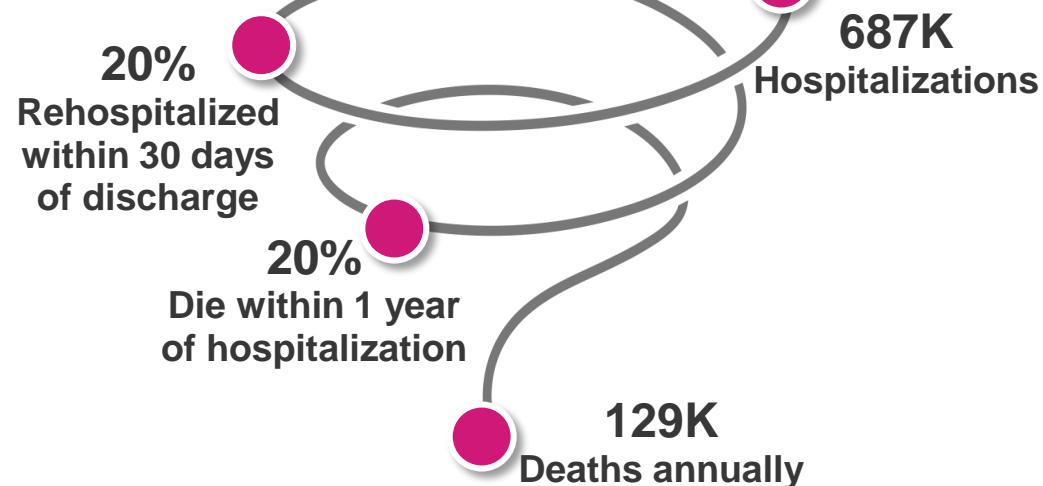
- Symptom control and relief
- Improve quality of life
- Improve lung function
- Reduce breathlessness
- Prevent exacerbations

Note: U.S. only data

## Acute (Hospital)



1.5M  
ER visits



**Number of COPD patients and hospitalizations remains high**

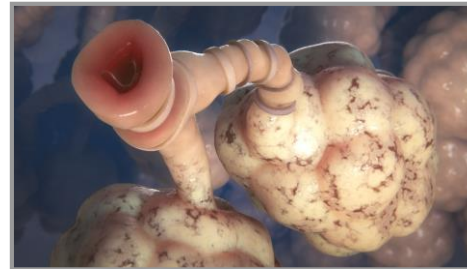
# RPL554 First-in-Class Candidate: Bronchodilator and Anti-inflammatory in a Single Compound



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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: Robust Product Pipeline

