



# Verona Pharma



## Breathtaking science

Developing respiratory drugs

to improve health and quality of life



**JP Morgan Conference**  
January 2019

**Nasdaq VRNA**  
[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 of its product candidate, 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 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.

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## RPL554

A **first-in-class** drug candidate with potential to **treat millions of patients** suffering from **deadly respiratory** disease by relieving **debilitating symptoms** like **breathlessness**, and the underlying **airway inflammation**

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## Verona Pharma

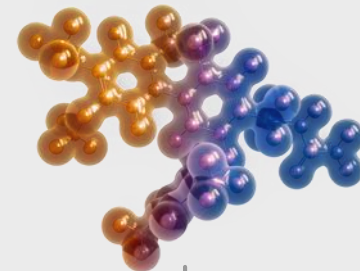
Taking our first-in-class product candidate for treatment of respiratory disease from Phase 2 to commercialization

### Initial Disease Focus



Chronic Obstructive Pulmonary Disease  
(COPD)

### Our Novel Drug RPL554



Inhaled  
Inhibitor of  
Enzymes  
PDE3 and  
PDE4

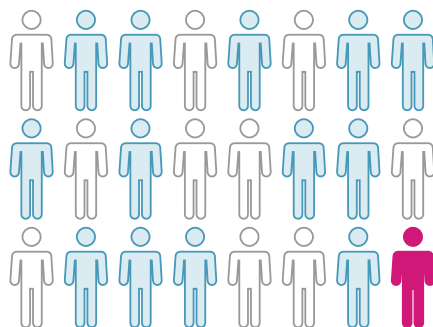
Bronchodilator **AND** Anti-inflammatory Agent  
... in a Single Compound

Demonstrated **dual effects** and well **tolerated** in 12 clinical trials with >730 subjects  
On track to commence **Phase 3** following end of Phase 2 meeting in 2019

# COPD: The Silent Epidemic

## Living with It

**24M** in US alone



## In the Workplace

- **70%** of COPD sufferers work
- **2<sup>nd</sup> leading cause** of disability

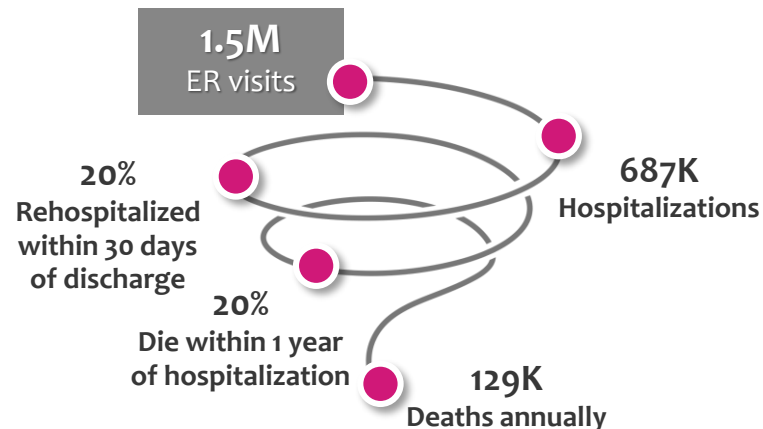
## Cost

**\$50B/year**

Indirect & Direct

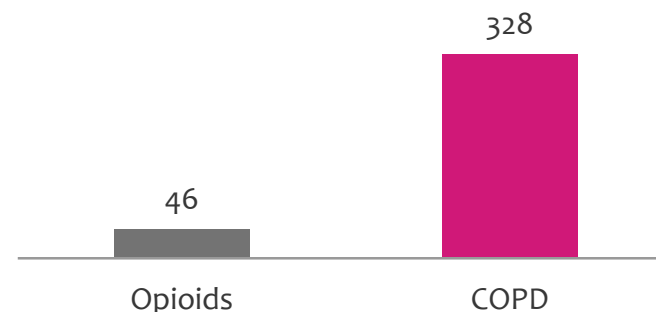
Sources: COPD Foundation

## Dying from It



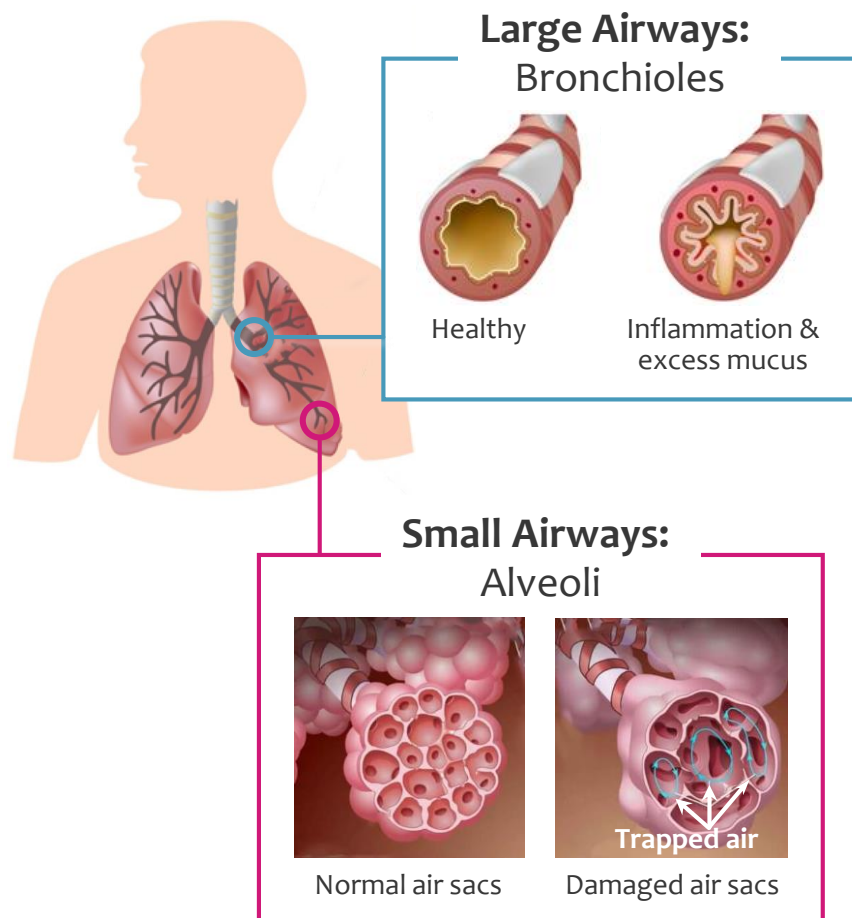
## 3<sup>rd</sup> Largest Chronic Disease Killer

Deaths/Day





# COPD: A Significant Unmet Medical Need



## Consequences and Symptoms

- Poor lung function
- Breathlessness
- Coughing, sputum
- Fatigue
- Exacerbations / flare-ups

*"When I bend over, I can't breathe. I can't unload the dishwasher, or make a bed ... I wake up but I can't move. I am so short of breath."*

– John Linnell, Living with COPD

*"These symptoms have a huge impact on our patients' lives. They become more limited in their activities and they have increasing shortness of breath"*

– US COPD KOL

# Living with COPD: More Treatment Options Needed



John Linnell

**A Year Later:  
2 Bronchodilators**  
LAMA and LABA  
(Long Acting Beta Agonist)

**Visits Doctor**  
“It takes me up to  
2 hours to get going in  
the morning”

**Diagnosed with COPD  
and prescribed an inhaler**  
(Long Acting Anti-  
Muscarinic - LAMA)

**Exacerbations/  
Flare Ups**  
“Each exacerbation makes  
it worse and you never  
fully recover”

**Still Symptomatic**

“I live and struggle with COPD  
every single day, and I too,  
**just want to breathe**”

