

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

**FORM 8-K**

**Current Report Pursuant  
to Section 13 or 15(d) of the  
Securities Exchange Act of 1934**

Date of Report (Date of earliest event Reported): **September 4, 2012**

**THERAVANCE, INC.**

(Exact Name of Registrant as Specified in its Charter)

**Delaware**

(State or Other Jurisdiction of  
Incorporation)

**000-30319**

(Commission File Number)

**94-3265960**

(I.R.S. Employer Identification Number)

**901 Gateway Boulevard  
South San Francisco, California 94080  
(650) 808-6000**

(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01 Regulation FD Disclosure.**

*The information contained in this Item 7.01 and in the accompanying exhibit shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing under the Exchange Act or the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.*

On September 4, 2012 at the European Respiratory Society (ERS) Annual Congress 2012 in Vienna, Austria, two oral presentations were made, one relating to a Phase 3 study of fluticasone furoate/vilanterol (FF/VI) and the other relating to a Phase 2b study of GSK961081 ('081). FF/VI, with proposed brand names of Relvar™ and Breo™, is an investigational once-daily inhaled corticosteroid (ICS)/long-acting beta-agonist (LABA) combination treatment for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD) and patients with asthma. '081 is a single molecule bifunctional bronchodilator with both muscarinic antagonist and beta<sub>2</sub> receptor agonist activities for the treatment of COPD. FF/VI and '081 are in development under the LABA collaboration and strategic alliance, respectively, between GlaxoSmithKline and Theravance, Inc. The slides from the oral presentations are furnished as Exhibit 99.1 and Exhibit 99.2 to this report and are incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

- (d) Exhibits

<b>Exhibit</b>	<b>Description</b>
Exhibit 99.1	Lung function effects and safety of fluticasone furoate (FF)/vilanterol (VI) in patients with COPD: low-mid dose assessment

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**THERAVANCE, INC.**

Date: September 4, 2012

By: /s/ Michael W. Aguiar  
**Michael W. Aguiar**  
**Chief Financial Officer**

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**EXHIBIT INDEX**

<u>Exhibit</u>	<u>Description</u>
Exhibit 99.1	Lung function effects and safety of fluticasone furoate (FF)/vilanterol (VI) in patients with COPD: low-mid dose assessment
Exhibit 99.2	A dual-acting muscarinic antagonist, beta 2-agonist (MABA) molecule (GSK961081) improves lung function in COPD: A randomised trial

# Lung function effects and safety of fluticasone furoate (FF)/vilanterol (VI) in patients with COPD: low-mid dose assessment

Kerwin EM<sup>1</sup>, Scott-Wilson C<sup>2</sup>, Sanford L<sup>3</sup>,  
Rennard SI<sup>4</sup>, Agusti A<sup>5</sup>, Barnes N<sup>6</sup>, Crim C<sup>2</sup>

1. Clinical Research Institute of Southern Oregon, Medford, OR, USA;
2. GlaxoSmithKline, Research Triangle Park, NC, USA;
3. GlaxoSmithKline, Stockley Park, London, UK;
4. University of Omaha, Nebraska, OH, USA;
5. Thorax Institute, Hospital Clinic, IDIBAPS, University of Barcelona and FISIB, CIBERES, Mallorca, Spain;
6. Respiratory Medicine, Barts and The London NHS Trust, London, UK

## CONFLICT OF INTEREST DISCLOSURE

**Edward Kerwin, M.D. has served on Advisory Boards for Astra Zeneca, Forest, Ironwood, Mylan, Pearl, Sanofi, Sunovion and Targacept; Speakers Panels for AstraZeneca, Pfizer, Sanofi, and Sunovion; and has received travel reimbursement from Merck, Forest and Novartis. He has conducted clinical trials for multiple pharmaceutical companies, including GlaxoSmithKline**

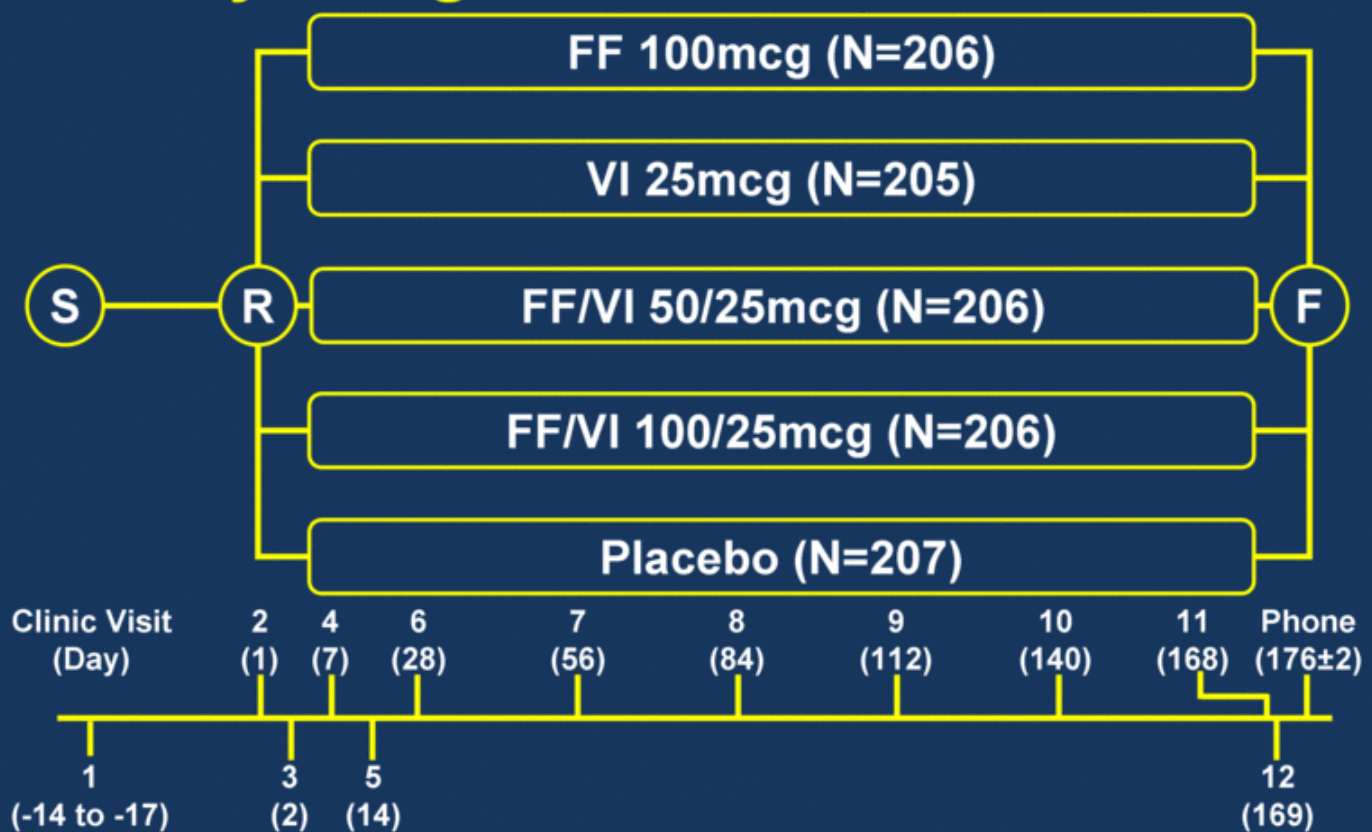
## Introduction

- **An inhaled corticosteroid (ICS) combined with a long-acting beta<sub>2</sub> agonist (LABA) is an established treatment for COPD patients experiencing impaired airway function or acute exacerbations**
- **Fluticasone furoate (FF) and vilanterol (VI) are respectively, a novel ICS and LABA, in development as a once-daily combination therapy for COPD and asthma**