*Completed twelve Phase 1 and 2 clinical trials  
and enrolled >730 subjects*

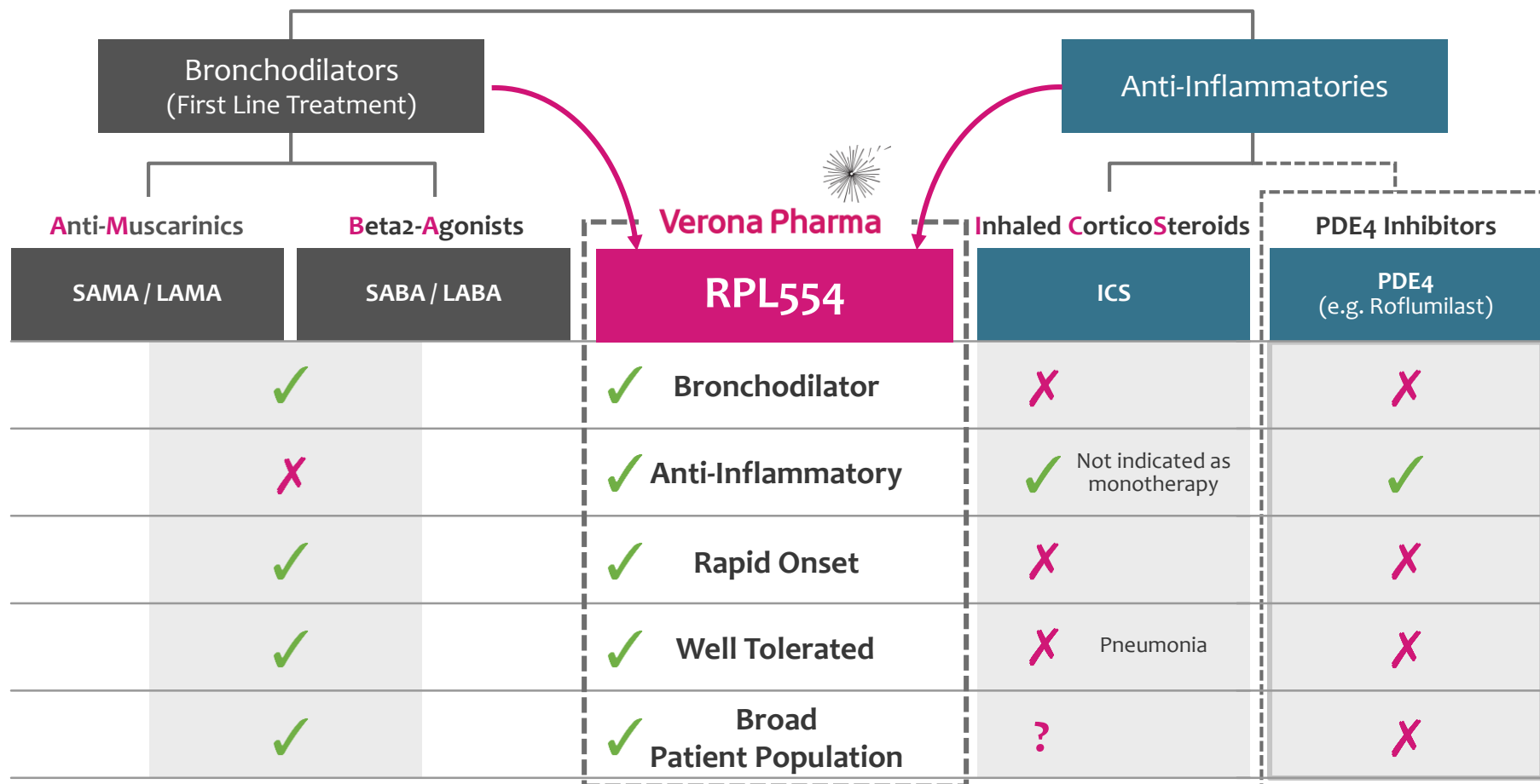


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Indication	Delivery	Pre-Clinical	Phase 1	Phase 2	Phase 3
<b>COPD</b> Maintenance (Home)	 Nebulizer				
<b>COPD</b> Acute (Hospital)					
<b>Cystic Fibrosis</b>					
<b>COPD</b> Maintenance (Home)	<b>MDI</b> 				
<b>COPD</b> Maintenance (Home)	<b>DPI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

*RPL554 has potential application in other significant respiratory diseases such as asthma.*

# RPL554: Potential to Address Limitations of Current Therapies



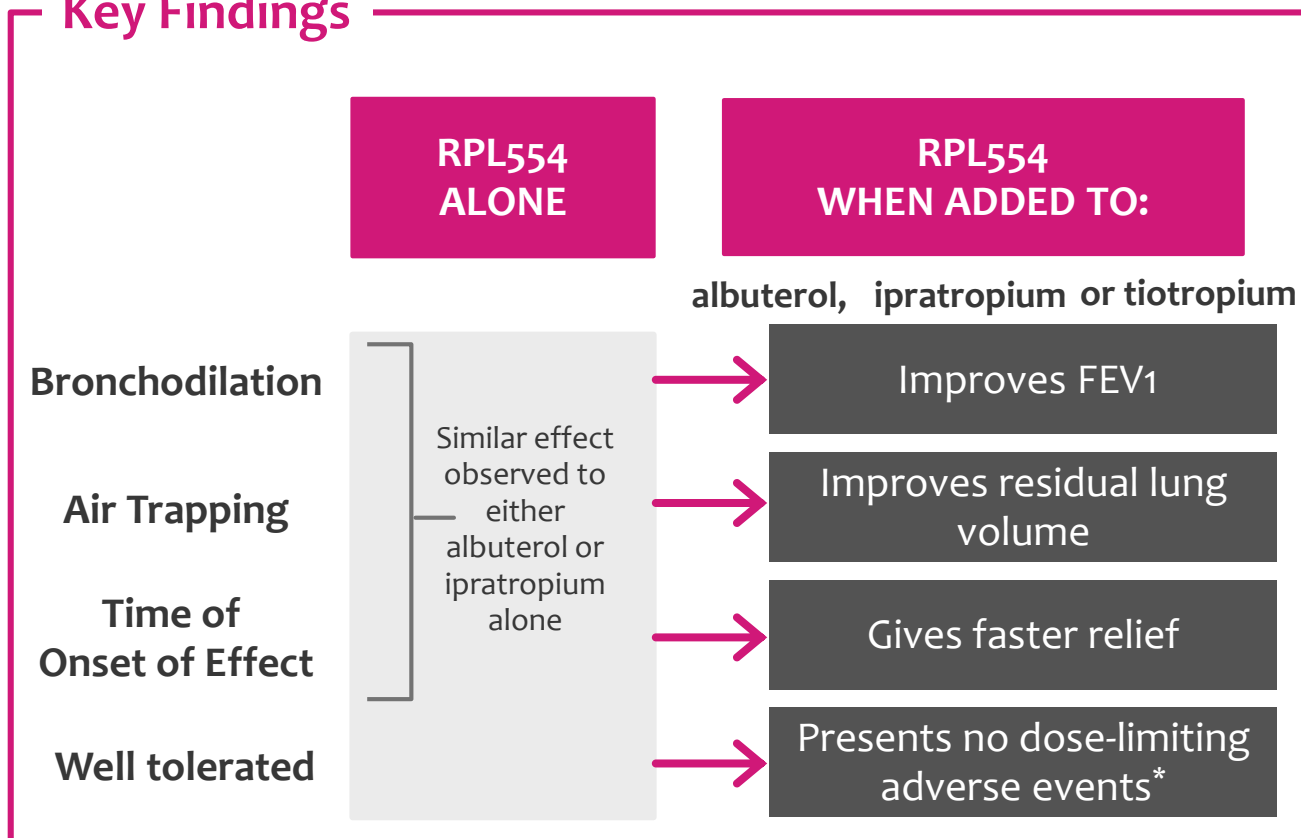
New therapies are required for patients with progressive disease and symptoms despite current treatment options

