NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Not applicable

Trial Indication(s)

Chronic Obstructive Pulmonary Disease (COPD)

Protocol Number

CQBW251B2201

Protocol Title

A 24-week multi-center, double-blind, placebo controlled dose-range finding study to investigate the efficacy and safety of oral QBW251 in COPD patients on triple inhaled therapy (LABA / LAMA / ICS)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2

Study Start/End Dates

Study Start Date: September 2019 (Actual)
Primary Completion Date: October 2021 (Actual)
Study Completion Date: February 2022 (Actual)

Study Design/Methodology

This study used a 6 treatment arm, parallel-group, randomized, double-blind study design. 974 male and female COPD patients were randomized into the trial.

Centers

149 centers in 26 countries: Australia(4), Japan(29), Czech Republic(4), United States(25), Hungary(5), Germany(14), Netherlands(2), Belgium(3), Slovakia (Slovak Republic)(7), Spain(3), Austria(3), Turkey(2), Greece(2), Canada(3), Denmark(3), Italy(3), Hong Kong(2), France(4), Poland(3), Korea, Republic of(3), Thailand(4), Philippines(5), Guatemala(3), Argentina(11), United Kingdom(1), Colombia(1)

Objectives:

- Primary:

Change From Baseline in Forced Expiratory Volume in One Second (FEV1) at week 12

- Secondary:

Change From Baseline in Forced Expiratory Volume in One Second (FEV1)

Change from baseline in Evaluating Respiratory Symptoms (E-RS); Total score
Change from baseline in Evaluating Respiratory Symptoms (E-RS); Cough and Sputum score
Number of Participants with a "Better" change in the Patient Global Impression of Severity (PGI-S) from baseline
Change from baseline in the Cough and Sputum Assessment Questionnaire (CASA-Q)
Change from baseline in St. George's Respiratory Questionnaire (SGRQ)
Minimum plasma concentration (Cmin) for QBW251
Maximum plasma concentration (Cmax) for QBW251
Maximum plasma concentration (Cmax) for QBW251 in Serial PK set
Area under the curve from time 0 to 24 hours (AUC0-24h) of QBW251 in Serial PK set

Test Product (s), Dose(s), and Mode(s) of Administration

QBW251 oral capsules (450, 300, 150, 75 and 25 mg) of identical appearance to ensure blinding administered twice a day (b.i.d) for 24 weeks

Statistical Methods

The Multiple Comparison Procedure – Modelling (MCP-Mod) methodology was employed to characterize the dose-response efficacy relationship among QBW251 arms (25, 75, 150, and 300mg) and placebo arms with regards to the change from baseline in trough FEV1 after 12 Weeks of treatment (primary objective) and 24 Weeks of treatment, E-RS cough and sputum score and E-RS total score after 12 and 24 weeks of treatment. In addition, the estimated treatment difference and the associated 90% confidence intervals were presented for the treatment contrast of each dose versus placebo.

The proportion of patients who achieve a clinically important improvement in the E-RS weekly mean scores (total and subscale) were analyzed using repeated measurements logistic regression. The model included the same terms as for the MMRM analysis of the Weekly scores.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Male and female COPD patients aged ≥40 years, who have signed an Informed Consent Form prior to initiation of any study-related procedure.
- Current or ex-smokers who have a smoking history of at least 10 pack years.
- Patients who have been treated with a triple combination of LABA/LAMA/ICS for the last 3 months prior to screening.
- Patients featuring chronic bronchitis

Exclusion Criteria:

- Patients who have had a COPD exacerbation that required treatment with antibiotics and/or oral corticosteroids and/or hospitalization, or a respiratory tract infection in the 4 weeks prior to screening, or between screening and randomization.

- Patients with any documented history of asthma, or with an onset of chronic respiratory symptoms, including a COPD diagnosis, prior to age 40 years.
- Patients with a body mass index (BMI) of more than 40 kg/m2.
- Use of other investigational drugs (approved or unapproved) within 30 days or 5 half-lives prior to screening, or until the expected pharmacodynamic effect has returned to baseline (e.g., biologics), whichever is longer; or longer if required by local regulations.
- Pregnant or nursing (lactating) women, and women of childbearing potential not willing to use acceptable effective methods of contraception during study participation.