“My doctor says there’s nothing more  
he can do: he’s reached **the end of  
currently available treatments**”

**“We sorely need new treatments: I’m going to die **with** COPD,  
but I’ll be damned if I’m going to die **from** it.”**

# COPD Maintenance Treatments

Compelling Need for Therapy with New Mode of Action



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## Current

### Bronchodilators

Long Acting Beta Agonist  
(LABA)

Long Acting Anti-Muscaric  
(LAMA)

40% of patients  
continue to be  
symptomatic

### Anti-Inflammatories

Inhaled Corticosteroids  
(ICS)

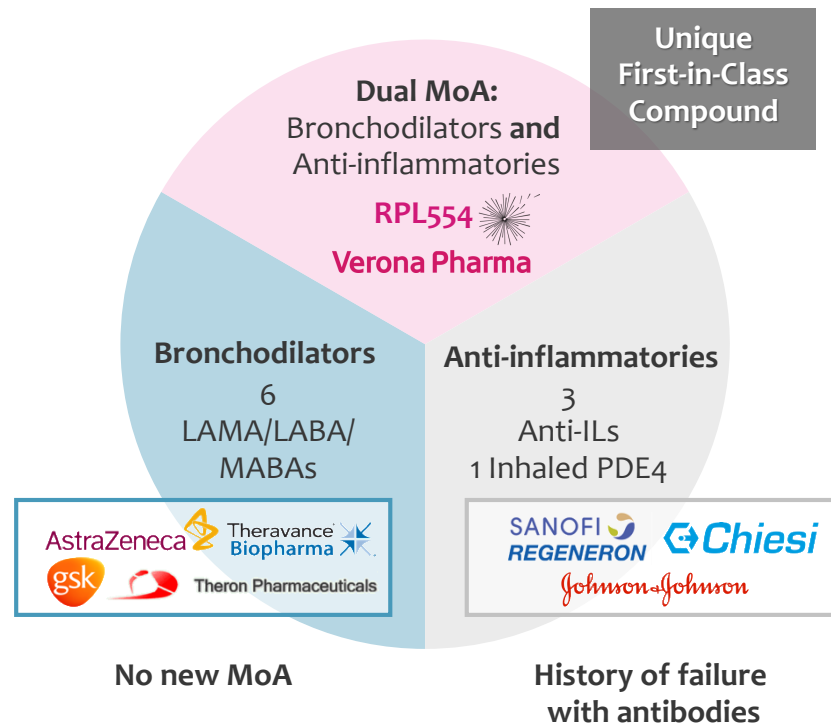
Unlike in asthma,  
do not work in  
early/moderate COPD

Oral - PDE4 Inhibitor  
• Roflumilast

Poorly tolerated  
(GI issues)

Significant Limitations

## In Development\*



Few with New MoA

\*See appendix slide 32



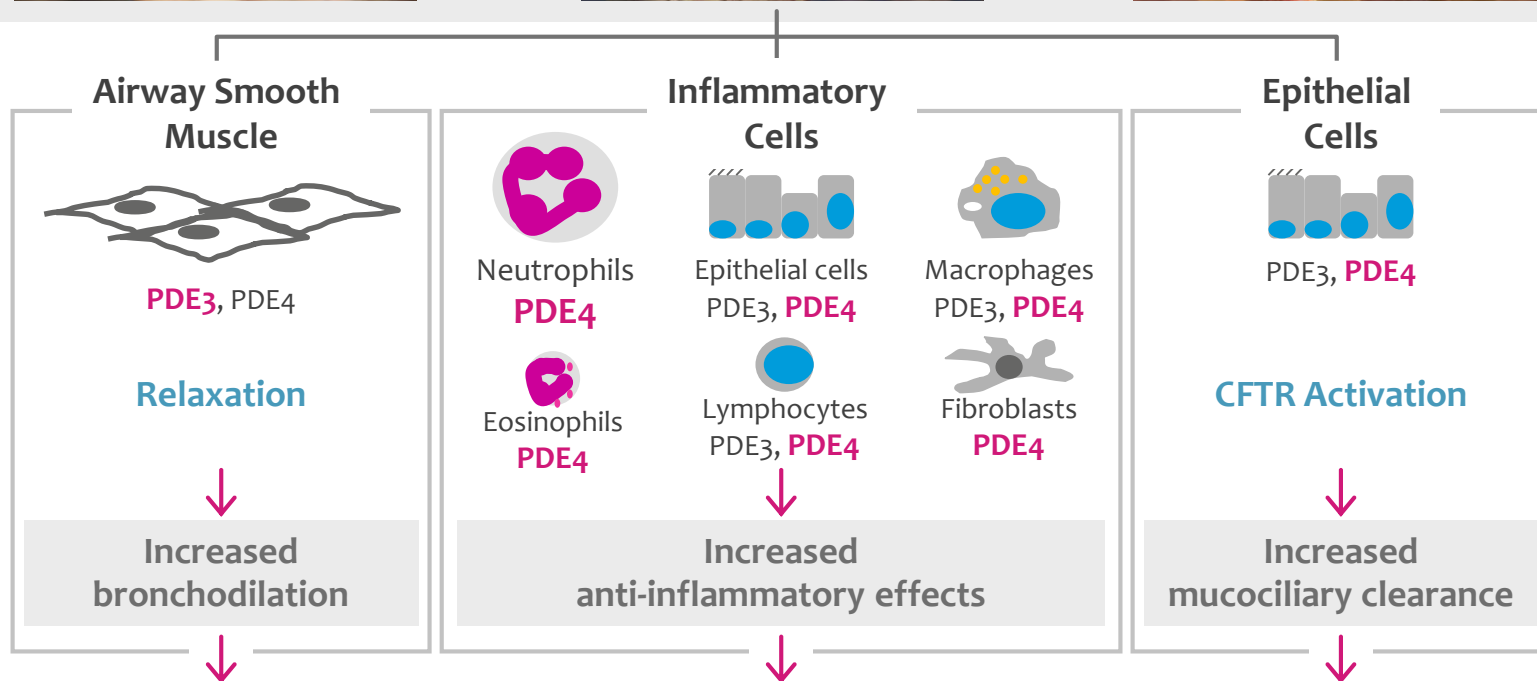
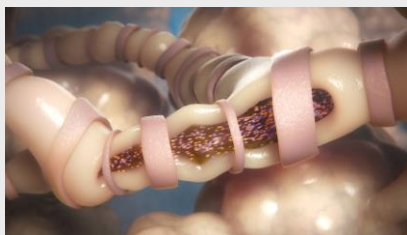
# RPL554 First-in-Class Candidate: Bronchodilator and Anti-inflammatory in a Single Compound



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## RPL554: Dual PDE3 and PDE4 Enzyme Inhibitor