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



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## Key Findings



\*in completed clinical trials

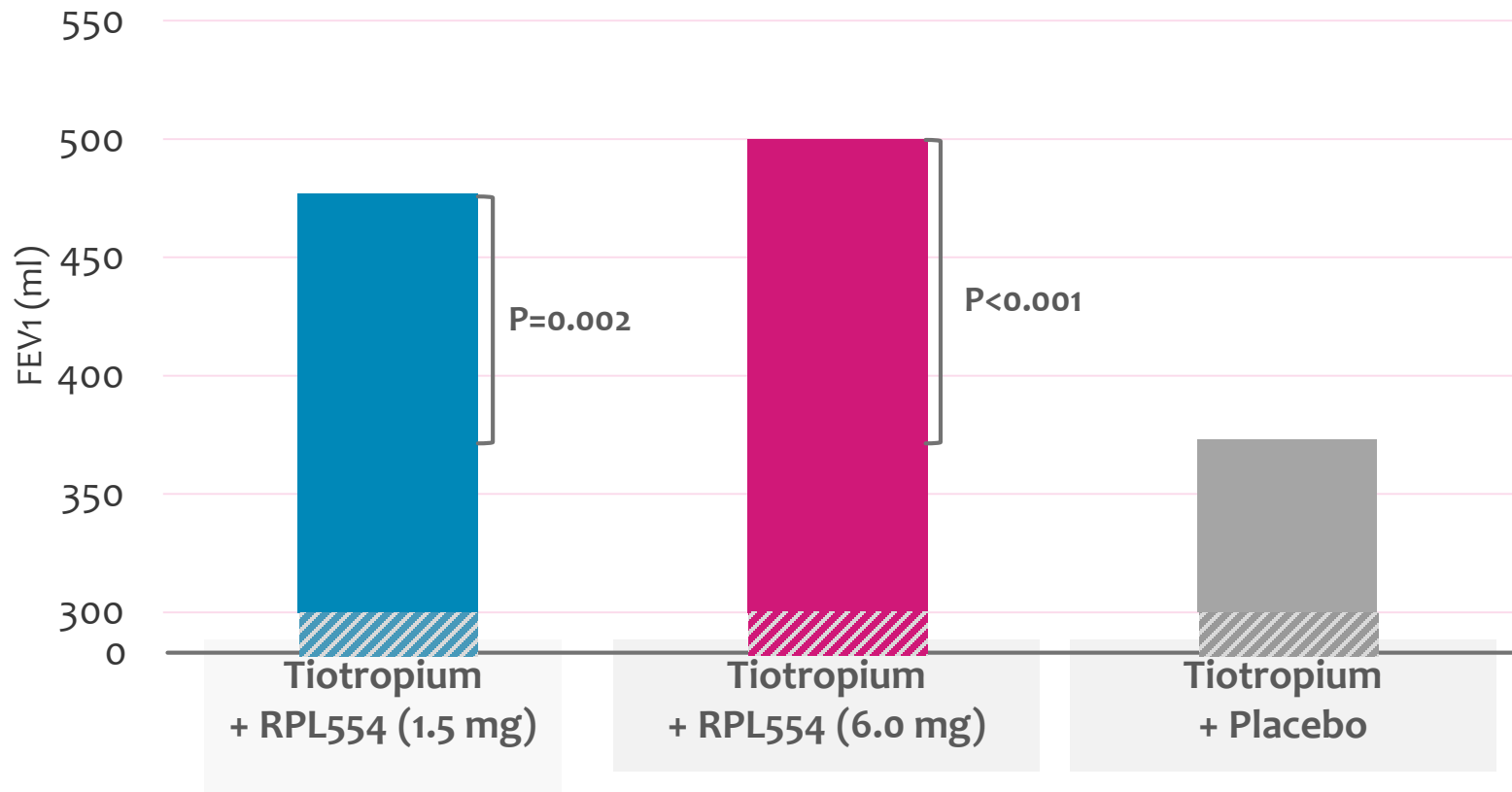
Source: Ph2 studies RPL554-009-2015; RPL554-CO-202