Participant Flow Table

Overall Study

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo	Total
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks	
Started	99	250	124	126	124	251	974
Pharmacokinetic (PK) Set	99	250	123	126	124	0	722
Serial Pharmacokinetic (PK) Set	14	21	14	13	14	0	76
Completed	91[1]	233	122	117	118	236	917
Not Completed	8	17	2	9	6	15	57
Withdrawal by Subject	3	8	1	3	3	13	31
Adverse Event	2	4	1	4	0	1	12
Physician Decision	2	0	0	0	0	1	3

Lost to Follow-up	1	3	0	0	0	0	4
Death	0	2	0	2	3	0	7

[1] QBW251 450 mg arm was discontinued early based on a pre-defined pharmacokinetic exposure stopping rule.

Baseline Characteristics

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo	Total
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks	
Number of Participants [units: participants]	99	250	124	126	124	251	974
Age Continuous (units: Years) Mean ± Standard Deviation							
	66.5±7.28	66.6±7.56	66.7±6.58	65.7±8.30	67.0±7.83	66.7±7.59	66.6±7.55
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)							
Female	36	99	47	50	49	92	373
Male	63	151	77	76	75	159	601
Race (NIH/OMB) (units: Participants) Count of Participants (Not Applicable)							
American Indian or Alaska Native	2	10	1	4	4	5	26

Asian	9	42	27	20	25	43	166
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0
Black or African American	1	5	2	6	2	5	21
White	87	193	94	96	93	198	761
More than one race	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0

Primary Outcome Result(s)

Change From Baseline in Forced Expiratory Volume in One Second (FEV1) at week 12

(Time Frame: Baseline and Week 12)

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	42	209	111	112	105	219
Change From Baseline in Forced Expiratory Volume in One Second (FEV1) at week 12 (units: Liter)						

Least Squares Mean ± Standard Error						
	0.013 ± 0.021	0.013 ± 0.0103	0.014 ± 0.0142	0.021 ± 0.0141	0.006 ± 0.0144	0.001 ± 0.0101

Statistical Analysis

Groups	QBW251 450 mg, Placebo
P Value	0.628
Method	ANCOVA
Other Least Squares Mean Difference	0.011
Standard Error of the mean	0.0235
90 % Confidence Interval 2-Sided	-0.027 to 0.050

Statistical Analysis

Groups	QBW251 300 mg, Placebo
P Value	0.425
Method	ANCOVA
Other Least Squares Mean Difference	0.012
Standard Error of the mean	0.0144

90 % Confidence Interval 2-Sided	-0.012 to 0.035

Statistical Analysis

Groups	QBW251 150 mg, Placebo
P Value	0.463
Method	ANCOVA
Other Least Squares Mean Difference	0.013
Standard Error of the mean	0.0174
90 % Confidence Interval 2-Sided	-0.016 to 0.041

Statistical Analysis

Groups	QBW251 75 mg, Placebo
P Value	0.244
Method	ANCOVA
Other Least Squares Mean Difference	0.020
Standard Error of the mean	0.0173
90 % Confidence Interval 2-Sided	-0.008 to 0.049

Statistical Analysis

Groups	QBW251 25 mg, Placebo
P Value	0.793
Method	ANCOVA
Other Least Squares Mean Difference	0.005
Standard Error of the mean	0.0176
90 % Confidence Interval 2-Sided	-0.024 to 0.034

Secondary Outcome Result(s)

Change From Baseline in Forced Expiratory Volume in One Second (FEV1)

(Time Frame: Baseline, weeks 4, 8, 16, 20 and 24)

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	99	250	124	126	124	251
Change From Baseline in Forced Expiratory Volume in One Second (FEV1) (units: Liter) Mean ± Standard Deviation						