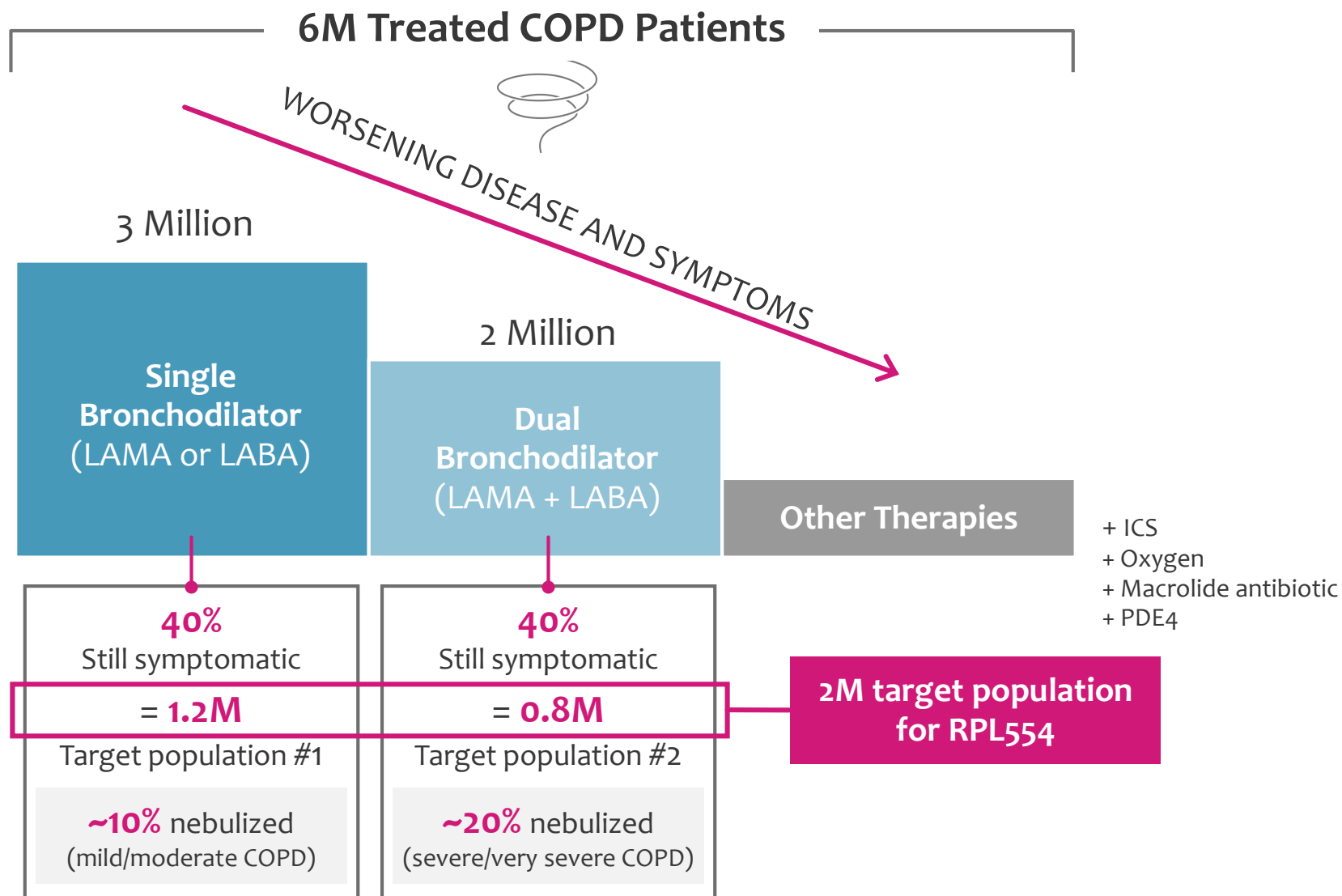
Impacts 3 Key Mechanisms in Respiratory Disease:



Leading to:

Improved lung function, symptom reduction and improved quality of life

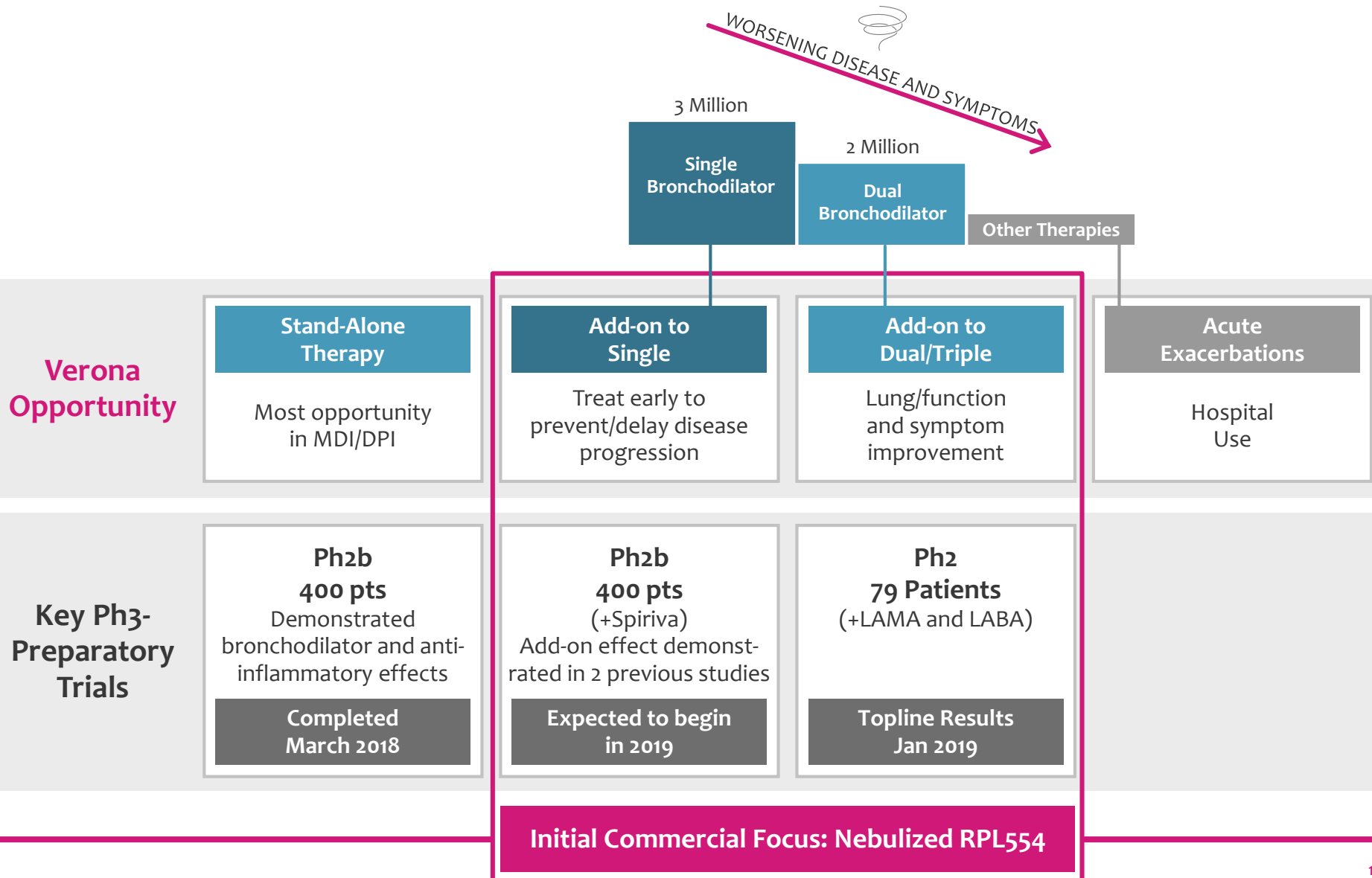
# Today's COPD Treatment Paradigm



# Nebulized RPL 554: Initial Opportunity as Add-on Therapy



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# Four Week Phase 2b Study: 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 centres 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