# 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: Phase 2 study RPL554-CO-202  
P values vs placebo

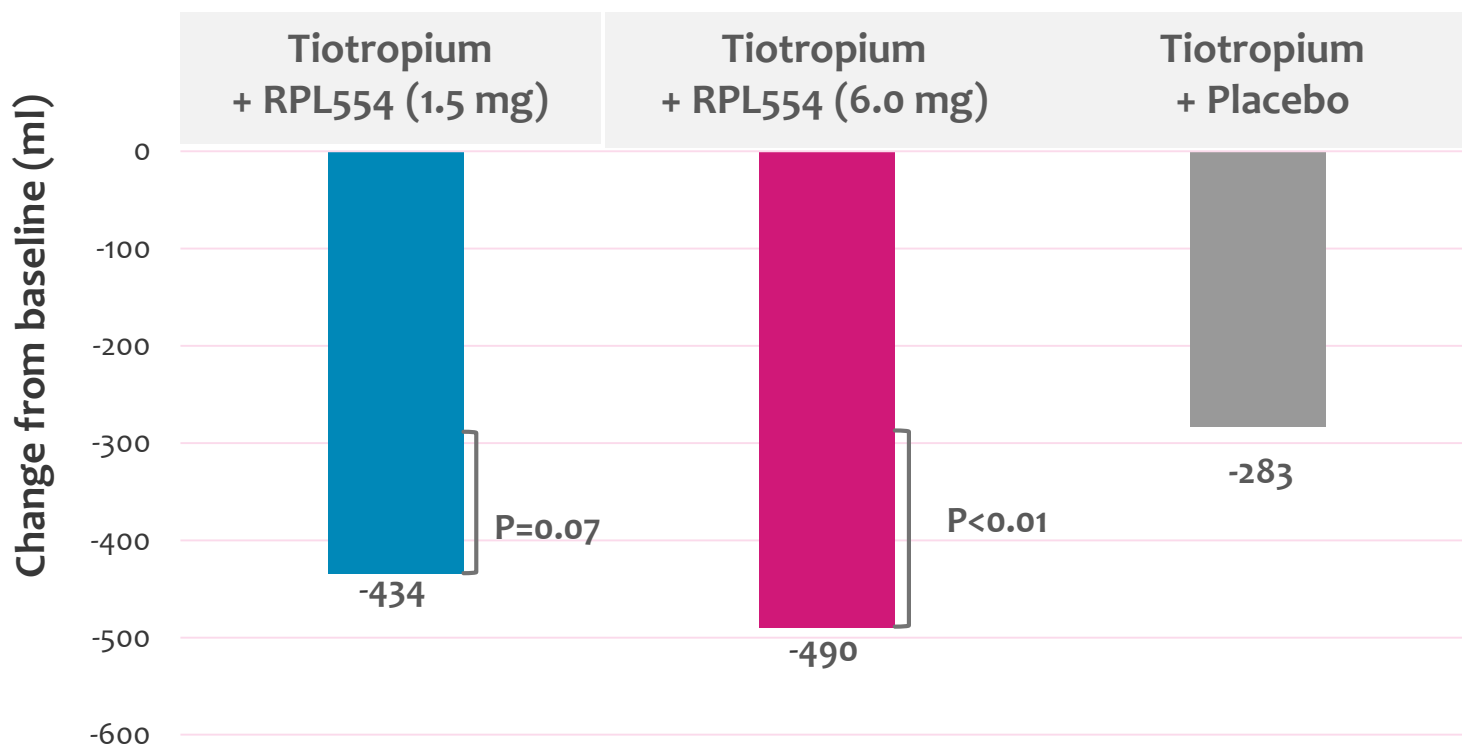
# RPL554: Marked Reduction in Hyperinflation, Residual Volume (RV, air trapping) as Compared to Tiotropium Alone



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## Reduction in Hyperinflation (ml) on Day 2

N=27-28



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

Source: RPL554-CO-202  
P values vs placebo

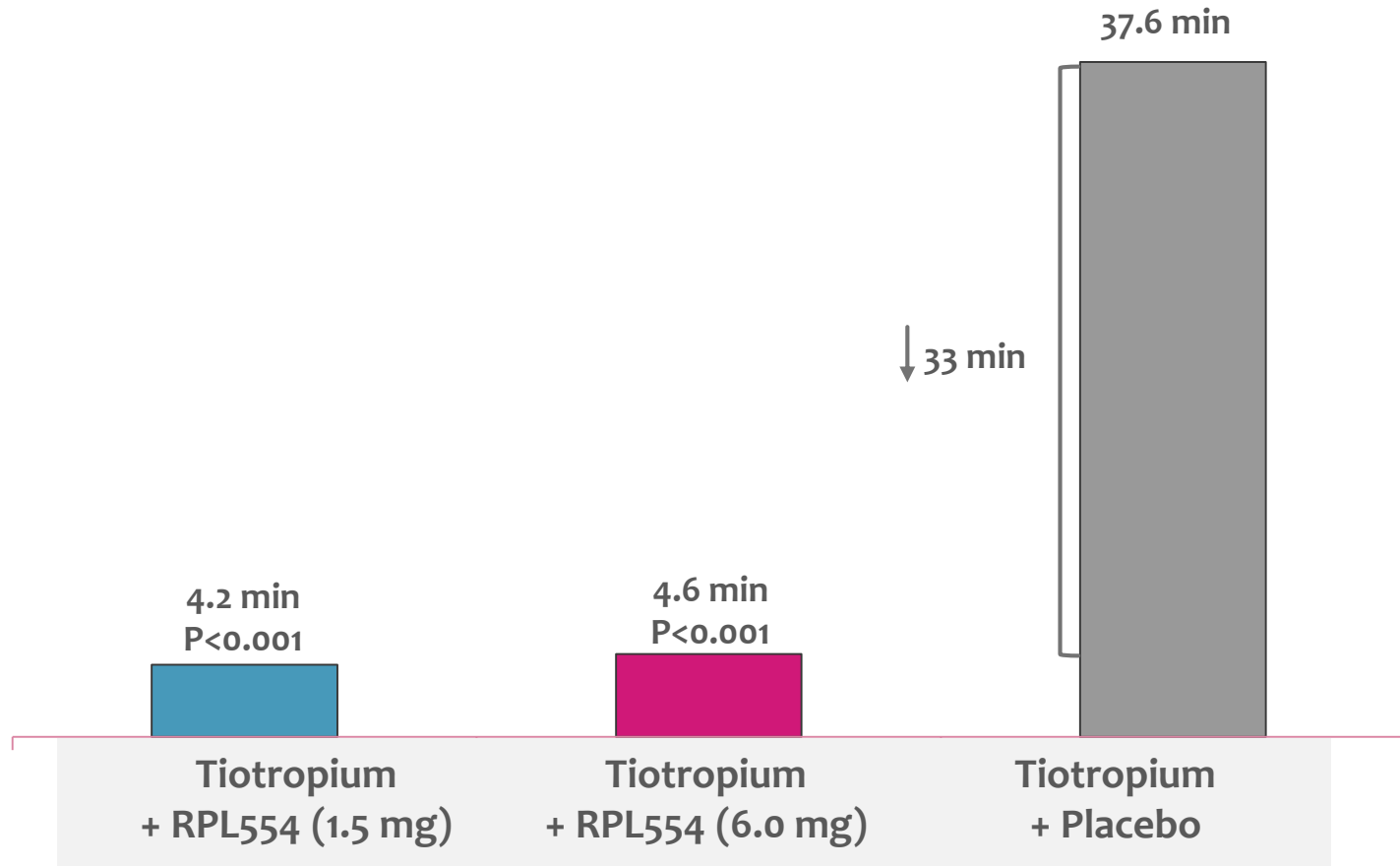
# RPL554: Combination Increases Speed of Onset of Bronchodilator Effect