Week 4	0.007 ± 0.14	0.007 ± 0.15	0.009 ± 0.13	0.000 ± 0.14	0.009 ± 0.14	0.005 ± 0.13
Week 8	0.028 ± 0.14	0.013 ± 0.16	-0.002 ± 0.13	0.002 ± 0.15	0.016 ± 0.16	0.009 ± 0.15
Week 16	0.013 ± 0.18	0.003 ± 0.16	0.005 ± 0.14	0.011 ± 0.15	0.007 ± 0.17	-0.011 ± 0.14
Week 20	-0.031 ± 0.20	0.005 ± 0.18	0.012 ± 0.13	0.001 ± 0.16	0.003 ± 0.16	-0.007 ± 0.15
Week 24	0.033 ± 0.13	0.023 ± 0.19	0.004 ± 0.16	0.003 ± 0.19	0.003 ± 0.17	-0.013 ± 0.16

Change from baseline in Evaluating Respiratory Symptoms (E-RS); Total score

(Time Frame: Baseline, weeks 12 and 24)

	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	250	124	126	124	251
Change from baseline in Evaluating Respiratory Symptoms (E-RS); Total score (units: Score on a scale) Least Squares Mean ± Standard Error					
Week 12	-1.75 ± 0.234	-1.26 ± 0.323	-1.66 ± 0.317	-1.30 ± 0.324	-1.41 ± 0.228
Week 24	-2.16 ± 0.239	-1.37 ± 0.327	-1.36 ± 0.325	-1.36 ± 0.333	-1.31 ± 0.232

Change from baseline in Evaluating Respiratory Symptoms (E-RS); Cough and Sputum score

(Time Frame: Baseline, weeks 12 and 24)

	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered	QBW251 was orally administered	QBW251 was orally administered	QBW251 was orally administered	Placebo was orally administered

	300 mg b.i.d for 24 weeks	150 mg b.i.d for 24 weeks	75 mg b.i.d for 24 weeks	25 mg b.i.d for 24 weeks	b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	250	124	126	124	251
Change from baseline in Evaluating Respiratory Symptoms (E-RS); Cough and Sputum score (units: Score on a scale) Least Squares Mean ± Standard Error					
Week 12	-0.78 ± 0.077	-0.63 ± 0.105	-0.52 ± 0.104	-0.22 ± 0.106	-0.44 ± 0.074
Week 24	-0.90 ± 0.078	-0.68 ± 0.107	-0.51 ± 0.106	-0.26 ± 0.109	-0.50 ± 0.076

Number of Participants with a "Better" change in the Patient Global Impression of Severity (PGI-S) from baseline

(Time Frame: Baseline, weeks 12 and 24)

	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	250	124	126	124	251
Number of Participants with a "Better" change in the Patient Global Impression of Severity (PGI-S) from baseline (units: Participants) Count of Participants (Not Applicable)					
Week 12 - Respiratory Symptoms	66 (30.28%)	27 (23.28%)	35 (30.7%)	33 (30.56%)	64 (29.36%)
Week 24 - Respiratory Symptoms	72 (35.29%)	28 (24.78%)	40 (36.7%)	31 (30.39%)	79 (36.57%)
Week 12 - Cough and mucus	85 (38.99%)	55 (47.41%)	54 (47.37%)	41 (37.96%)	78 (35.78%)

Week 24 - Cough and mucus	104 (41.6%)	57 (45.97%)	50 (39.68%)	37 (29.84%)	96 (38.25%)

Change from baseline in the Cough and Sputum Assessment Questionnaire (CASA-Q)

(Time Frame: Baseline, weeks 12 and 24)

	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	250	124	126	124	251
Change from baseline in the Cough and Sputum Assessment Questionnaire (CASA-Q) (units: Score on a scale) Least Squares Mean ± Standard Error					
Cough symptoms score, week 12	6.06 ± 1.082	8.82 ± 1.488	6.68 ± 1.498	6.73 ± 1.535	6.06 ± 1.077
Cough symptoms score, week 24	10.49 ± 1.148	10.59 ± 1.556	8.04 ± 1.575	5.84 ± 1.623	7.25 ± 1.118
Cough impact score, week 12	4.97 ± 0.983	5.94 ± 1.352	5.89 ± 1.359	5.03 ± 1.394	5.26 ± 0.978
Cough impact score, week 24	7.08 ± 0.983	8.29 ± 1.334	7.51 ± 1.349	4.02 ± 1.391	7.12 ± 0.958
Sputum symptoms score, week 12	7.74 ± 1.142	8.51 ± 1.571	7.01 ± 1.580	5.74 ± 1.620	6.96 ± 1.136
Sputum symptoms score, week 24	10.52 ± 1.242	11.34 ± 1.685	5.81 ± 1.704	4.64 ± 1.756	9.05 ± 1.211
Sputum impact score, week 12	5.88 ± 1.011	6.58 ± 1.391	6.98 ± 1.398	4.35 ± 1.433	4.72 ± 1.005