**Ph2b  
400 pts**

Demonstrated  
bronchodilator and anti-  
inflammatory effects

**Completed  
March 2018**

Initial Commercial Focus: Nebulized RPL554

# RPL554 Rapidly Improved Lung Function and Provided Progressive Symptom Relief in Phase 2b trial

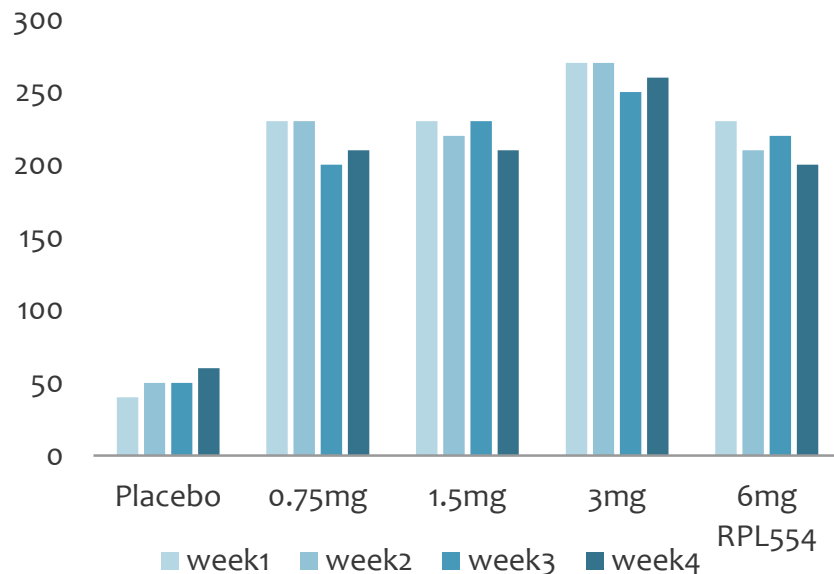


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## Lung Function

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

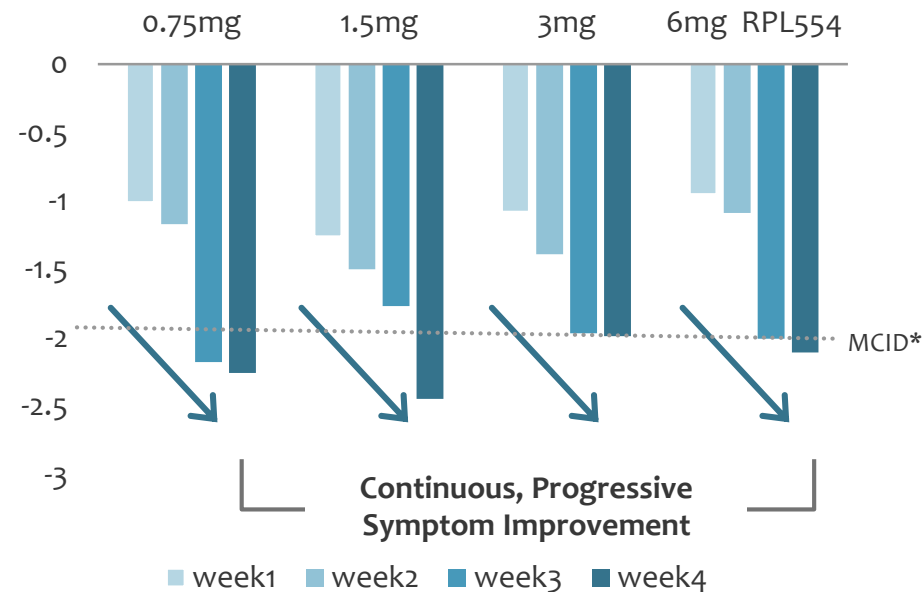
N=403



## Symptom Relief

Total Score E-RS: COPD by Week (Placebo Corrected, p<0.02)

N=403



\*Minimal clinically important difference

**Triple effect** of increased bronchodilation, anti-inflammatory effect and mucociliary clearance **improved lung function, relieved symptoms** and potentially leads to **reduction in COPD exacerbations**

# RPL554: Add-on Effect to Single Bronchodilator Reproduced in Two Independent Studies



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## Key Findings

**RPL554 Alone**

**RPL554 When Added to:**  
Albuterol, ipratropium  
or tiotropium

**Bronchodilation**

Similar effect observed to either albuterol or ipratropium alone

Improved FEV<sub>1</sub>

**Air Trapping**

Improved residual lung volume

**Time of Onset of Effect**

Provided faster relief

**Well Tolerated**

Presented no dose-limiting adverse events\*

**Ph2b 400 pts (+Spiriva)**  
**Add-on effect demonstrated in 2 previous studies**

**Expected to begin in 2019**

\*in completed clinical trials  
Source: Ph2 studies RPL554-009-2015; RPL554-CO-202

**79 Patients (+LAMA and LABA)**

**Topline Results Jan 2019**

**Initial Commercial Focus: Nebulized RPL554**

**Verona Opportunity**

**Stand-Alone Therapy**

Most opportunity in MDI/OPI

**Key P3-Preparatory Trials**

**Ph2b 400 pts**

Proven efficacy bronchodilator and anti-inflammatory

**Completed March 2018**



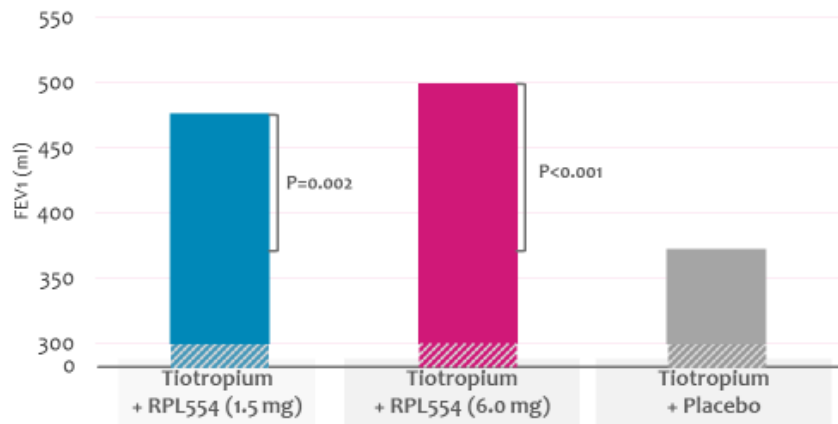
# RPL554: Significant Additional Bronchodilator Response when Inhaled on Top of Tiotropium (Spiriva)



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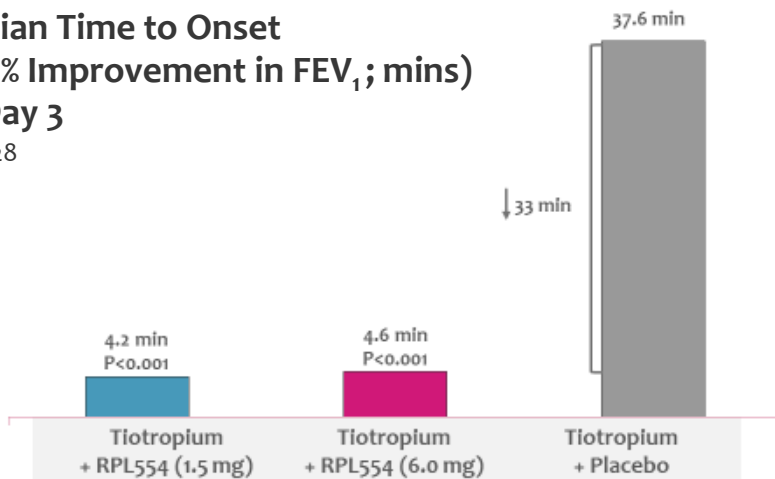
## Peak Change from Baseline in FEV<sub>1</sub> (ml) on Day 3