# Objectives

- Post-Dose & Trough Lung Function Effects
  - 24-week efficacy of VI
  - Addition of FF to VI
  - Dose Range FF when added to VI
- Symptoms
- Safety

# Study design



# Endpoints

- **Co-primary**

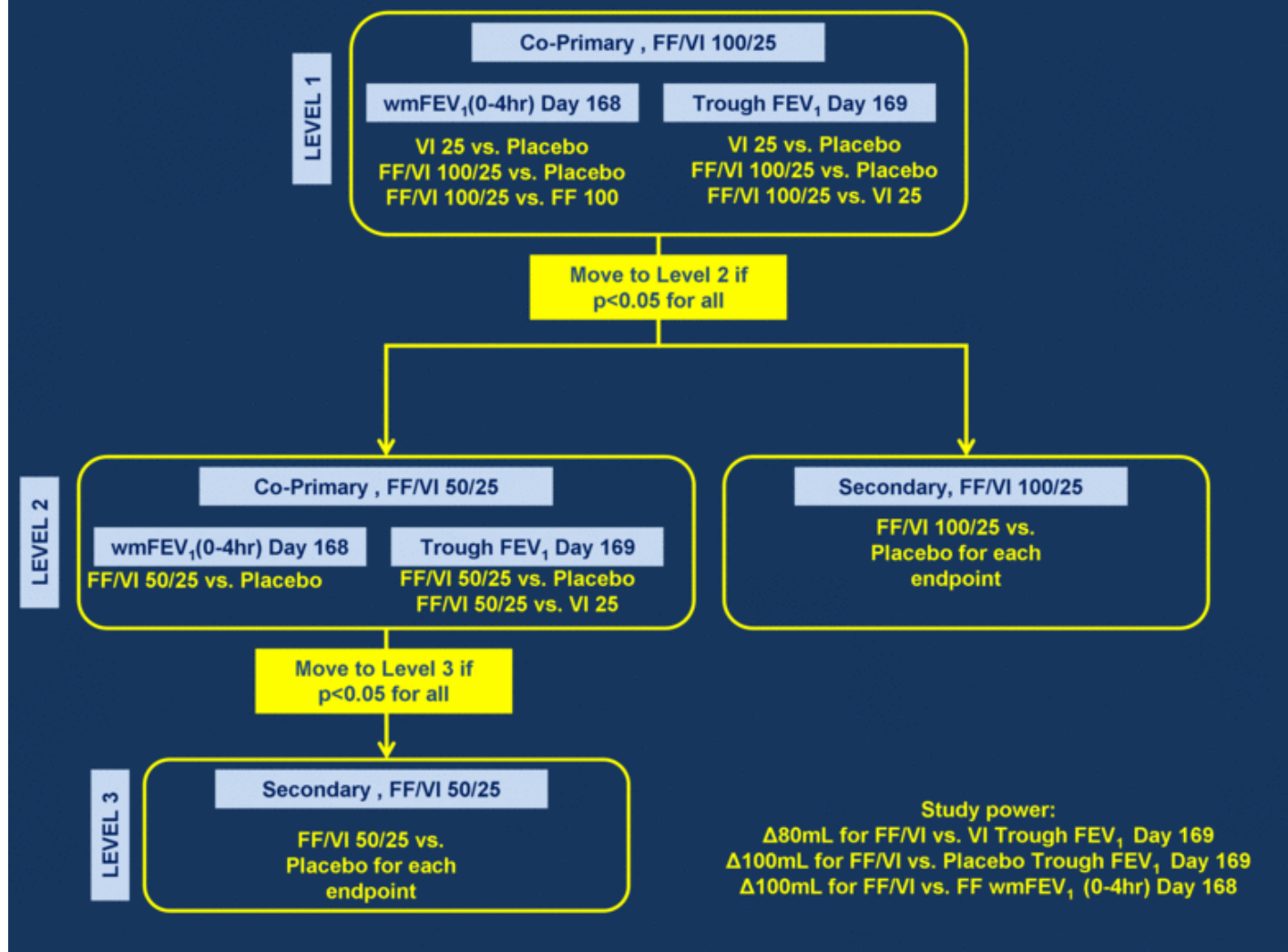
- Weighted mean FEV<sub>1</sub> (0-4hr) post-dose, Day 168
- Change from baseline Trough FEV<sub>1</sub>, Day 169

- **Secondary**

- CRQ-SAS dyspnoea domain
- Peak FEV<sub>1</sub> (0-4hr) post-dose, Day 1
- Time to  $\Delta$ 100mL (0-4hr) post-dose, Day 1

- **Safety**



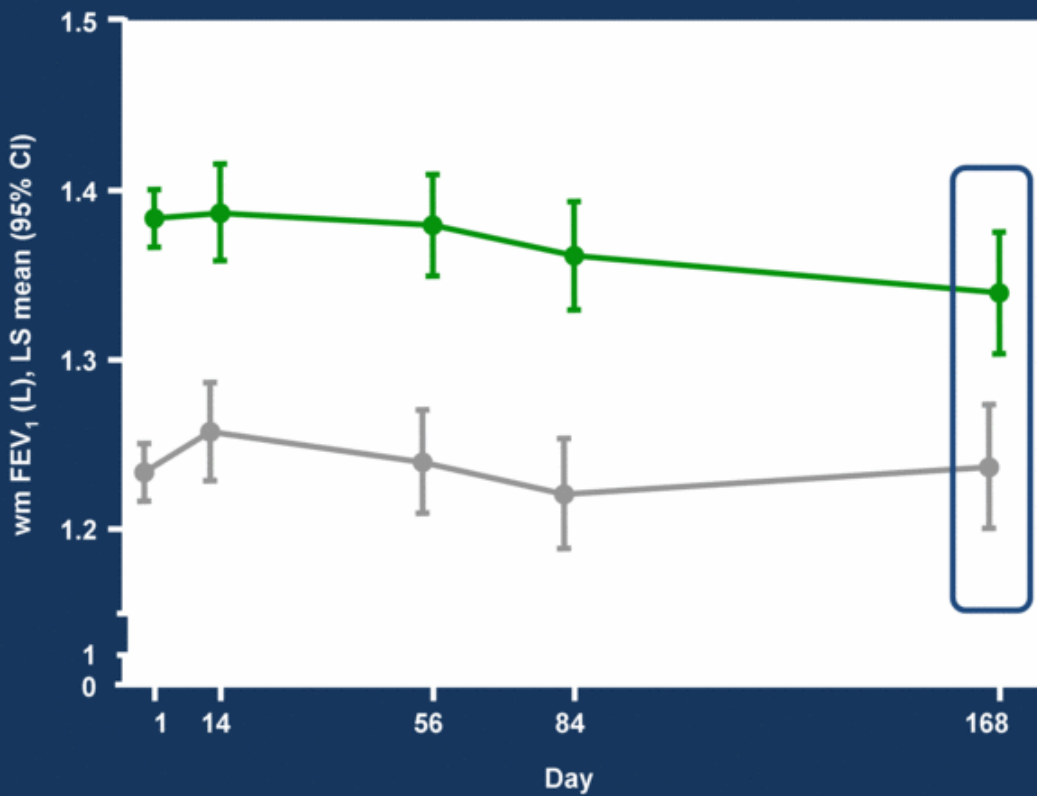


# Characteristics

		Total (N=1030)
Mean Age, yr (SD)		62.7 (9.09)
Male Sex, n (%)		685 (67)
Mean Post-BD FEV <sub>1</sub> , L (SD)		1.406 (0.48)
Mean Post-BD %pred FEV <sub>1</sub> , % (SD)		48.3 (12.45)
GOLD stage, n (%)	II	487 (47)
	III	445 (43)
	IV	94 (9)
Mean mMRC dyspnoea, score (SD)		2.4 (0.5)
Moderate* exacerbations, n (%)	0	787 (76)
	1	202 (20)
	2	31 (3)
	>2	10 (<1)