Sputum impact score, week 24	7.14 ± 1.032	7.66 ± 1.401	7.75 ± 1.417	4.40 ± 1.460	7.04 ± 1.007	

Change from baseline in St. George's Respiratory Questionnaire (SGRQ)

(Time Frame: Baseline, weeks 12 and 24)

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg	Placebo
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	99	250	124	126	124	251
Change from baseline in St. George's Respiratory Questionnaire (SGRQ) (units: Score on a scale) Least Squares Mean ± Standard Error						
Week 12 - Total score	-0.34 ± 11.17	-5.84 ± 14.82	-3.14 ± 12.67	-6.78 ± 14.64	-3.85 ± 10.82	-3.36 ± 13.27
Week 24 - Total score	-2.93 ± 10.58	-6.48 ± 15.35	-3.69 ± 12.39	-6.06 ± 14.88	-1.70 ± 10.97	-4.37 ± 13.00
Week 12 - Symptoms score	-5.24 ± 21.16	-8.23 ± 18.73	-5.70 ± 18.39	-6.93 ± 19.29	-5.59 ± 16.52	-6.07 ± 17.14
Week 24 - Symptoms score	-7.90 ± 22.47	-10.59 ± 21.06	-7.09 ± 17.02	-8.42 ± 18.21	-5.16 ± 15.61	-6.97 ± 17.39
Week 12 - Activity score	-2.00 ± 10.83	-4.80 ± 17.67	-4.72 ± 17.35	-7.27 ± 17.48	-4.06 ± 14.68	-2.40 ± 15.21
Week 24 - Activity score	-1.25 ± 12.50	-5.12 ± 17.36	-3.69 ± 16.37	-5.80 ± 20.47	-1.20 ± 14.36	-4.27 ± 16.07
Week 12 - Impacts score	2.03 ± 14.28	-5.69 ± 17.06	-1.49 ± 13.88	-6.42 ± 16.63	-3.13 ± 13.11	-3.11 ± 15.90
Week 24 - Impacts score	-2.21 ± 8.24	-6.04 ± 17.455	-2.63 ± 14.18	-5.44 ± 16.05	-1.04 ± 13.95	-3.68 ± 14.95

Minimum plasma concentration (Cmin) for QBW251

(Time Frame: Pre-dose on Days 15, 29, 57, 85, 113, 141 and 169)

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	99	250	123	126	124
Minimum plasma concentration (Cmin) for QBW251 (units: ng/mL) Mean ± Standard Deviation					
Day 15	1280 ± 1700	619 ± 1230	143 ± 158	44.0 ± 49.0	12.7 ± 15.5
Day 29	951 ± 1050	571 ± 923	125 ± 123	47.8 ± 47.3	10.1 ± 10.1
Day 57	1040 ± 1330	572 ± 833	116 ± 103	47.7 ± 62.2	14.2 ± 25.5
Day 85	1080 ± 1360	587 ± 951	119 ± 147	49.7 ± 71.2	9.93 ± 10.3
Day 113	859 ± 1150	593 ± 1000	120 ± 130	52.7 ± 73.9	9.89 ± 9.20
Day 141	1150 ± 1150	552 ± 923	118 ± 103	66.8 ± 226	15.9 ± 45.7
Day 169	637 ± 349	465 ± 618	128 ± 147	44.9 ± 61.1	8.97 ± 8.08

Maximum plasma concentration (Cmax) for QBW251

(Time Frame: Days 1, 15 and 169)