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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: Four Week Phase 2b Study in Moderate to Severe COPD



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## **Trial Description:**

- Phase 2b randomized, double blind, placebo controlled, dose ranging study
- Assess nebulized RPL554 in patients with moderate to severe COPD
- Outpatient setting
- No background bronchodilator therapy (stable ICS regimen can be maintained)

## **Patient Population:**

- 403 moderate-to-severe COPD patients, diagnosed >12 months previously
- Males and females, age 40-75

## **Location:**

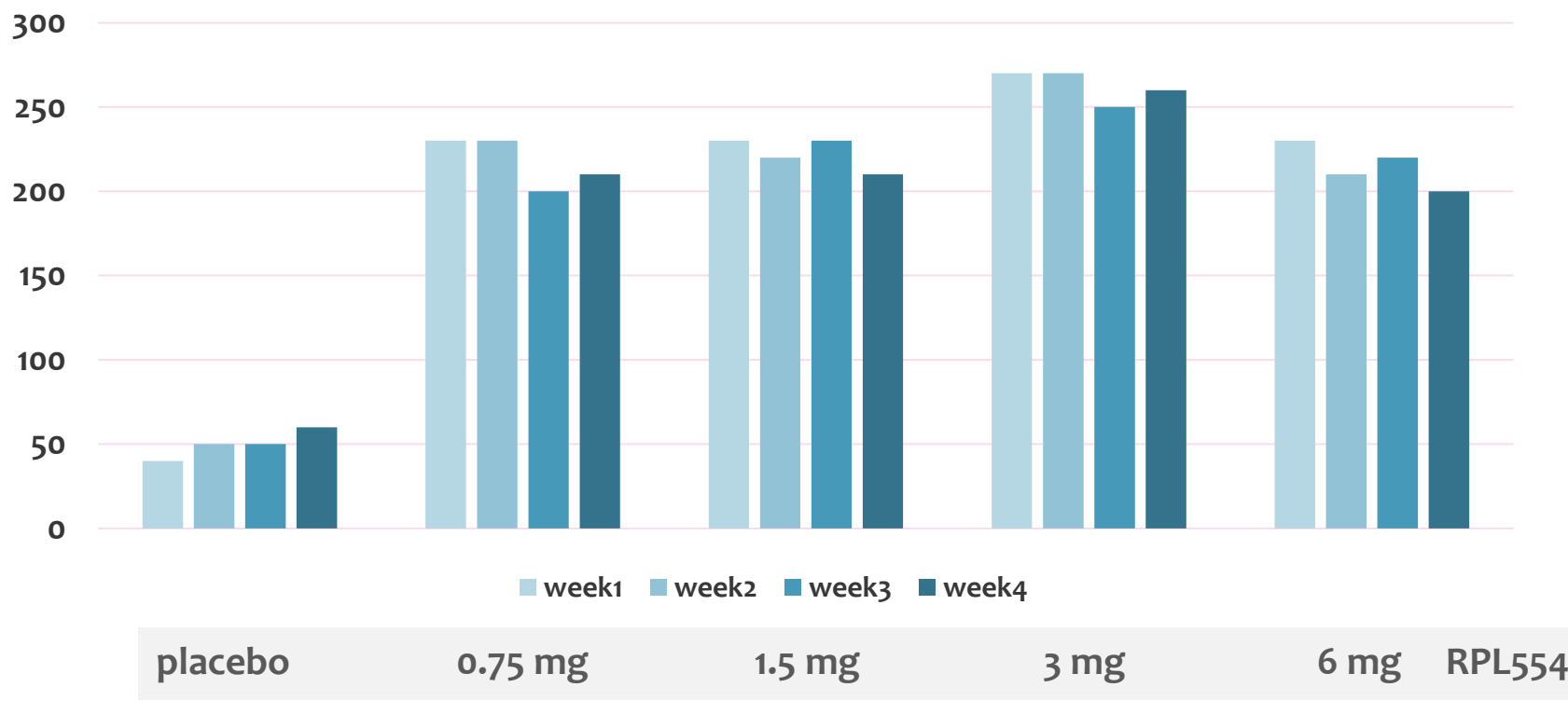
- Approximately 45 centers in Western & Eastern Europe

## **RPL554 Dosage:**

- Five arms, twice daily dosing with RPL554 at 0.75 mg, 1.5 mg, 3 mg, 6 mg or placebo