\*requiring systemic corticosteroids and/or antibiotics

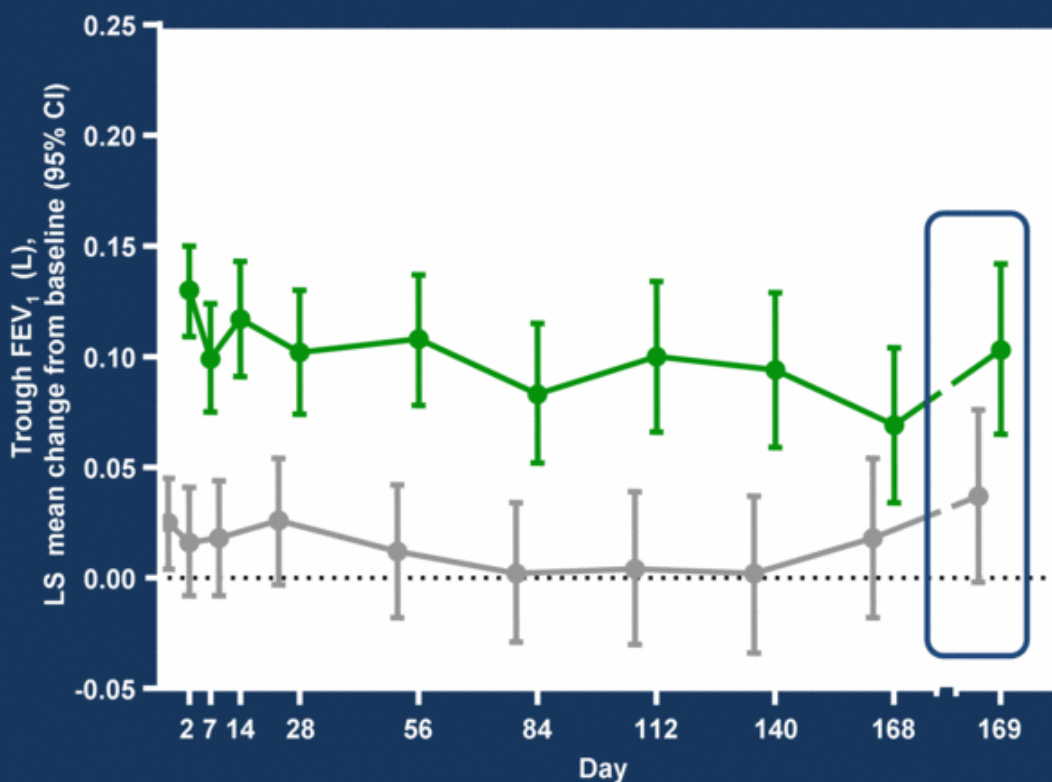
# wmFEV<sub>1</sub> (0-4hr): VI vs. PBO



Day 168		
Test	ΔmL (95% CI)	p
VI - PBO	103 (52, 153)	<0.001

◆ VI 25  
◆ Placebo

# Trough FEV<sub>1</sub>: VI vs. PBO

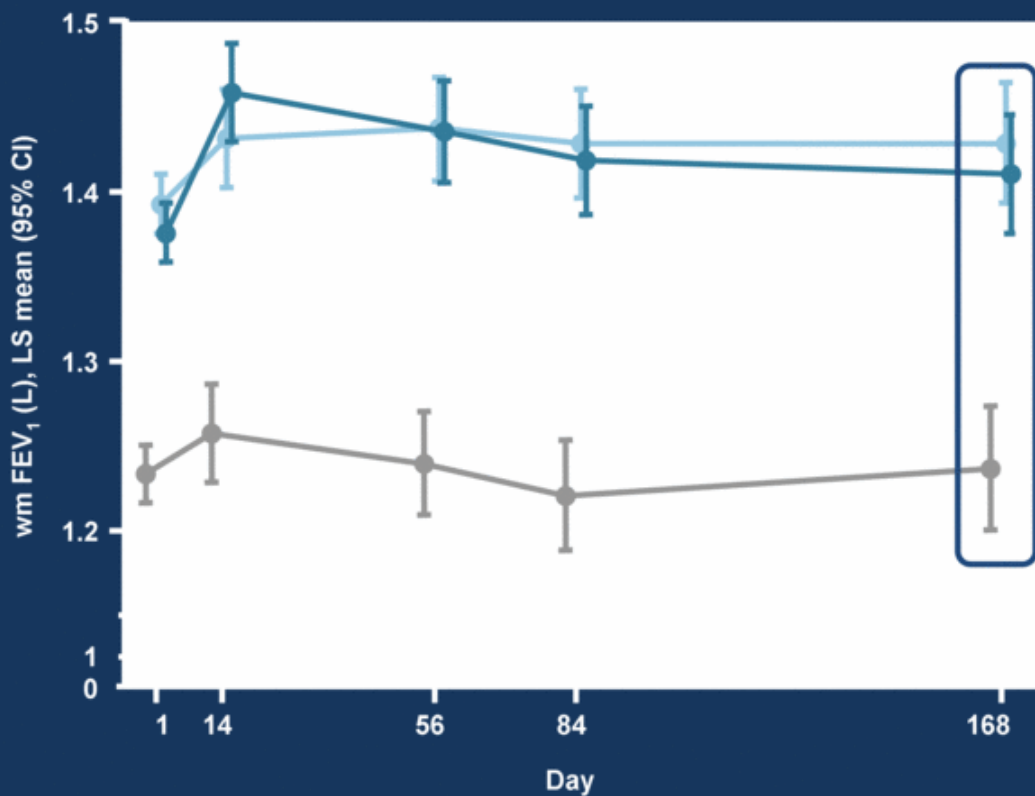


Day 169		
Test	ΔmL (95% CI)	p
VI - PBO	67 (12, 121)	0.017

◆ VI 25  
◆ Placebo



# wmFEV<sub>1</sub> (0-4hr): FF/VI vs. PBO

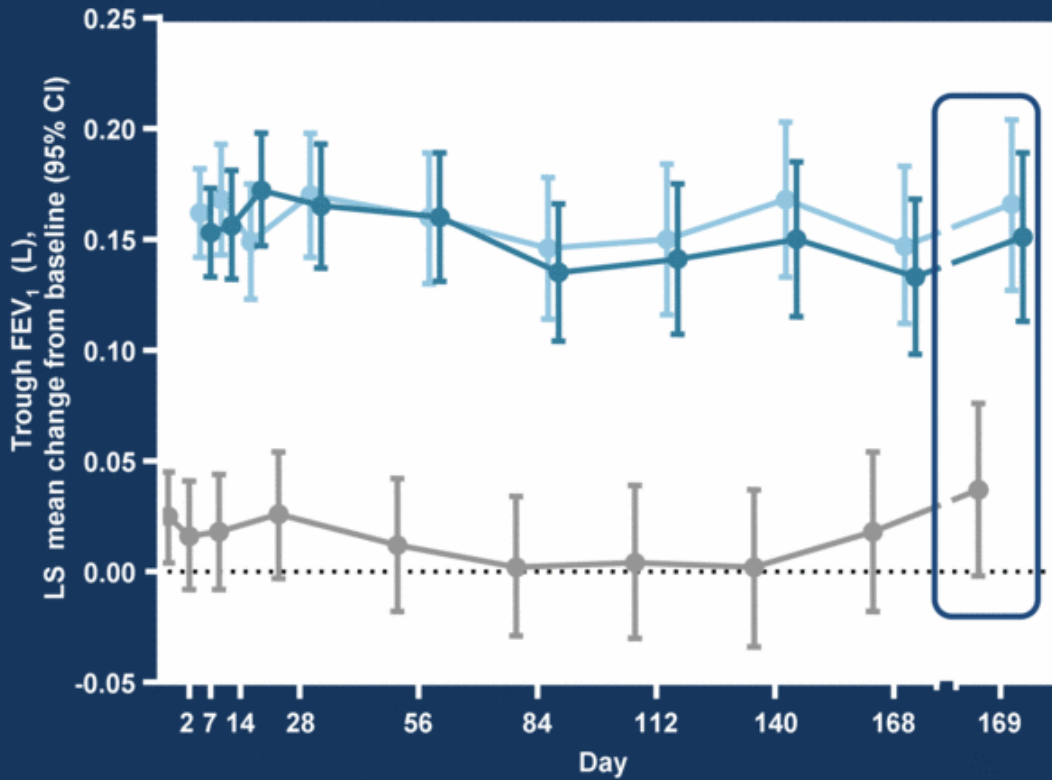


Day 168		
Test	ΔmL (95% CI)	p
FF/VI 100/25 - PBO	173 (123, 224)	<0.001
FF/VI 50/25 - PBO*	192 (141, 243)	-

