Verona Pharma

Late-breaking oral presentation at ERS 2018: "RPL554, a first-in-class dual PDE3/4 inhibitor, causes significant bronchodilation and symptom relief; a Phase 2b COPD study,"
D Singh, M.D., Professor, MEU, University of Manchester
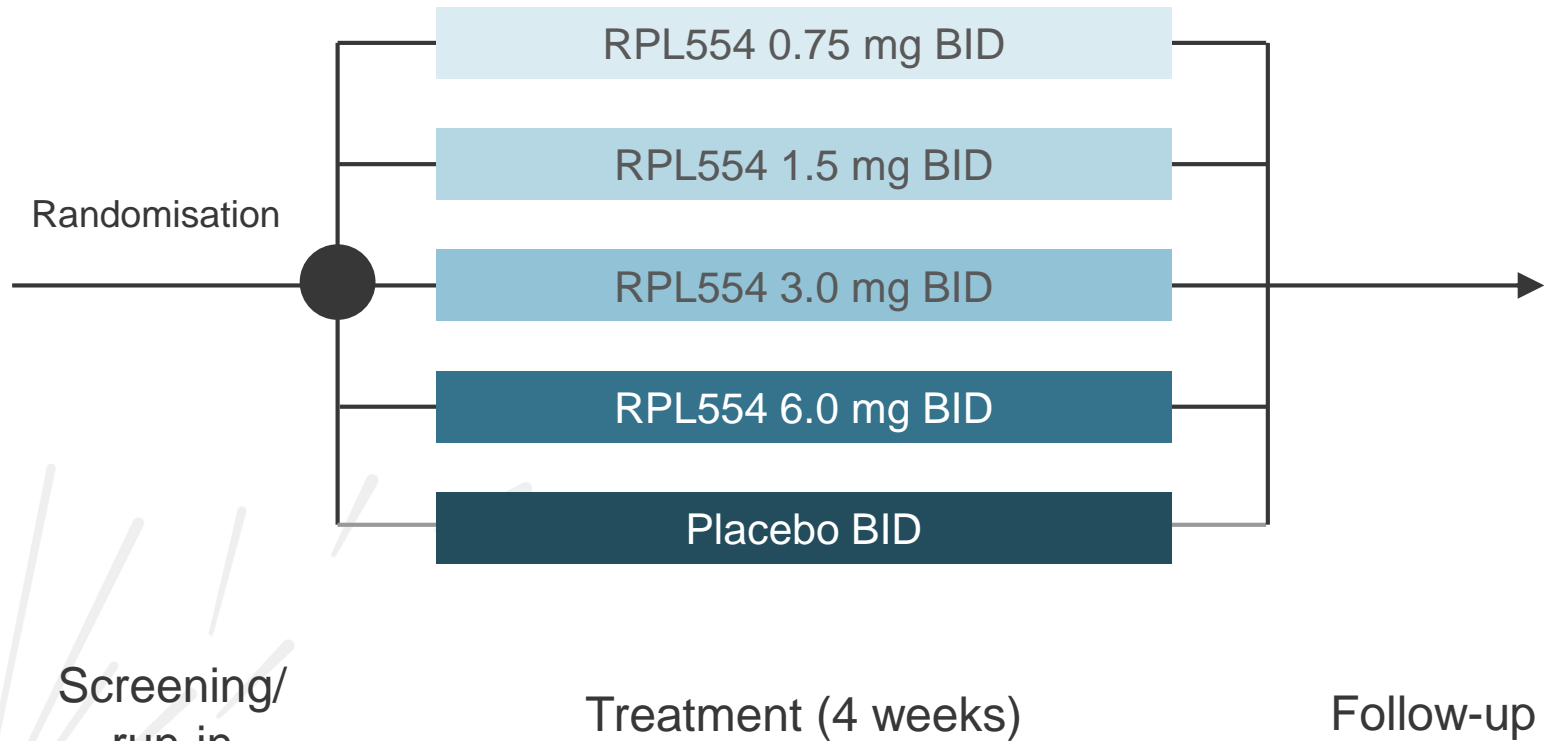
September 18, 2018

Study Design

- **Description:**
  - Phase 2b randomized, double blind, placebo controlled, dose ranging study

- **Patient Population:**
  - 403 patients with moderate-to-severe COPD, diagnosed >12 months previously
  - males and females, age 40-75