# Significant, Clinically Meaningful Bronchodilator Response Maintained over Four Weeks

Peak Change from Day 1 in Baseline in FEV<sub>1</sub> (mL) on week 4  
(p<0.001)  
N=403

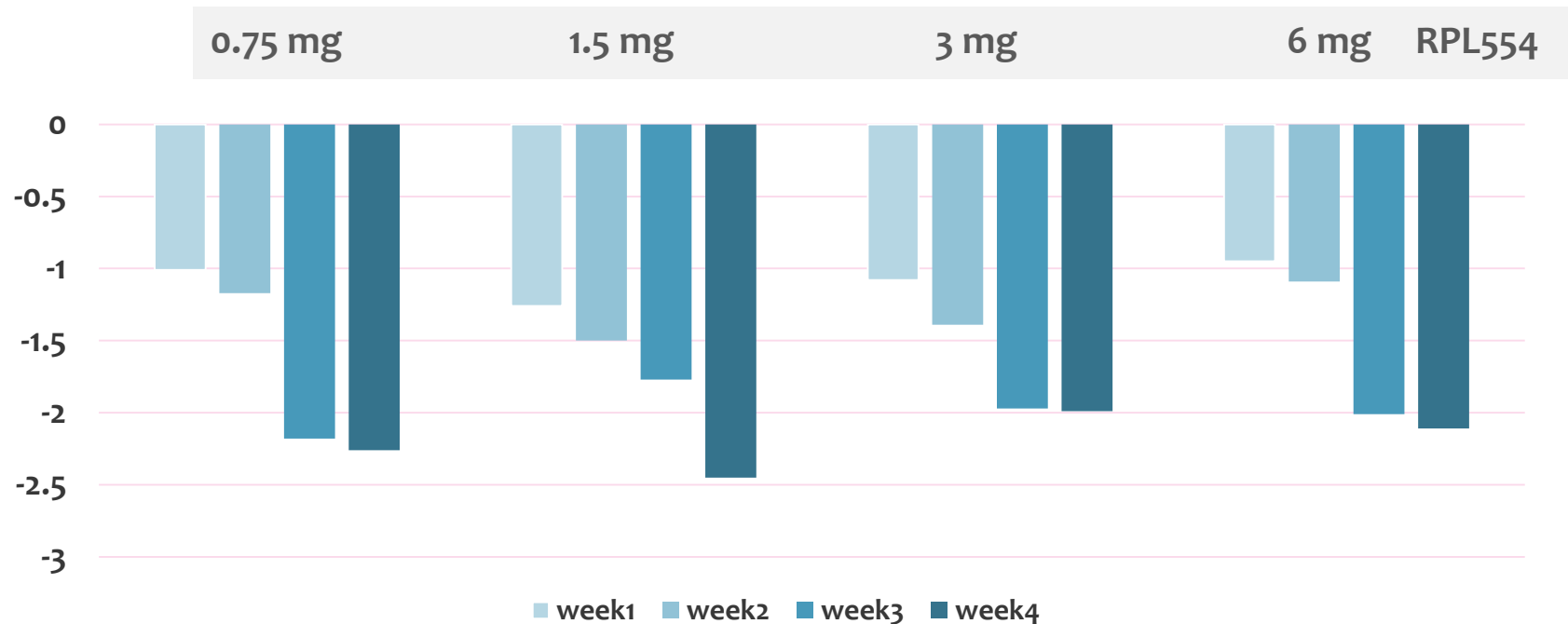




# RPL554: Rapid and Progressive Improvement of COPD Symptoms with All Doses from Weeks 1 to 4

**Total score E-RS\*: COPD by week (placebo corrected,  $p < 0.02$ )**

**N=403**

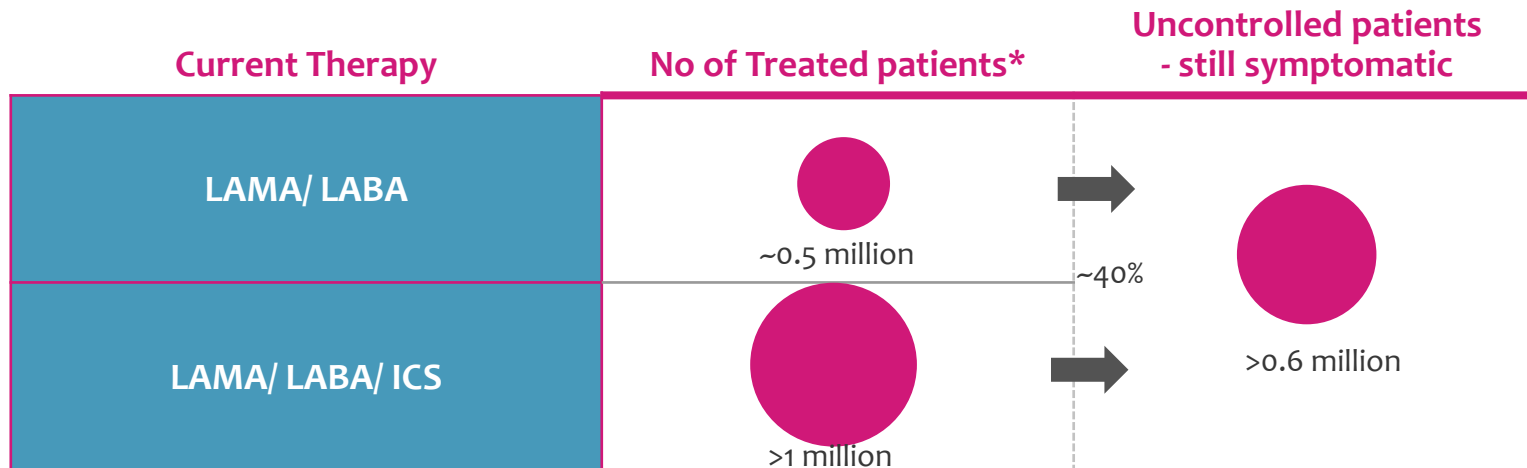


(\*E-RS (EXACT-PRO) - a recognized patient-reported outcome measure for use in clinical studies of COPD)