- ◆ FF/VI 100/25
- ◆ FF/VI 50/25
- ◆ Placebo

\*p-value not shown due to statistical hierarchy; difference is descriptive only

# Trough FEV<sub>1</sub>: FF/VI vs. PBO

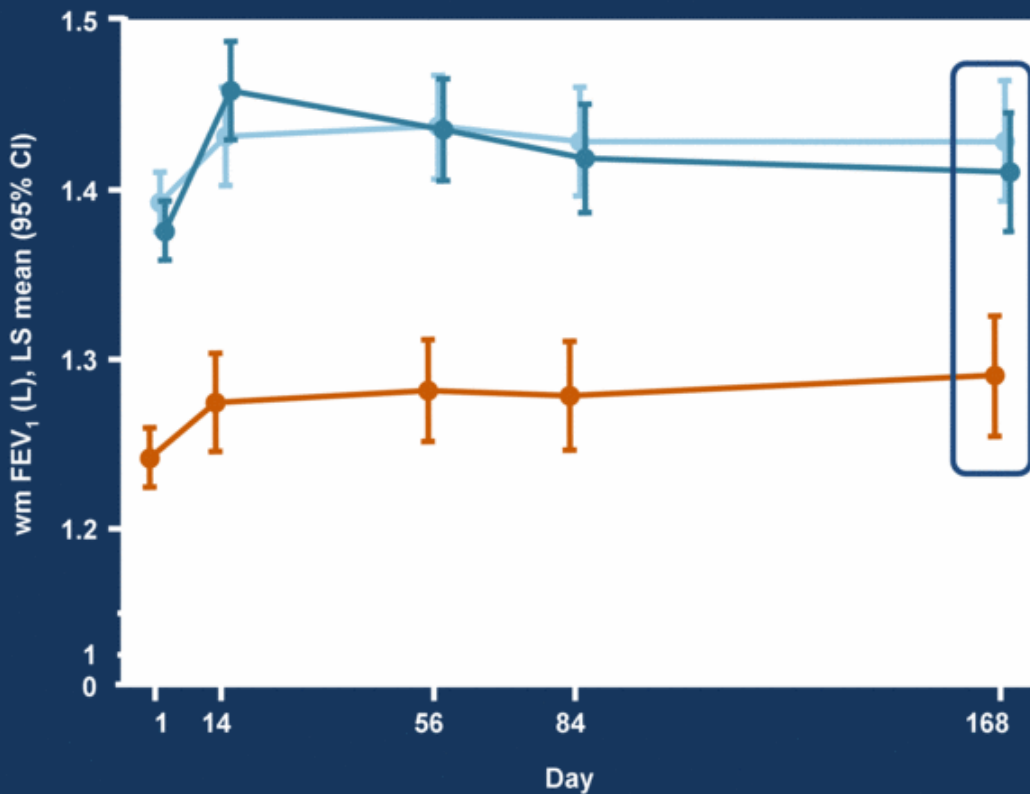


Day 169		
Test	ΔmL (95% CI)	p
FF/VI 100/25 - PBO	115 (60, 169)	<0.001
FF/VI 50/25 - PBO*	129 (74, 184)	-

- FF/VI 100/25
- FF/VI 50/25
- Placebo

\*p-value not shown due to statistical hierarchy; difference is descriptive only

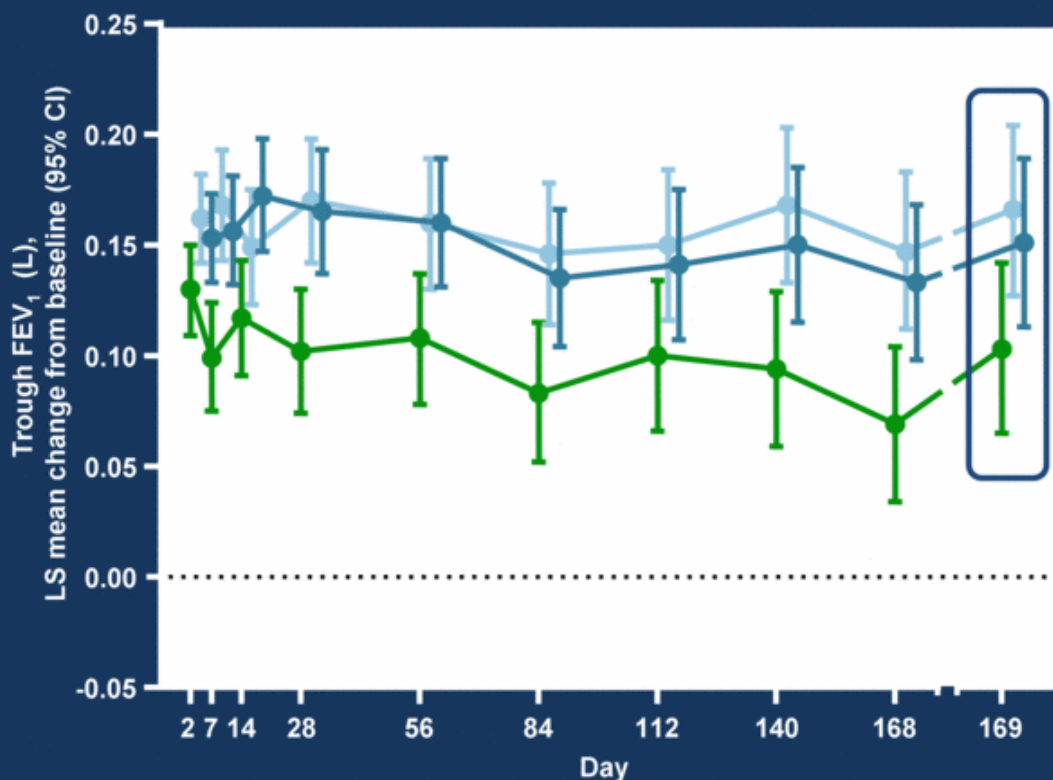
# wmFEV<sub>1</sub> (0-4hr): FF/VI vs. FF



Day 168		
Test	ΔmL (95% CI)	p
FF/VI 100/25 - FF	120 (70, 170)	<0.001

- FF/VI 100/25
- FF/VI 50/25
- FF 100

# Trough FEV<sub>1</sub>: FF/VI vs. VI



Day 169		
Test	ΔmL (95% CI)	p
FF/VI 100/25 – VI	48 (-6, 102)	0.082
FF/VI 50/25 – VI*	62 (8, 117)	-

- FF/VI 100/25
- FF/VI 50/25
- VI 25

\*p-value not shown due to statistical hierarchy; difference is descriptive only

# CRQ-SAS dyspnoea domain: Day 168

Test	Δ Units(95% CI)
VI – Placebo	0.14 (-0.10, 0.38)
FF 100 – Placebo	0.06 (-0.18, 0.30)
FF/VI 50/25 – Placebo	0.19 (-0.05, 0.43)
FF/VI 100/25 – Placebo	0.30 (0.06, 0.54)
FF/VI 50/25 – VI 25	0.05 (-0.19, 0.29)
FF/VI 100/25 – VI 25	0.16 (-0.08, 0.40)
FF/VI 100/25 – FF 100	0.24 (0.01, 0.48)