- **Location:**
  - approx. 45 out-patient centers in Western & Eastern Europe

- **Background therapy:**
  - no background bronchodilator therapy
 - stable ICS regimen could be maintained

Study Design

Randomisation

RPL554 0.75 mg BID

RPL554 1.5 mg BID

RPL554 3.0 mg BID

RPL554 6.0 mg BID

Placebo BID

Screening/
run-in

Treatment (4 weeks)

Follow-up

Demographics

Parameter	Patients (N=403)
Age	63.2 years
Gender, male	60.5%
Race, Caucasian	100%
Disease characteristics	
COPD duration	7.8 years
Chronic bronchitis	62%
MRC ≥2	93.6%
Smoking, current smoker	54.8%
Pack-years	42.1
Screening spirometry	
FEV_1, post-salbutamol	55.8% predicted normal
FEV_1, post-salbutamol	1.64 L
FEV_1 reversibility	11.7%

Lung function: Highly reproducible peak FEV_1 over 4 weeks
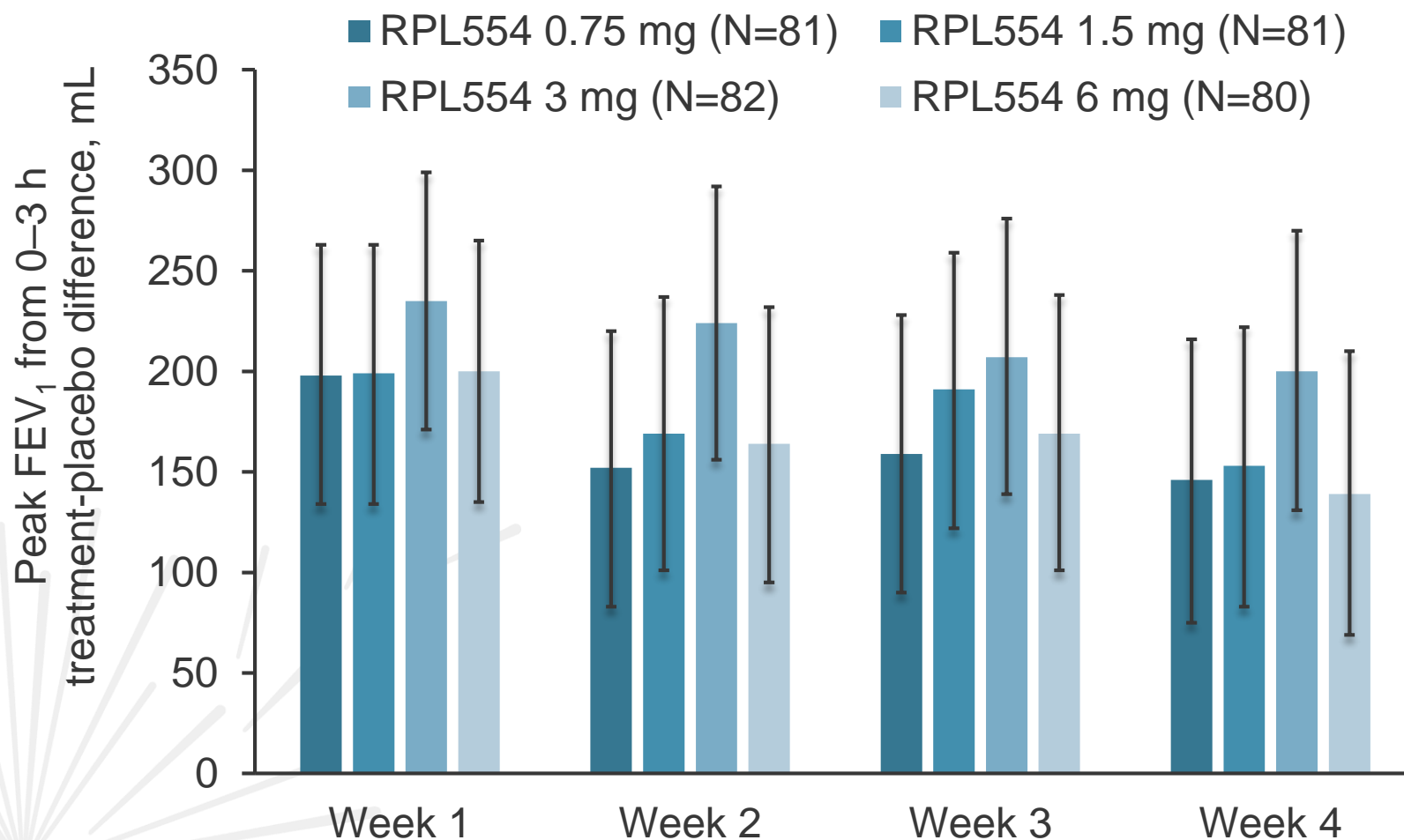
FEV$_1$, forced expiratory volume in 1 second.
All treatment–placebo differences $p < 0.001$. Data are LS mean and 95% confidence intervals.
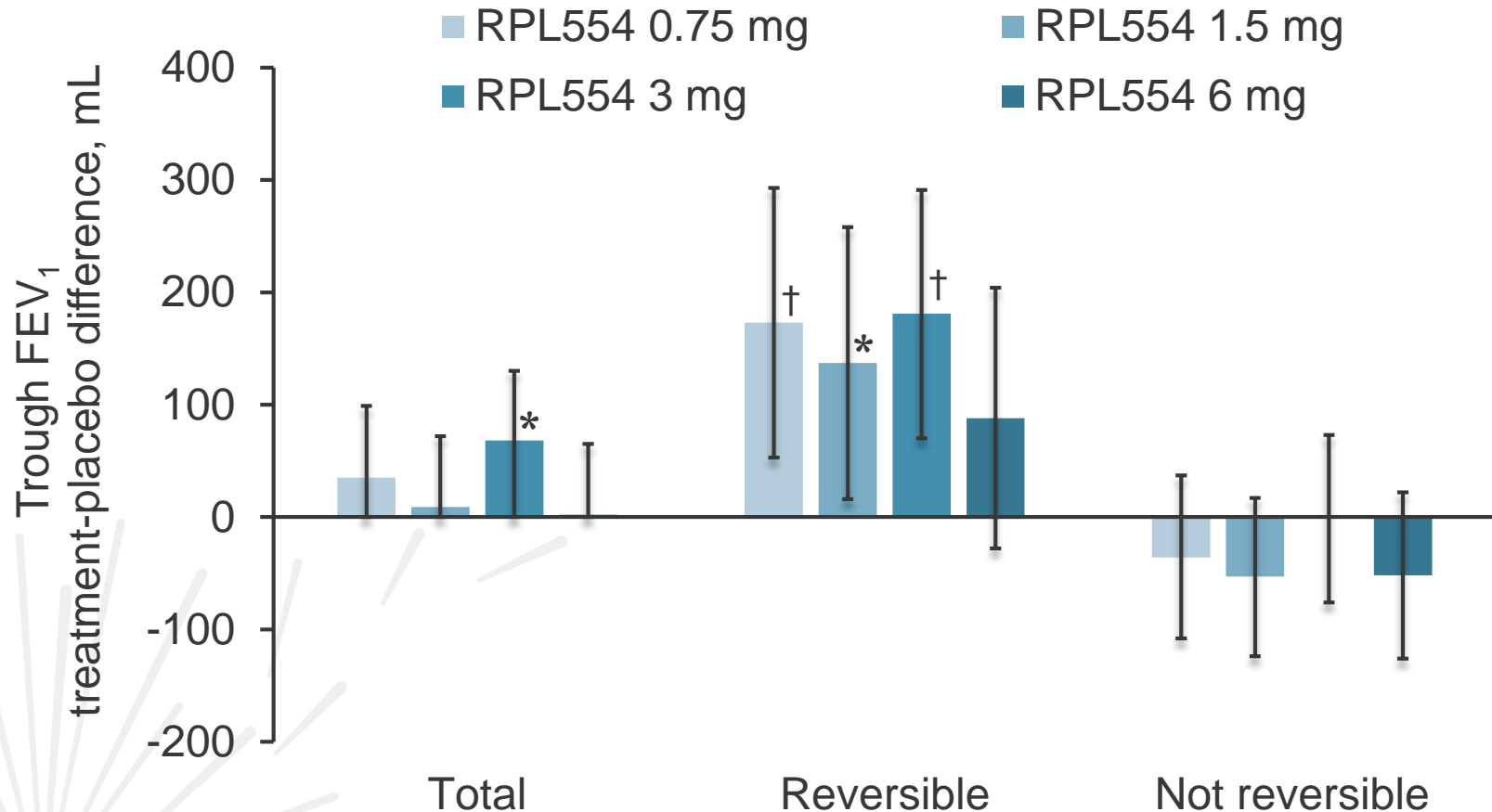