N=27-28



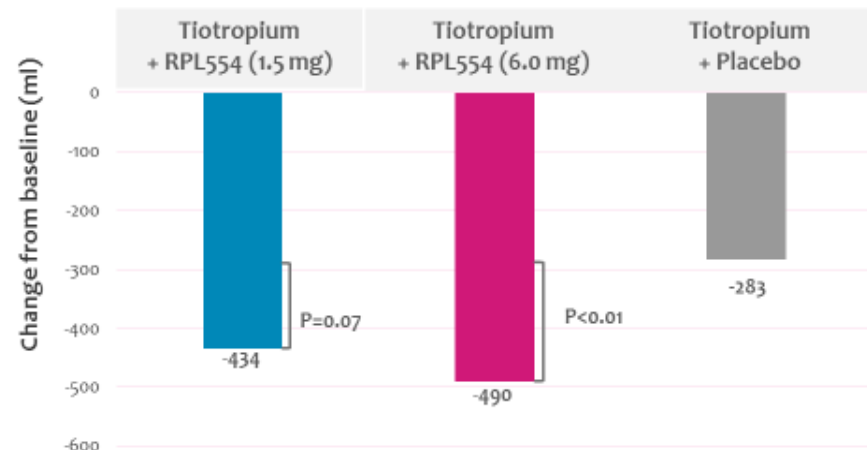
## Median Time to Onset (≥ 10% Improvement in FEV<sub>1</sub>; mins) on Day 3

N=27-28



## Reduction in Hyperinflation (ml) on Day 2

N=27-28



- Additional improvement in peak FEV<sub>1</sub>
- Reduction of hyperinflation - typically correlated with improvement in symptoms
- Rapid onset of action
- Well tolerated

# Evaluating RPL554 as Add-on to Dual Bronchodilator Treatment in COPD Patients



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## Trial Description:

- Phase 2 randomized, double blind, placebo controlled, cross-over study
- Three day treatment with baseline to peak FEV1 on Day 3 as primary endpoint
- Assess nebulized RPL554 as add-on to LAMA/LABA treatment; some patients maintained stable dose of ICS providing a triple background

## Patient Population:

- Enrolled 79 moderate-to-severe COPD patients; treatment phase completed
- Males and females, age 40-75

## Location:

- 2 Centers in US; 1 in UK

## RPL554 Dosage:

- Three arms, twice daily dosing with RPL554 at 1.5 mg and 6 mg and placebo

Initial Commercial Focus: Nebulized RPL554

WORSENING DISEASE AND SYMPTOMS

3 Million

Single  
Bronchodilator  
[1.2M]

2 Million

Dual  
Bronchodilator  
[0.8M]

800K

Still Symptomatic

Standard  
Therapy

Add-on to  
Single

Add-on to  
Dual/Triple

Acute  
Exacerbations

Hospital  
Use

Treat early to  
prevent/delay disease  
progression

Lung/function  
and symptom  
improvement

Ph2b

400 pts

(+Spiriva)

Proven add-on effect  
in 2 previous studies

Begins

Ph2

79 Patients  
(+LAMA and LABA)

Topline Results  
Jan 2019

400 pts

Proven efficacy  
in previous studies  
and anti-inflammatory

Completed

Verona  
Opportunity

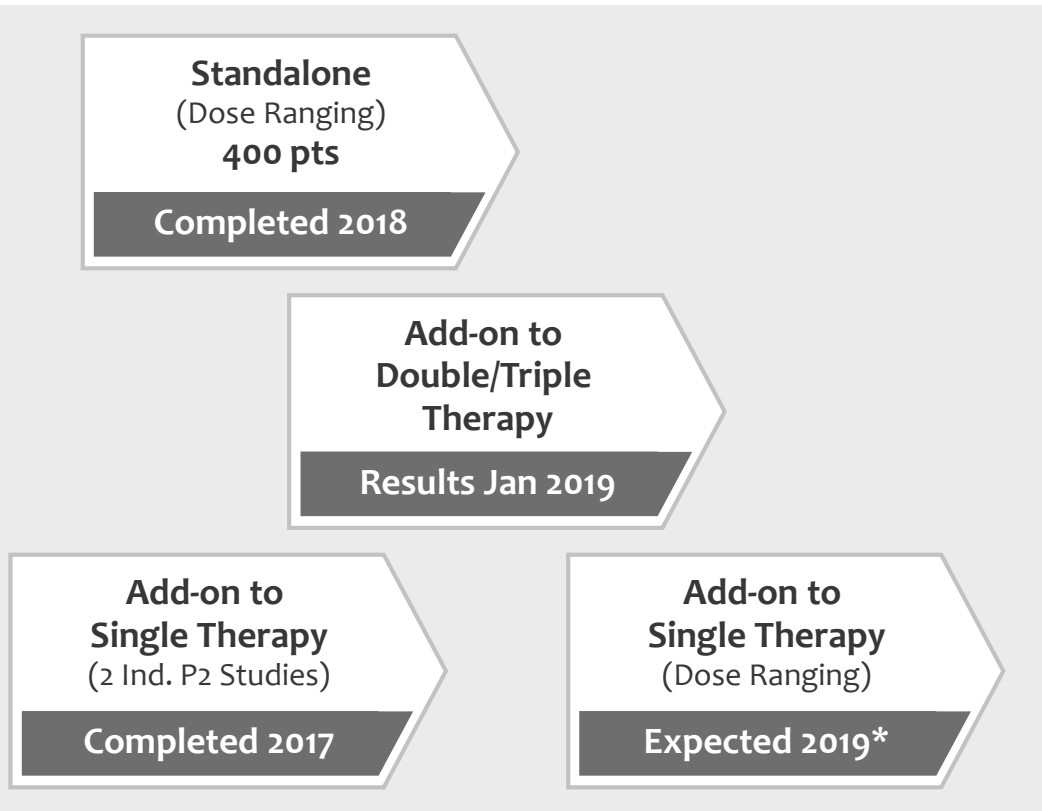
Key  
Preparatory  
Trials

# Advancing to Phase 3 – Planned Development Pathway



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## Phase 3-Preparatory Trials



## Phase 3 Development

Nebulized add-on to current  
**“Standard-of-Care”**

Two trials, each 3 - 6 months duration;  
12 months safety data

Potential endpoints: **lung function**  
(e.g. FEV<sub>1</sub>), **symptom improvement**,  
**explore exacerbations**

... plus significant potential opportunity  
for inhalers (DPI/MDI) **and**  
progression in other indications