Differences are descriptive only due to statistical hierarchy  
 Range: 1 – maximum impairment, 7 – no impairment; MCID > 0.5 Units

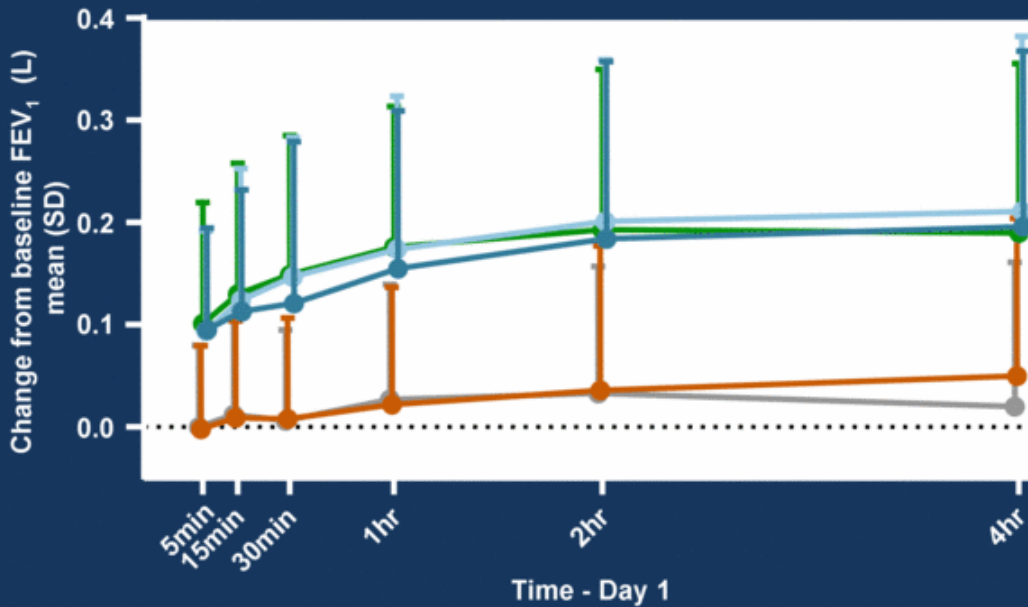
## Peak FEV<sub>1</sub> (0-4hr): Day 1

Test	Δ mL(95% CI)
VI – Placebo	142 (114, 169)
FF 100 – Placebo	12 (-15, 39)
FF/VI 50/25 – Placebo	148 (120, 175)
FF/VI 100/25 – Placebo	139 (112, 166)
FF/VI 50/25 – VI 25	6 (-22, 33)
FF/VI 100/25 – VI 25	-3 (-30, 25)
FF/VI 100/25 – FF 100	127 (100, 154)

Differences are descriptive only due to statistical hierarchy

# Time to $\Delta 100\text{mL}$ (0-4h): Day 1

## Serial FEV<sub>1</sub>: Day 1 (0-4h)



MEDIAN TIME $\Delta 100\text{mL}$	
Treatment	Min
Placebo	n/a
FF 100	n/a
VI 25	16
FF/VI 100/25	17
FF/VI 50/25	17

n/a = not applicable as >50% of patients did not achieve a  $\geq 100\text{mL}$  improvement by 4hr

## Safety

	Placebo N=207	FF 100 N=206	VI 25 N=205	FF/VI 50/25 N=206	FF/VI 100/25 N=206
<b>ANY EVENT, n (%)</b>					
On-Treatment AEs	100 (48)	123 (60)	111 (54)	114 (55)	111 (54)
On-Treatment SAEs	11 (5)	16 (8)	15 (7)	6 (3)	11 (5)
<b>EVENTS OF SPECIAL INTEREST, n (%)</b>					
Cardiovascular Effects	16 (8)	18 (9)	15 (7)	15 (7)	11 (5)
Local Steroid Effects	7 (3)	13 (6)	6 (3)	24 (12)	16 (8)
LRTI excluding pneumonia	8 (4)	8 (4)	6 (3)	3 (1)	5 (2)
Pneumonia	3 (1)	4 (2)	5 (2)	3 (1)	5 (2)
Hypersensitivity	2 (<1)	5 (2)	3 (1)	1 (<1)	6 (3)
Effects on Glucose	1 (<1)	4 (2)	1 (<1)	3 (1)	5 (2)
Bone Disorders	4 (2)	2 (<1)	2 (<1)	1 (<1)	1 (<1)
Ocular Effects	1 (<1)	2 (<1)	1 (<1)	1 (<1)	1 (<1)
Systemic Steroid Effects	2 (<1)	0	0	2 (<1)	1 (<1)
Effects on Potassium	1 (<1)	1 (<1)	0	0	0
Tremor	0	1 (<1)	0	0	0



## Summary

- **VI 25mcg provides sustained bronchodilation over 24 weeks in moderate-to-severe COPD**
- **Addition of FF to VI provides further bronchodilation**
- **Additional lung function effect not statistically significantly greater than VI alone**
- **VI has a negligible effect on dyspnoea**
  - Addition of FF at 100mcg provides a numerical improvement
- **VI provides rapid substantial post-dose bronchodilation from Day 1 onward**
  - Addition of FF provides no more rapid or increased bronchodilation
- **FF/VI exhibits a safety profile similar to that of its components and placebo**

## Conclusion

- **FF/VI represents a once-daily treatment option for moderate-to-severe COPD which is efficacious and well tolerated**





# A dual-acting muscarinic antagonist, beta 2-agonist (MABA) molecule (GSK961081) improves lung function in COPD: A randomised trial

**Pascal Wielders\***, Andrea Ludwig-Sengpiel, Nicholas Locantore, Suus Baggen, Robert Chan and John H. Riley

\* Catharina Hospital Eindhoven, The Netherlands, on behalf of The Investigators

The study was registered on the Clinical Trials Register NCT01319019, used the study code MAB115032 and was funded by GlaxoSmithKline.

My institution has received grants from GSK, AstraZeneca and Novartis  
Speakers fee from GSK, AstraZeneca, Boehringer Ingelheim, Novartis