	QBW251 450 mg	QBW251 300 mg	QBW251 150 mg	QBW251 75 mg	QBW251 25 mg
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks

Number of Participants Analyzed [units: participants]	99	250	123	126	124
Maximum plasma concentration (Cmax) for QBW251 (units: ng/mL) Mean ± Standard Deviation					
Day 1	1280 ± 847	751 ± 598	251 ± 238	68.9 ± 64.5	14.4 ± 15.2
Day 15	2500 ± 1710	1320 ± 1030	411 ± 368	114 ± 101	26.1 ± 20.6
Day 169	2370 ± 1160	1210 ± 797	361 ± 303	104 ± 86.6	22.5 ± 16.4

Maximum plasma concentration (Cmax) for QBW251 in Serial PK set

(Time Frame: 1, 2, 4, 6, and 8 hours post-dose on Days 1 and 15)

	QBW251 450 mg	**QBW251 300 mg**	**QBW251 150 mg**	**QBW251 75 mg**	**QBW251 25 mg**
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	14	21	14	13	14
Maximum plasma concentration (Cmax) for QBW251 in Serial PK set (units: ng/mL) Mean ± Standard Deviation					
Day 1	1510 ± 928	1280 ± 622	478 ± 241	96.6 ± 72.7	25.3 ± 29.7
Day 15	2700 ± 1170	1870 ± 844	542 ± 523	175 ± 127	39.4 ± 27.0

Area under the curve from time 0 to 24 hours (AUC0-24h) of QBW251 in Serial PK set

(Time Frame: 1, 2, 4, 6, and 8 hours post-dose on Days 1 and 15)

	QBW251 450 mg	**QBW251 300 mg**	**QBW251 150 mg**	**QBW251 75 mg**	**QBW251 25 mg**

Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks
Number of Participants Analyzed [units: participants]	14	21	14	13	14
Area under the curve from time 0 to 24 hours (AUC0-24h) of QBW251 in Serial PK set (units: ng*h/mL) Mean ± Standard Deviation					
Day 1	10900 ± 3740	8480 ± 3660	2920 ± 1140	769 ± 330	185 ± 107
Day 15	30000 ± 22600	16500 ± 8380	4740 ± 2390	1390 ± 679	333 ± 209

Safety Results

All-Cause Mortality

	QBW251 450 mg N = 99	QBW251 300 mg N = 250	QBW251 150 mg N = 124	QBW251 75 mg N = 126	QBW251 25 mg N = 124	Placebo N = 251	Total N = 974
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks	Total
Total participants affected	0 (0.00%)	2 (0.80%)	0 (0.00%)	2 (1.59%)	3 (2.42%)	0 (0.00%)	7 (0.72%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were reported from the start of treatment to 30 days after end of treatment, assessed up to maximum duration of 199 days.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (24.1)
Assessment Type for Table Default	Systematic Assessment

	QBW251 450 mg N = 99	QBW251 300 mg N = 250	QBW251 150 mg N = 124	QBW251 75 mg N = 126	QBW251 25 mg N = 124	Placebo N = 251	Total N = 974
Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks	Total
Total participants affected	10 (10.10%)	33 (13.20%)	6 (4.84%)	14 (11.11%)	12 (9.68%)	15 (5.98%)	90 (9.24%)
Blood and lymphatic system disorders							
Anaemia	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Cardiac disorders							
Acute myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Aortic valve stenosis	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Atrial fibrillation	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Bundle branch block left	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Cardiac arrest	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)

Cardiac failure congestive	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Cor pulmonale	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Coronary artery disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Coronary artery stenosis	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Supraventricular tachycardia	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Ventricular fibrillation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Eye disorders							
Cataract	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Retinal detachment	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Vitreous haemorrhage	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	1 (0.40%)	2 (0.21%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Acute abdomen	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Colitis ulcerative	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Duodenal ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Erosive oesophagitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Gastric haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Haemorrhoidal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Oesophagitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Vomiting	0 (0.00%)	1 (0.40%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.21%)