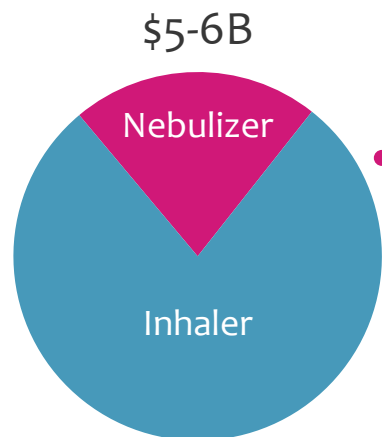


End of Phase 2 Meeting with FDA  
planned for 2H 2019

\*Expected to begin in 1H 2019, results expected in 2H 2019

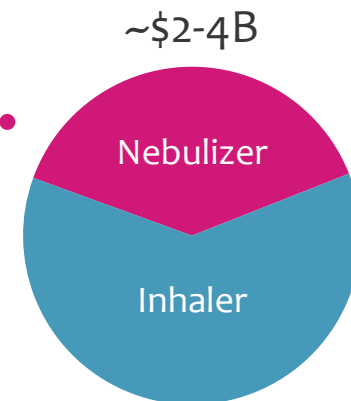
# Substantial and Addressable US Market Opportunity

## Add-on to Single Therapy



Attractive Medicare  
Part B Reimbursement

## Add on to Double/Triple Therapy



### Assumptions

Nebulizer		Inhaler	Nebulizer		Inhaler
\$1K	\$400	Avg. Monthly WAC Price	\$1K	\$400	
10%	90%	% of Patients	20%	80%	
0.12M	1.08M	Total Patients	0.16M	0.64M	

<sup>1</sup> See appendix slide 31

# Verona's Go-to-Market Strategy for Maintenance COPD



## Payors

### Nebulized therapy could be well reimbursed in US

- Reimbursed under favourable Medicare Part B
- 66% of payors report they would reimburse RPL554 at premium price (\$1K/month)\*

## Physicians

### Reach with Targeted Specialty Sales Force

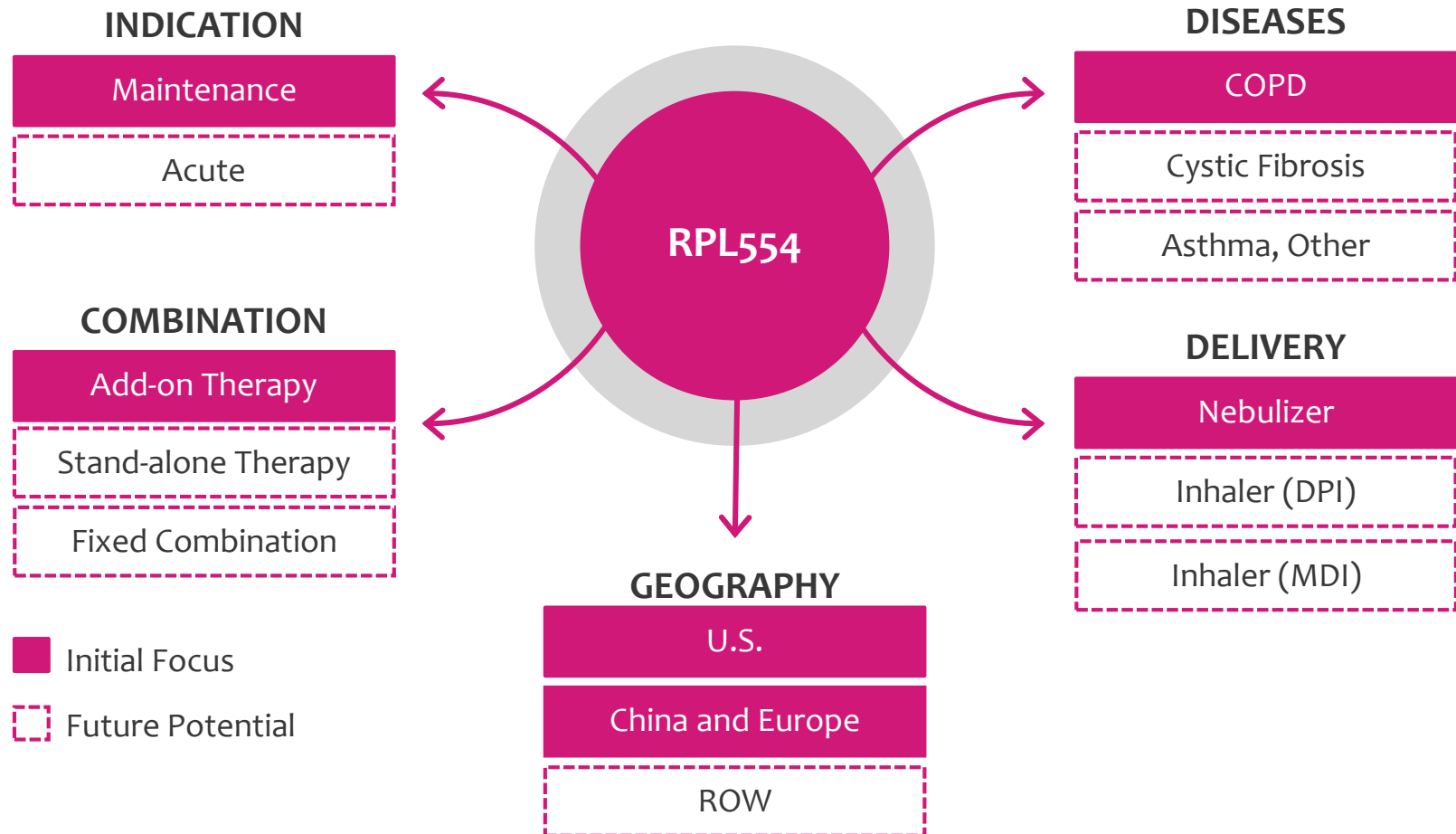
- Focused on high prescribing physicians & influential pulmonologists

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**Multiple additional opportunities** after initial market entry