# GSK961081 a dual pharmacophore



Muscarinic Antagonist

Linker

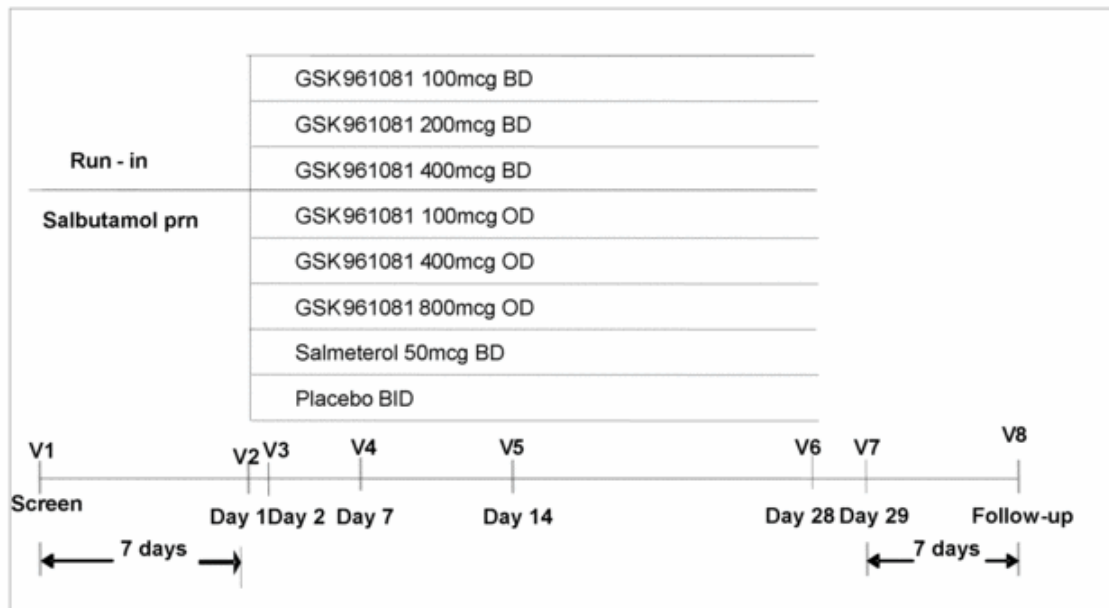
Beta Agonist

MABA

## Study aims

- ▶ To assess the safety and efficacy of GSK961081 in moderate and severe COPD subjects
- ▶ To assess the dose and dosing regimen
- ▶ MAB115032 – Design. A phase IIb multicentre, randomised, double-blind, double-dummy, placebo- and active-controlled, parallel-group, dose-ranging and dose-interval study.

# Study design



## Inclusion Criteria

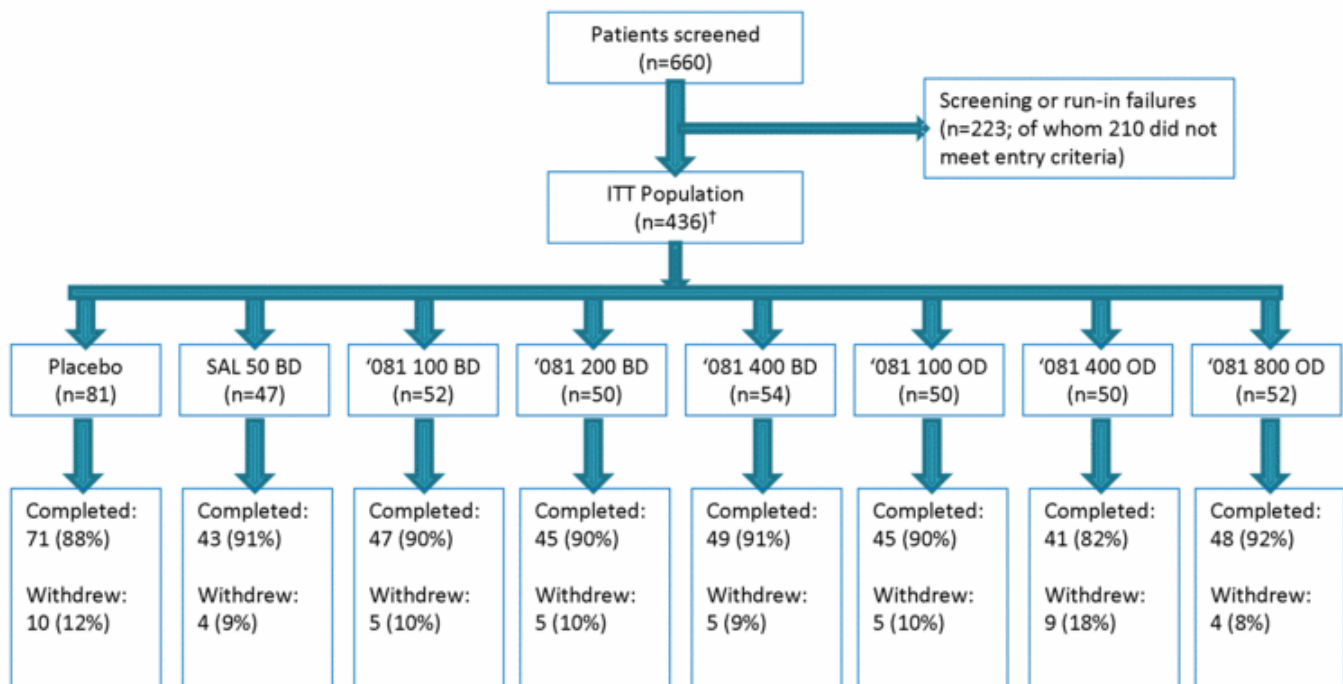
1. Males or females age:  $\geq 40$  years of age
2. COPD Diagnosis:
3. Tobacco Use: Current and former.  $\geq 10$  pack years
4. Severity of Disease:
  - i. Post-salbutamol FEV1 /FVC ratio of  $< 0.70$
  - ii. Post-salbutamol FEV1  $\geq 30$  and  $\leq 70\%$

# Notable Exclusion Criteria

1. **Asthma:** a current diagnosis of asthma or other respiratory disorder
2. **Lung Resection:**
3. **Chest X-Ray:** Chest X-ray (or CT scan) with significant abnormalities
4. **COPD Medications\*:** oral corticosteroids or antibiotics 6 weeks prior
5. **Hospitalisation:** for COPD or pneumonia in 12 weeks prior.
6. **Other Disease/Abnormalities:** symptomatic (or documented history of) laryngopharyngeal /extraesophageal reflux or posterior laryngitis; previous history of laryngopharyngeal ulcerations and erosions.

\* ICS was allowed





## Efficacy Endpoints

### ▶ Primary:

- Mean change from baseline for Trough FEV1 on Day 29

### ▶ Others

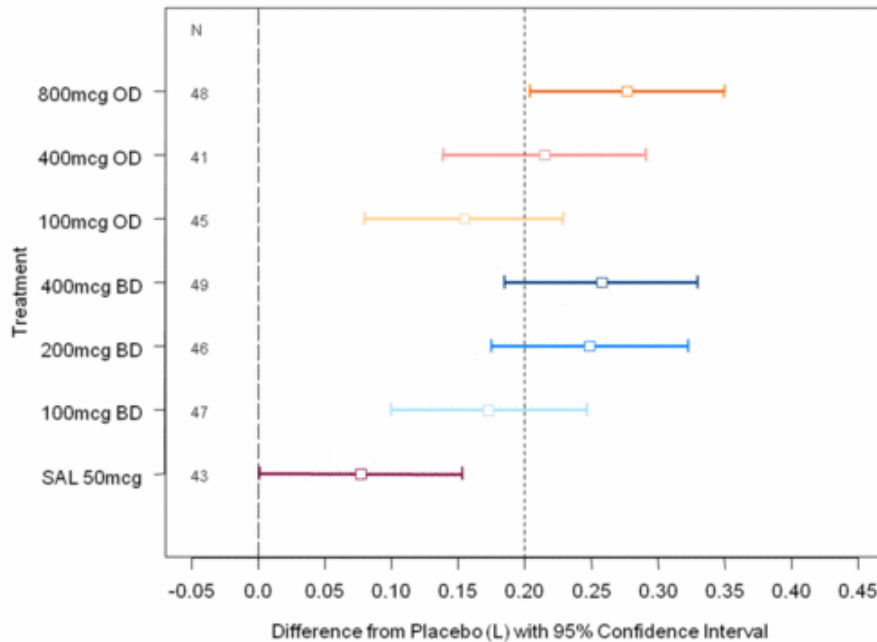
- Weighted mean change from baseline FEV1 over 0-12hrs on Day 28
- Weighted mean change from baseline FEV1 over 0-24hrs on Day 28 in subjects with overnight visits
- Serial FEV1 profile on Day 1 and Day 28
- FVC
- Rescue medication use
- Safety Profile