Lung function: Average FEV_1 from 0–12 hours after 4 weeks
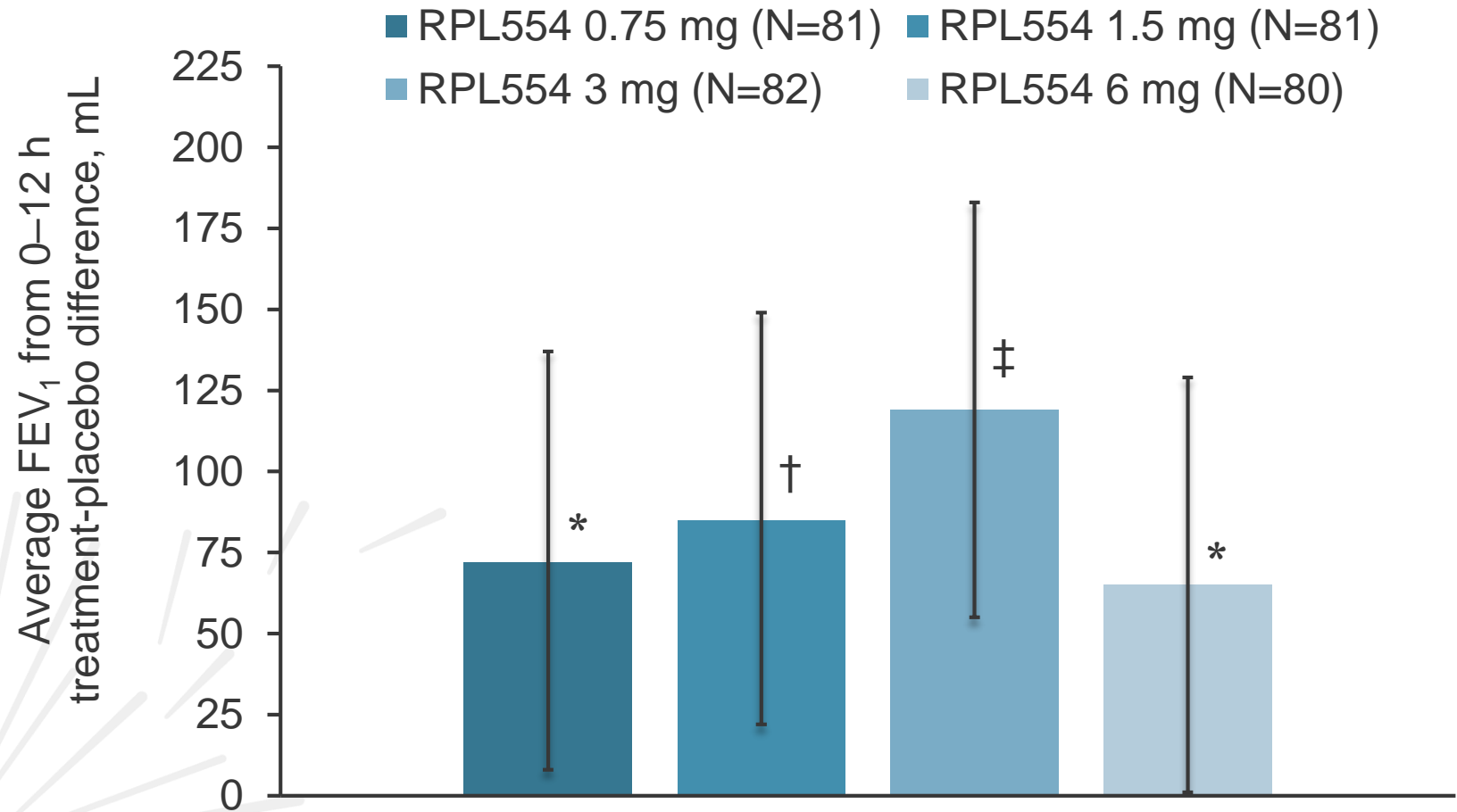
FEV$_1$, forced expiratory volume in 1 second. Treatment–placebo difference: *p<0.05; †p<0.01; ‡p<0.001. Data are LS mean and 95% confidence intervals
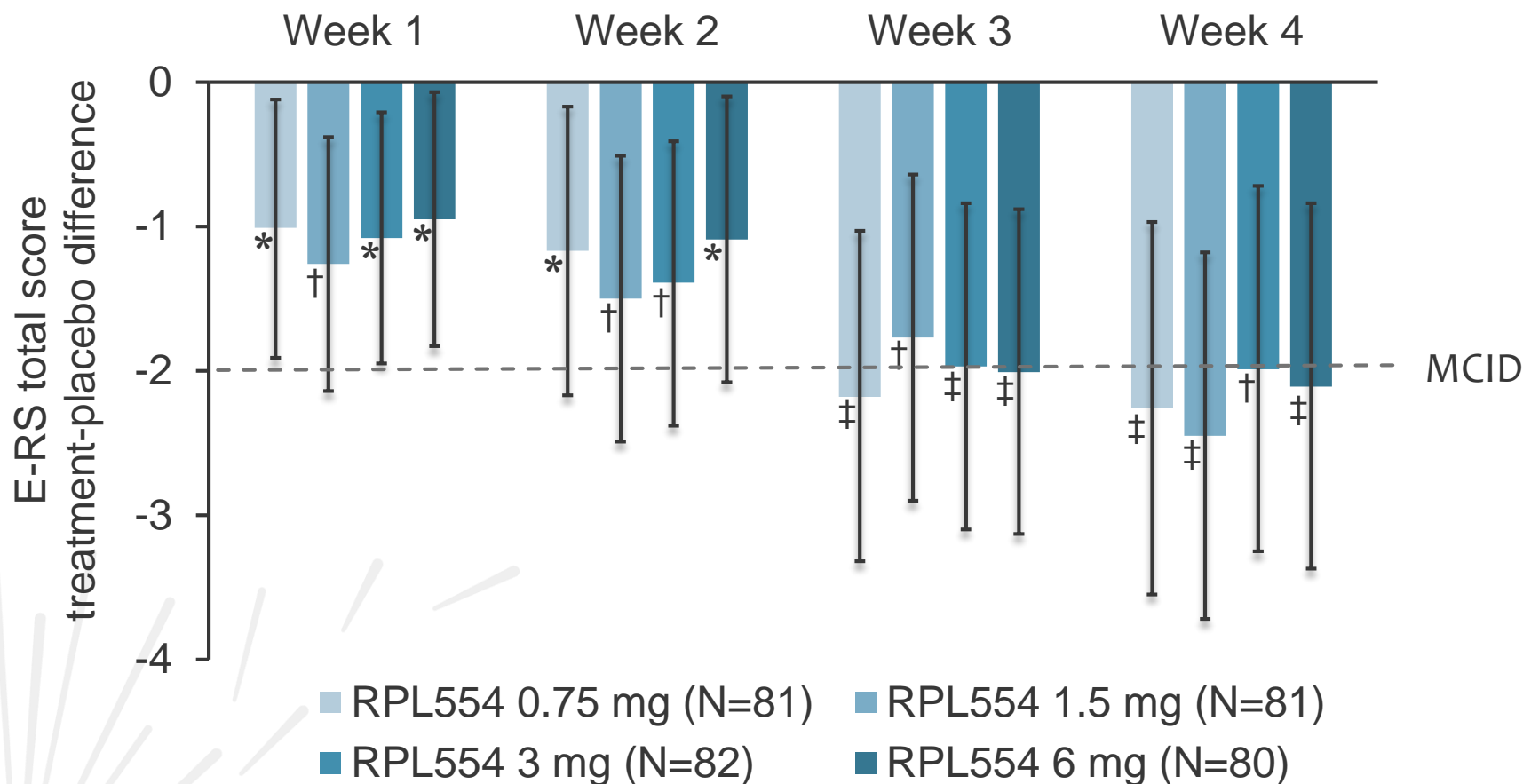
Lung function: Trough FEV$_1$ after 4 weeks