# Nebulized RPL554 for COPD: > 600,000 Potentially Eligible Patients in U.S.



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Physicians see the value of a novel MoA in this high unmet need population  
with very limited alternatives\*

Estimate ~40% of patients receiving dual bronchodilators are uncontrolled\*\*

Source: \*IQVIA claims data analysis Q2 2017 & Verona market research Q1 2018

\*\*Vestbo J, et al. Lancet 2017; 389: 1919-29.

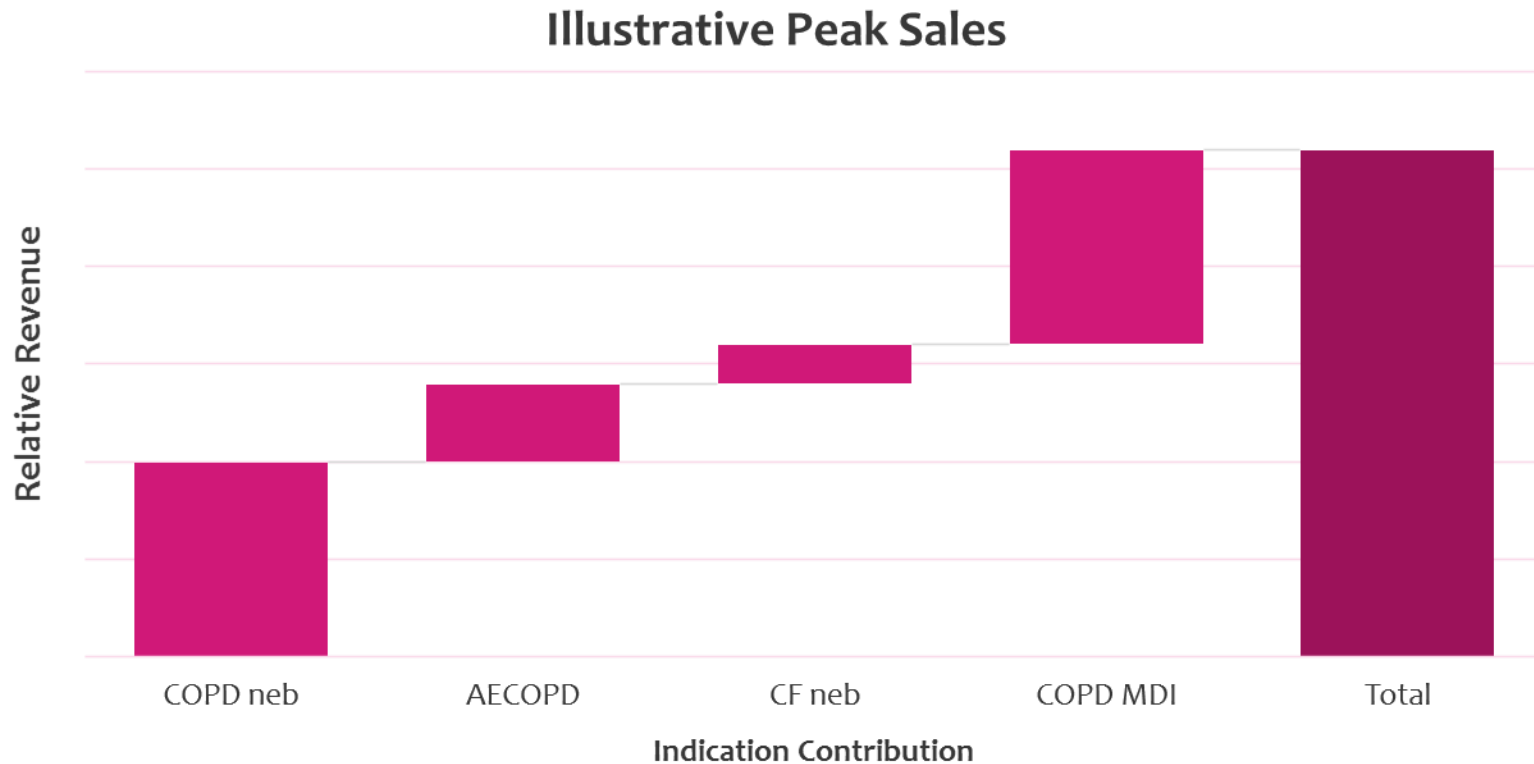
Mullerova H, et al. Am J Respir Crit Care Med 2017; 195: A4986.

Mahler, D. A., et al. European Respiratory Journal 2014, 43(6), 1599–609.