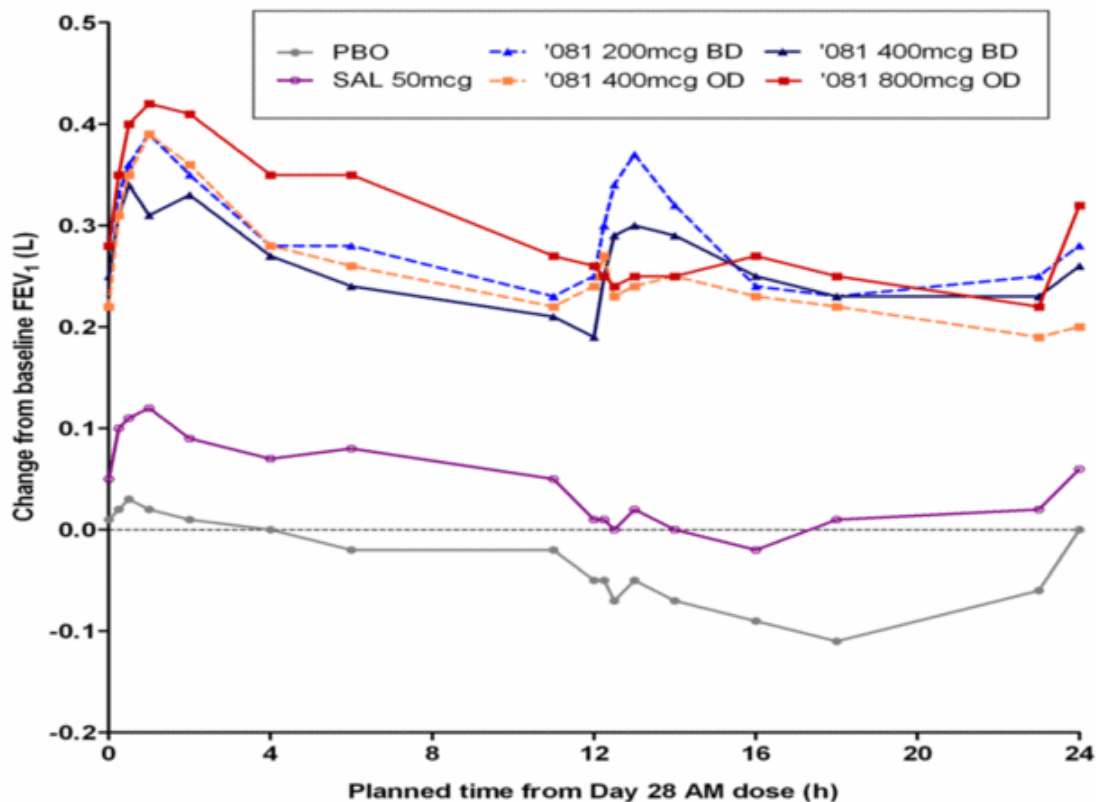
# Primary Efficacy Endpoint – Trough FEV<sub>1</sub> Day 29

Treatment	SAL 50	100 BD	200 BD	400 BD	100 OD	400 OD	800 OD
N	43	47	46	49	45	41	48
LSMean Diff	77mL	173mL	249mL	258mL	155mL	215mL	277mL
95% CI	(0, 150)	(100, 250)	(170, 320)	(190, 330)	(80, 230)	(140, 290)	(200, 350)
p-value	0.046	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

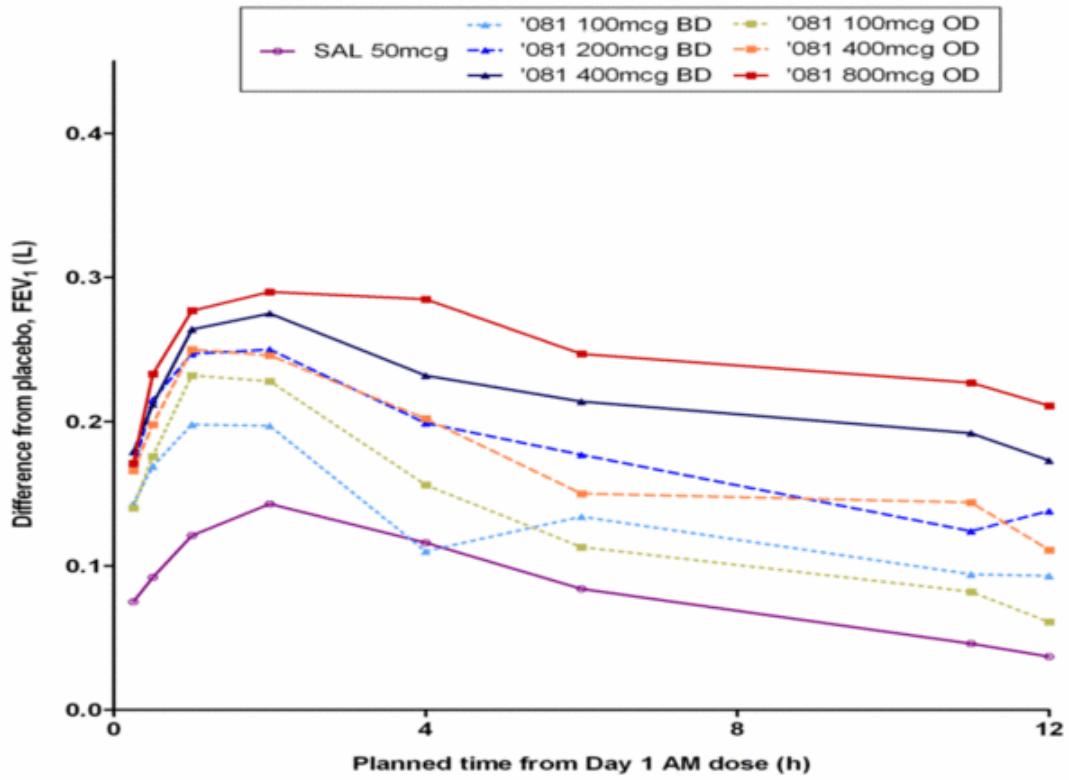
Adjusted Difference from Placebo, Change from Baseline in Trough FEV<sub>1</sub> (L) at Day 29



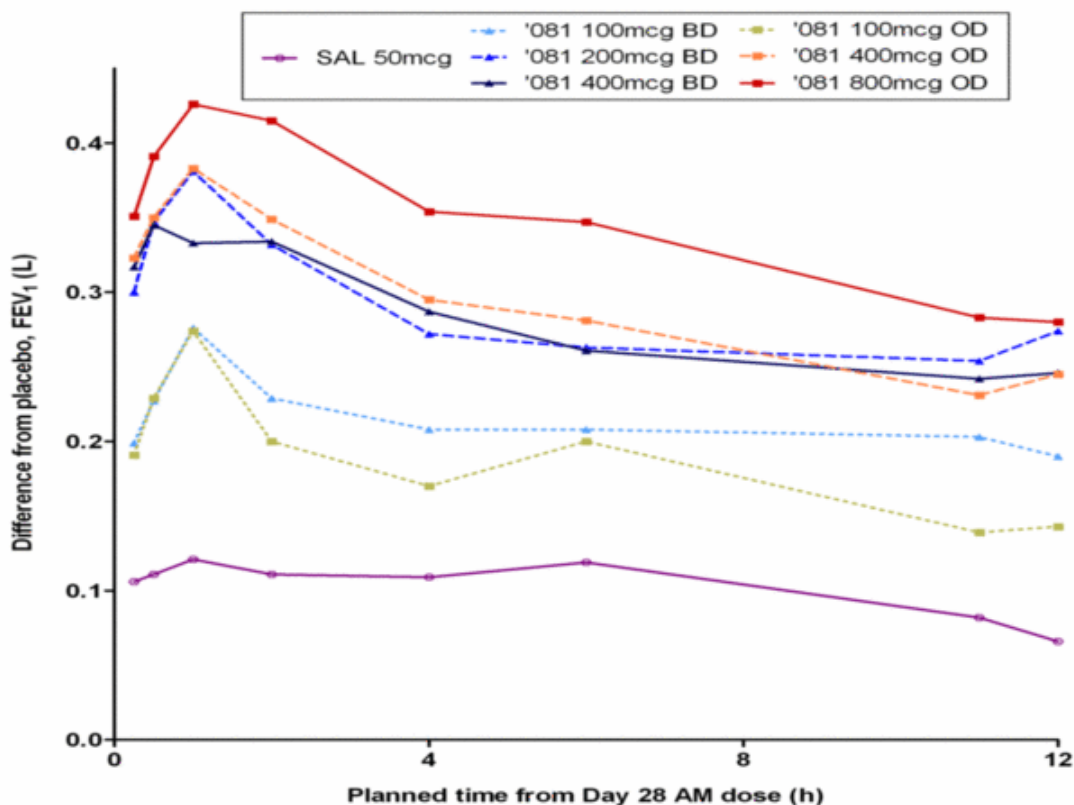
# Comparison of dosing regimen in Subset at Day 28