# Significant Future Growth Potential



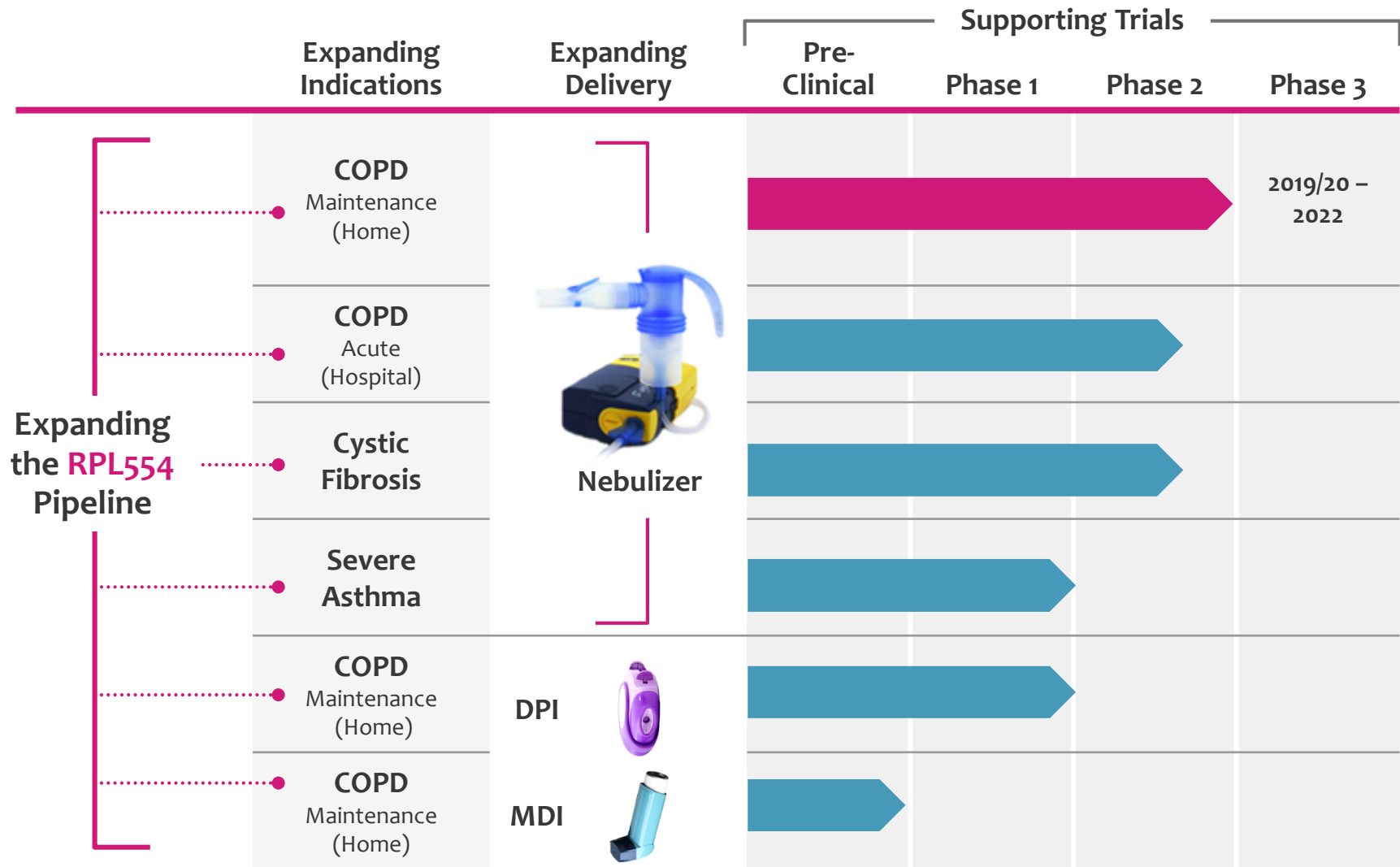
Worldwide Commercialization Rights; Patent Runway beyond 2030





# RPL554 Lifecycle: Expanding the Pipeline Over Time

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# Inhaled RPL554 - Potential to Expand Clinical Utility and Commercial Opportunity

## Inhaler Usage for Maintenance Therapy (U.S. Estimates)

- ~90% of 3.7 million mild/moderate COPD patients
- ~80% of 2.7 million severe/very severe COPD patients

## Next Steps in DPI and MDI Formulation Development

- DPI clinical trials started December 2018
- MDI clinical trials planned to start 1H 2019



**Potential to broaden use in other indications,  
such as asthma**

**Available for out-licensing**

# CF: A Devastating Orphan Disease

*RPL554: Favorable PK and PD Profile in CF Patients*



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- 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
  - Designed to reduce airway obstruction and inhibit inflammation



**Pre-clinical Studies and Phase 2a Study, Data Reported March 2018**



- RPL554 has the potential to be an effective bronchodilator in asthma patients
- Clear dose-response relationship and well tolerated in asthmatics in Phase 2a clinical study
- Little effect on heart rate and plasma potassium levels compared to nebulized albuterol

## Potential Positioning

- Severe asthma, before start of treatment with biologics
- Steroid-sparing

## Potential Device

DPI or MDI inhaler device may be more convenient for asthma patients



# RPL554: Long Patent Runway (until mid-2030s)

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## Robust Patent Portfolio

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- Composition of Matter – granted US, EU, Japan, other; expires 2020
  - Polymorph – granted US, EU, Japan, other; expires 2031
  - Formulations – granted US, EU, other; expires 2035
  - Manufacturing, use, salt forms, combinations: granted and pending in US, EU, and other territories; expires 2031 – 2037
  - Additional IP opportunities being explored
- 

## New Chemical Entity

- US: Market exclusivity up to 5 years post NDA approval
- EU: Market & Data exclusivity up to 10 years post Marketing Authorization

## Verona Pharma Has Global Rights

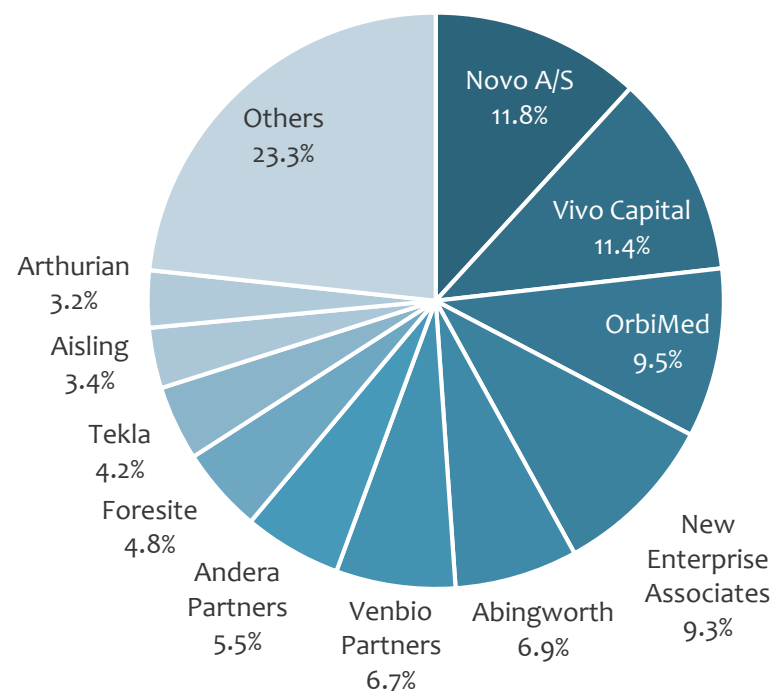


# Well Financed with Major Healthcare Investors

## Financial Overview September 30, 2018

Cash and Cash Equivalents	\$89.9M <sup>1</sup>
Operating Expenses Year To Date 3Q18	\$23.9M <sup>1</sup>
Market cap	\$146M <sup>2</sup>

## Shareholdings<sup>3</sup>



<sup>1</sup>Exchange rate used (US dollars per pound sterling): September 30, 2018: \$1.3053

<sup>2</sup>Fully diluted 127m shares or 15.9m ADSs, share price 91p and exchange rate £1 : \$1.2625 on January 3, 2019