FEV$_1$, forced expiratory volume in 1 second. Reversible defined as FEV$_1$ change from pre- to post-salbutamol ≥12% and ≥200 mL; not reversible <12% or <200 mL. Treatment–placebo difference: *p<0.05; †p<0.01. Data are LS mean and 95% confidence intervals.

# Respiratory symptoms (E-RS): Progressive improvement over 4 weeks

MCID, minimum clinically important difference; E-RS, EXAcerbations of Chronic Pulmonary Disease Tool-Respiratory Symptoms. Treatment–placebo difference: *p<0.05; †p<0.01; ‡p≤0.001. Data are LS mean and 95% confidence intervals.

Health status (SGRQ-C) at Week 4

RPL554 0.75 mg (N=81) RPL554 1.5 mg (N=81) RPL554 3 mg (N=82)
RPL554 6 mg (N=80) Placebo (N=79)
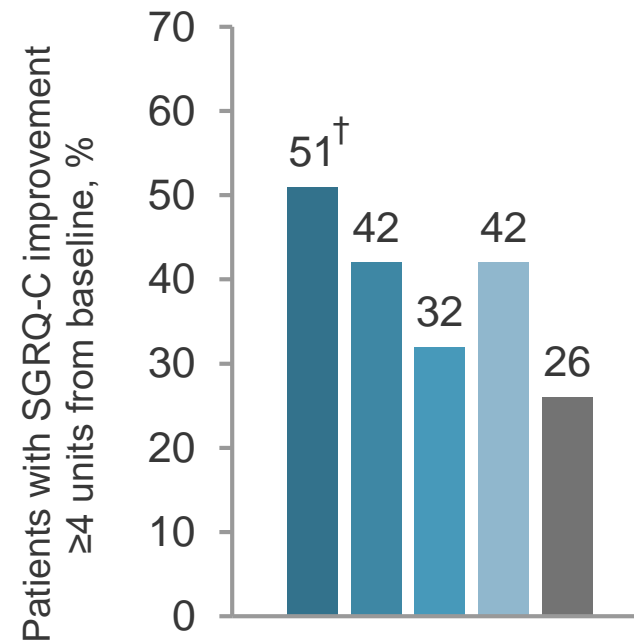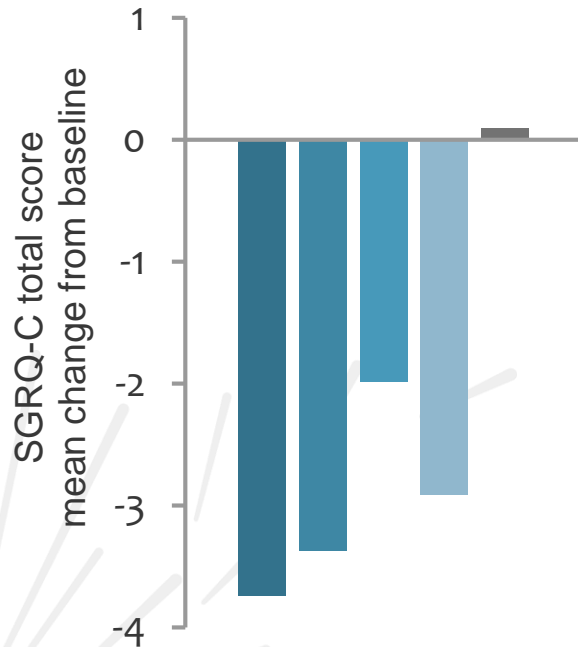
SGRQ-C, St George's Respiratory
Questionnaire – COPD. Treatment–placebo difference: [†]p<0.01.

Adverse events

Patients, n (%)	RPL554				Placebo (N=79)
	0.75 mg (N=81)	1.5 mg (N=81)	3 mg (N=82)	6 mg (N=80)	
Any AE	27 (33.3)	36 (44.4)	29 (35.4)	29 (36.3)	31 (39.2)
Drug-related	8 (9.9)	11 (13.6)	12 (14.6)	8 (10.0)	10 (12.7)
Severe AE	4 (4.9)	1 (1.2)	2 (2.4)	1 (1.3)	2 (2.5)
Serious AE	2 (2.5)	2 (2.5)	1 (1.2)	1 (1.3)	1 (1.3)
Drug-related	1 (1.2)	1 (1.2)	0	0	0
AE leading to death	0	1 (1.2)	0	1 (1.3)	0

Conclusions

- RPL554 – first-in-class, dual PDE3/4 inhibitor

- In patients with COPD, 4 weeks treatment with RPL554:
  - improved lung function
  - reduced symptoms

- The improvement in symptoms was progressive and clinically meaningful
  - Probably due to an anti-inflammatory effect

- RPL554 was well tolerated, all doses having a placebo-like adverse event profile

- RPL554 demonstrates benefit as standalone and add-on treatment