# Placebo subtracted 12 hour FEV1 profile at Day 1

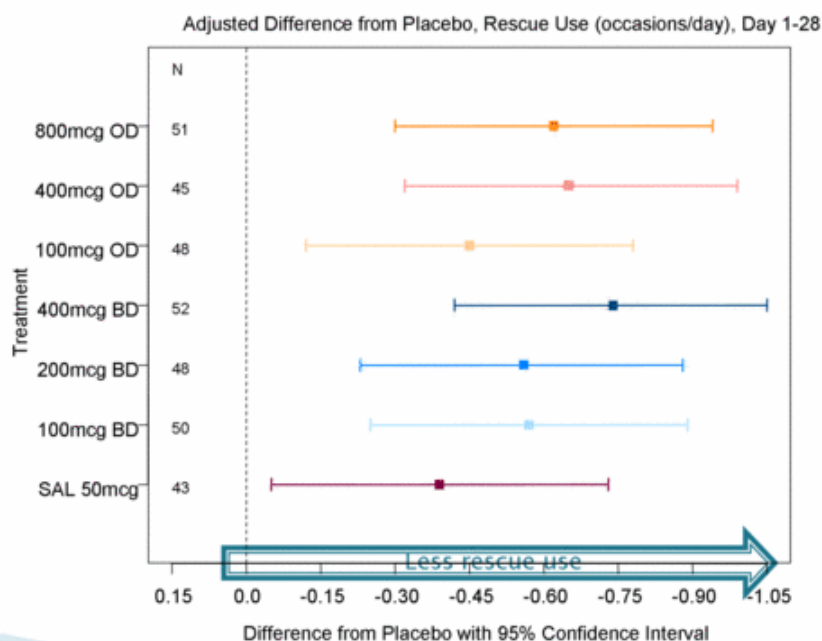


# Placebo subtracted 12 hour FEV<sub>1</sub> profile at Day 28



## Rescue Med Use, Weeks 1-4 (occasions per day)

Treatment	SAL 50	100 BD	200 BD	400 BD	100 OD	400 OD	800 OD
N	43	50	48	52	48	45	51
LSMean Diff	-0.39	-0.57	-0.56	-0.74	-0.45	-0.65	-0.62
95% CI	(-0.7, -0.1)	(-0.9, -0.3)	(-0.9, -0.2)	(-1.1, -0.4)	(-0.8, -0.1)	(-1.0, -0.3)	(-0.9, 0.3)
p-value	0.026	<0.001	<0.001	<0.001	0.007	<0.001	<0.001



Note: Placebo LSMean Change was -0.29 occasions/day

## Safety Results–On–Therapy AE’s (> 3% in any group)

AE Preferred Term	PBO (n=81)	SAL 50 (n=47)	100 BD (n=52)	200 BD (n=50)	400 BD (n=54)	100 OD (n=50)	400 OD (n=50)	800 OD (n=52)
Headache	5 (6%)	2 (4%)	2 (4%)	0	5 (9%)	5 (10%)	5 (10%)	2 (4%)
Cough	2 (2%)	0	2 (4%)	4 (8%)	1 (2%)	5 (10%)	5 (10%)	4 (8%)
Dysgeusia*	0	0	2 (4%)	3 (6%)	4 (8%)	3 (6%)	2 (4%)	1 (2%)
Nasopharyngitis	3 (4%)	0	1 (2%)	3 (6%)	0	3 (6%)	1 (2%)	0
Back pain	2 (2%)	0	1 (2%)	0	0	0	2 (4%)	0
Dysphonia	2 (2%)	0	0	0	0	0	1 (2%)	2 (4%)
Muscle spasms	0	1 (2%)	1 (2%)	0	2 (4%)	0	0	1 (2%)
Nausea	2 (2%)	0	0	0	0	1 (2%)	1 (2%)	0
Myalgia	1 (1%)	1 (2%)	0	0	0	0	2 (4%)	0
Palpitations	0	1 (2%)	0	0	2 (4%)	0	0	0


\* - Dysgeusia here combines the preferred terms "Dysgeusia" and "Product taste abnormal"

## Safety Results–On Therapy AE’s Leading to Withdrawal

AE Preferred Term	PBO (n=81)	SAL 50 (n=47)	100 BD (n=52)	200 BD (n=50)	400 BD (n=54)	100 OD (n=50)	400 OD (n=50)	800 OD (n=52)
Any event	2 (2%)	0	1 (2%)	2 (4%)	2 (4%)	2 (4%)	0	1 (2%)

- ▶ Placebo
  - Contusion, pain, wheezing
- ▶ 100 BD
  - Tachycardia
- ▶ 200 BD
  - Cough, dysgeusia, Wolff-Parkinson-White syndrome
- ▶ 400 BD
  - Bundle branch block left, dermatitis allergic
- ▶ SAL 50
  - none
- ▶ 100 OD
  - 1<sup>st</sup> degree atrioventricular block, 7<sup>th</sup> nerve paralysis
- ▶ 400 OD
  - none
- ▶ 800 OD
  - Cough

## Conclusions

- ▶ GSK961081 is a dual pharmacophore having both muscarinic antagonist and beta 2-agonist activities
  - ▶ GSK961081 appears safe and well tolerated
  - ▶ GSK961081 provides rapid symptom relief in moderate and severe COPD subjects
  - ▶ GSK961081 is a potent bronchodilator in moderate and severe COPD subjects
- 



# Acknowledgements

- ▶ The GSK study team including Helen Griffiths, Francis Arkhurst, the medical monitor Dmitriy Galkin and Ginny Norris for Scientific advice.
  - ▶ The Subjects for taking part in the trial. The investigators for their collection of subjects and running of the trial: Abdullah I (SA), Arpasova K (RS), Aisanov Z (RU), Bantje T (NL), Bateman E (SA), Bjermer L (SW), Blazhko V (UE), Bruning A (SA), De Munck D (NL), Dzurilla M (RS), Feshchenko Y (UE), Foerster K (GE), Gavrysiuk V (UE), Goossens M (NL), Hajkova M (RS), Hukelova H (RS), Iashyna L (UE), Irusen E (SA), Jogi R (ES), Joubert J (SA), Kornmann O (GE), Kuulpak EM (ES), Leshchenko I (RU), Lindberg A (SW), Linnhoff A (GE), Löfdahl M (SW), Lundback B (SW), Ludwig-Sengpiel A (GE), Mihaescu T (RO), Mihaicuta S (RO), Mostovoy Y (UE), Nemes R (RO), Ogorodova L (RU), Ostrovskyy M (UE), Pertseva T (UE), Pribulova E (RO), Rascu A (RO), Richter (SA), Samaruutel P (ES), Schenkenberger I (GE), Schroeder-Babo W (GE), Sinninghe Damste H(NL), Sooru E (ES), Stallaert R (NL), Sushko V (UE), Trofimov V (RU), Wielders P(NL), Wuerziger J (GE), Zorin V (UE)
- 