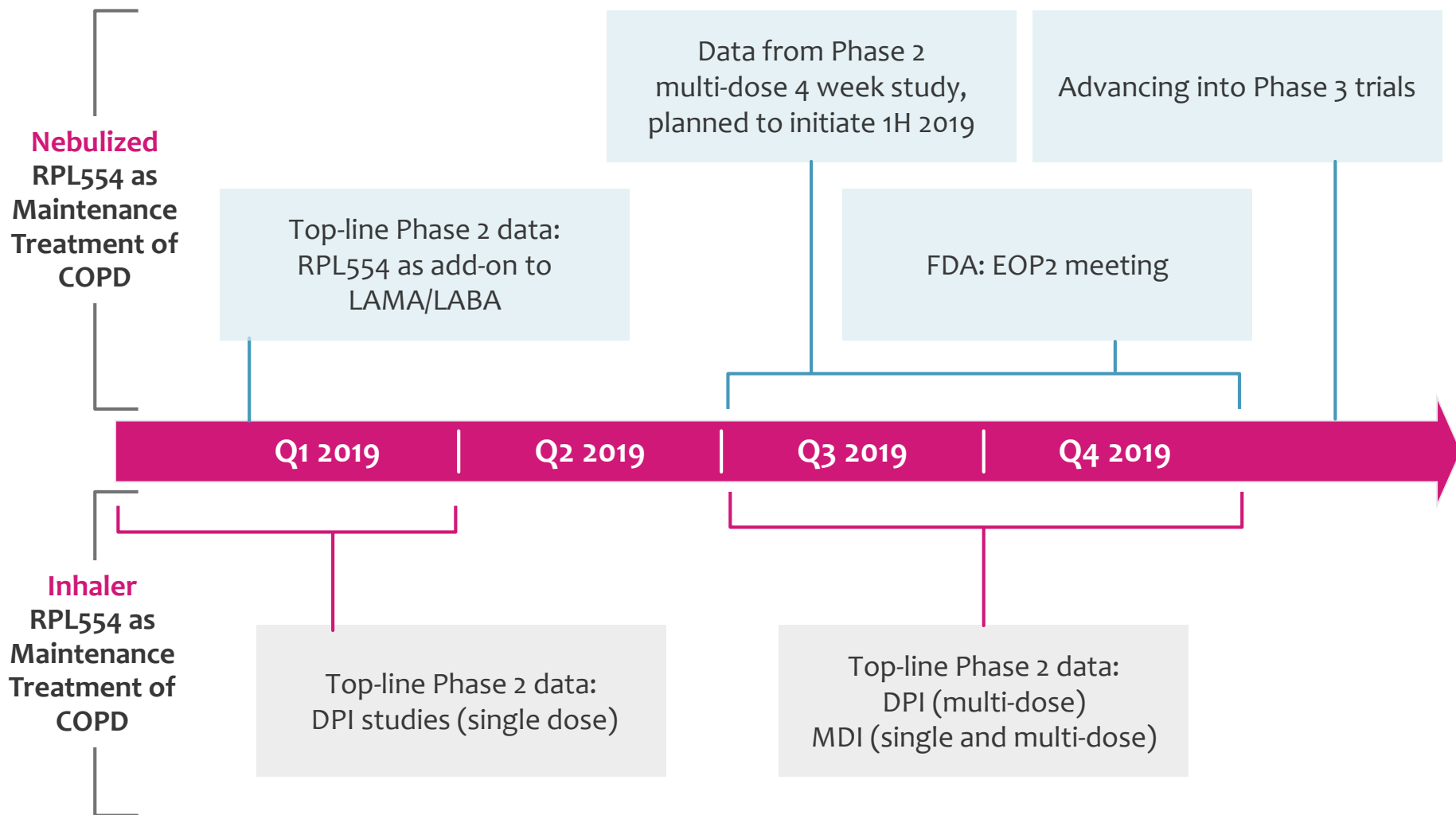
<sup>3</sup>As disclosed to the Company in accordance with AIM Rule 26, or through s80 notices and 13G filings



# 2019: An Important Year with Potential for Multiple Value Inflection Points



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## RPL554: Promising Novel Treatment for Patients with COPD

### Realizing Significant Opportunity in COPD:



RPL554 – unique PDE3/4 inhibitor with **bronchodilator and anti-inflammatory effects observed in clinical studies**, and well tolerated



In clinical studies improved symptoms in **moderate to severe**, symptomatic COPD patients on twice daily dosing



Potential as both a **stand-alone drug** and as an **add-on** to standard COPD treatments

**Nebulized RPL554:** Planning FDA End of P2 meeting in **2H 2019** and subsequent P3 trials

Advancing **Inhaled RPL554** and potential to broaden in **other indications**



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**Appendix**





# Experienced Management Team and Board

## Management

<b>Jan-Anders Karlsson, PhD</b> Chief Executive Officer	   
<b>Piers Morgan, MA, ACA</b> Chief Financial Officer	   
<b>Kathy Rickard, MD</b> Chief Medical Officer (from 1 Feb -19)	 
<b>Richard Hennings, BSc</b> Commercial Director	  
<b>Peter Spargo, PhD</b> SVP CMC	  
<b>Claire Poll, LLB</b> Legal Counsel	 
<b>Desiree Luthman, DDS</b> VP Regulatory Affairs	  
<b>Tara Rheault</b> VP R&D Ops & Global Proj Mgmt	 

## 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:



# Nebulized RPL554: 12 Completed Clinical Trials with >800 Subjects Enrolled



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## Recent Trials

Trial	Program	# of Subjects	Duration	Status
Phase 1/2	SAD MAD study with new suspension formulation	112	Single dose and twice daily for 5 days	Completed Sept 2015
Phase 2a	Dose ranging in asthma	29	Single dose	Completed March 2016
Phase 2a	Add-on to each of albuterol or ipratropium	30	Single dose	Completed May 2016
Phase 2a	Add-on to tiotropium (Spiriva®)	30	Dosed twice-daily for three days	Completed Sept 2017
Phase 1	Pharmacokinetic trial, US FDA new IND	12	Single dose	Completed Sept 2017
Phase 2b	Maintenance treatment	403	Dosed twice daily for four weeks	Completed March 2018
Phase 2	Add-on to dual bronchodilator therapy (LAMA/LABA: Stiolto)	79 enrolled	Dose twice daily for three days	LPFV Oct 2018 Top-line Jan 2019

# Maintenance Treatment of COPD: Substantial Market with Premium Pricing in Nebulized Segment



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US Sales of Common Bronchodilators	Administration	Class	Avg Monthly \$ WAC price <sup>1</sup>	US Only Sales \$M <sup>2</sup>
Brovana (Sunovion)	Nebulizer - open	LABA	971	339
Perforomist (Mylan)	Nebulizer - open	LABA	972	155
Lonhala (Sunovion) <sup>3</sup>	Nebulizer - closed	LAMA	1,190 <sup>4</sup>	-
Revefenacin (Mylan/Theravance)	Nebulizer - open	LAMA	FDA approval Nov 9, 2018	
Advair (GSK)	Inhaler	LABA / ICS	398	1,094
Spiriva (Boehringer-I)	Inhaler	LAMA	398	1,779
Anoro (GSK)	Inhaler	LAMA / LABA	398	277
Trelegy (GSK) <sup>3</sup>	Inhaler	LAMA / LABA / ICS	530	-

1. Oct 17 – Jan 18
2. May 2016 – April 2017
3. Launched April 2018
4. Retail price, [www.drug.com](http://www.drug.com)

Sources: Q2 2017 US COPD patient database & physician survey research, IQVIA MIDAS Sales. Mullerova H., et al., Characterization of COPD Patients Treated With Inhaled Triple Therapy Containing Inhaled Corticosteroid [ICS], Long-Acting Beta2-Agonists [LABA], and Long-Acting Muscarinic Antagonists [LAMA] in the UK, American Journal of Respiratory and Critical Care Medicine 2017;195: A4986. Vestbo J, et al., Single inhaler extrafine triple therapy versus long-acting muscarinic antagonist therapy for chronic obstructive pulmonary disease (TRINTY); a double-blind, parallel group, randomised controlled trial, The Lancet, Vol 389, p. 1919-1929; May 13, 2017



# Compelling Need for Therapy with New Mode of Action for COPD

... but Few Such Drugs in Development for COPD