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



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# RPL554: Phase 3 Plan for Nebulized RPL554 Development as Maintenance Treatment of COPD



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- Pivotal trials in **moderate to very severe COPD patients and/or patients with COPD symptoms** who prefer/accept nebulizer treatment
- Position **RPL554 as “add-on” to standard of care**
  - Supported by quantitative market research
- Potential key endpoints: **lung function** (eg. FEV<sub>1</sub>, residual volume) **and/or symptoms**
- Focus on speed and cost in pivotal trials with nebulizer treatment
  - **Two trials (3 to 6 months duration) with 12 months safety data**
  - **Pivotal trials planned to commence in 2019**
  - **NDA filing planned for 2021**



# 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 2018**



# RPL554: Demonstrates Favorable PK and PD Profile in CF Patients in Phase 2a Trial



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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 consistent with that observed in COPD patients, although with lower peak serum levels of RPL554 in CF patients
    - Serum half-life was dose-dependent; 7.5 to 10.1 hours for 1.5 mg and 6 mg
  - 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
    - RPL554 was well-tolerated with an adverse event profile consistent with other studies

**Results support further development in CF**



# Well Financed with Major Healthcare Investors

## Financial Overview Mar 31, 2018

Cash and Cash  
Equivalents

\$101.9M<sup>1</sup>

Operating  
Expenses 1Q18

\$8.2M<sup>1</sup>

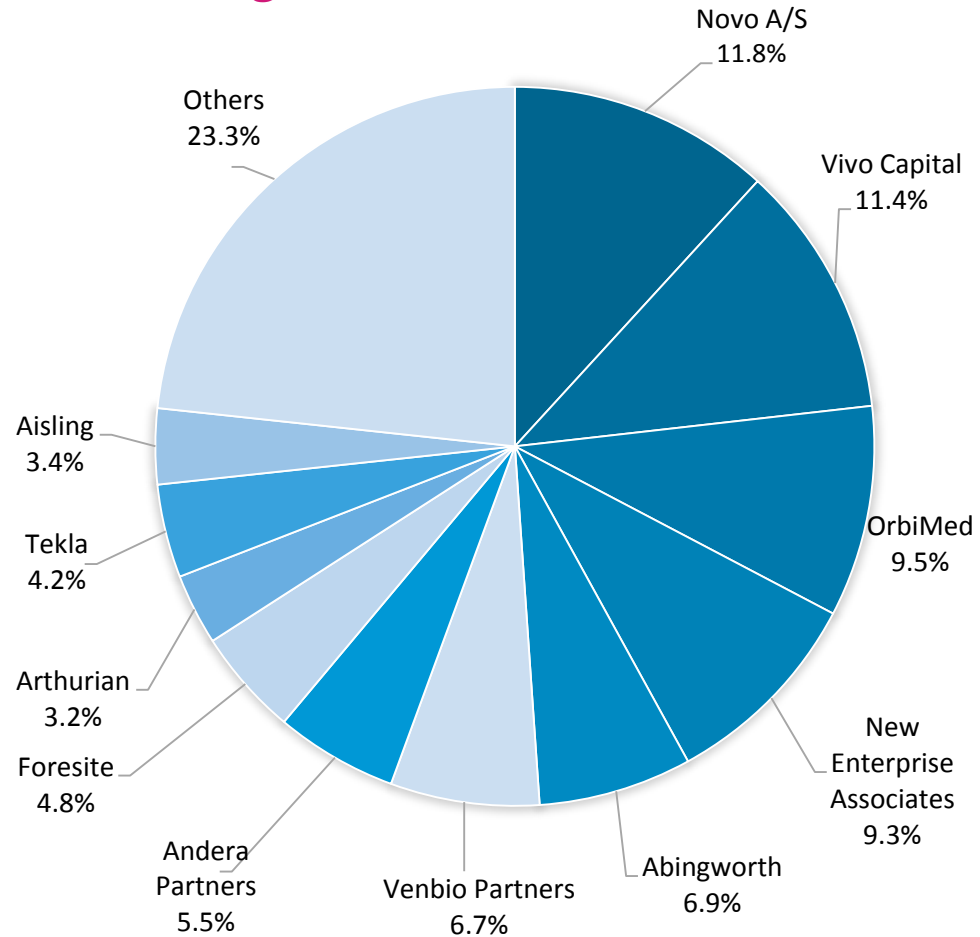
Market cap

\$253M<sup>2</sup>

<sup>1</sup>Exchange rate used (US dollars per pound sterling): March 31, 2018 \$1.4027

<sup>2</sup>Fully diluted 125m shares or 15.6m ADSs, ADS price \$16.22 May 11, 2018

## Shareholdings



# Significant Value Inflection Points over next 12 Months, Ahead of Commencing Phase 3



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## RPL554 nebulized formulation as maintenance treatment of COPD

- Planned Phase 2a study start: RPL554 as add-on to LAMA/LABA w/wo ICS 3Q 2018
- Phase 2a clinical data read out from “add-on study” above 1H 2019
- Decision on viability of drug product in plastic ampules mid 2019
- Regulatory agreement to proceed into Phase 3 studies 2019

## RPL554 pMDI and DPI formulations (out-licensing)

- Expected completion of pre-clinical studies 2018/19
- Expected start of clinical Phase 2 trials 2018/19
- Clinical data read out DPI/MDI Phase 2 trials 2019

## RPL554 anti-inflammatory treatment in Cystic Fibrosis

- Clinical anti-inflammatory/ Proof-of-concept study TBD