General disorders and administration site conditions							
Chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Pyrexia	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Vascular stent thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Hepatobiliary disorders							
Cholelithiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Infections and infestations							
COVID-19	0 (0.00%)	3 (1.20%)	0 (0.00%)	1 (0.79%)	2 (1.61%)	0 (0.00%)	6 (0.62%)
COVID-19 pneumonia	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	2 (0.21%)
Diverticulitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Endocarditis bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Erysipelas	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Lower respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Peritoneal abscess	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Pneumonia	1 (1.01%)	6 (2.40%)	0 (0.00%)	3 (2.38%)	2 (1.61%)	3 (1.20%)	15 (1.54%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Injury, poisoning and procedural complications							
Ankle fracture	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Bone graft lysis	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Fall	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)

Foot fracture	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Limb injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Procedural intestinal perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Tibia fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Wrist fracture	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Investigations							
Blood potassium increased	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Musculoskeletal and connective tissue disorders							
Intervertebral disc disorder	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Osteoarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Plantar fasciitis	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Abdominal neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Basal cell carcinoma	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	2 (0.21%)
Breast cancer	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Gallbladder adenocarcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Hepatic cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Lung neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Lung neoplasm malignant	1 (1.01%)	3 (1.20%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (0.41%)

Metastases to lymph nodes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Metastases to peritoneum	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Non-small cell lung cancer stage IIIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Oesophageal adenocarcinoma	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Prostate cancer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Renal neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Squamous cell carcinoma	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Squamous cell carcinoma of skin	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Nervous system disorders							
Aphasia	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Embolic stroke	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Hypoaesthesia	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Polyneuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Reproductive system and breast disorders							
Benign prostatic hyperplasia	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Respiratory, thoracic and mediastinal disorders							
Acute respiratory failure	0 (0.00%)	1 (0.40%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	2 (0.21%)
Bronchospasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)

Chronic obstructive pulmonary disease	5 (5.05%)	9 (3.60%)	1 (0.81%)	5 (3.97%)	2 (1.61%)	5 (1.99%)	27 (2.77%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Lung consolidation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Pneumothorax	0 (0.00%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	1 (0.10%)
Vascular disorders							
Arteriosclerosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	1 (0.10%)
Hypertensive emergency	0 (0.00%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.79%)	0 (0.00%)	0 (0.00%)	1 (0.10%)
Peripheral arterial occlusive disease	1 (1.01%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.10%)

Other Adverse Events by System Organ Class

Time Frame	Adverse events were reported from the start of treatment to 30 days after end of treatment, assessed up to maximum duration of 199 days.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment
Source Vocabulary for Table Default	MedDRA (24.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	QBW251 450 mg N = 99	**QBW251 300 mg N = 250**	**QBW251 150 mg N = 124**	**QBW251 75 mg N = 126**	**QBW251 25 mg N = 124**	**Placebo N = 251**	**Total N = 974**

Arm/Group Description	QBW251 was orally administered 450 mg b.i.d for 24 weeks	QBW251 was orally administered 300 mg b.i.d for 24 weeks	QBW251 was orally administered 150 mg b.i.d for 24 weeks	QBW251 was orally administered 75 mg b.i.d for 24 weeks	QBW251 was orally administered 25 mg b.i.d for 24 weeks	Placebo was orally administered b.i.d for 24 weeks	Total
Total participants affected	48 (48.48%)	117 (46.80%)	59 (47.58%)	55 (43.65%)	60 (48.39%)	107 (42.63%)	446 (45.79%)
Cardiac disorders							
Atrial fibrillation	2 (2.02%)	1 (0.40%)	2 (1.61%)	0 (0.00%)	1 (0.81%)	3 (1.20%)	9 (0.92%)
Gastrointestinal disorders							
Diarrhoea	6 (6.06%)	7 (2.80%)	1 (0.81%)	2 (1.59%)	3 (2.42%)	6 (2.39%)	25 (2.57%)
Nausea	5 (5.05%)	4 (1.60%)	2 (1.61%)	3 (2.38%)	1 (0.81%)	5 (1.99%)	20 (2.05%)
Vomiting	1 (1.01%)	2 (0.80%)	0 (0.00%)	3 (2.38%)	1 (0.81%)	4 (1.59%)	11 (1.13%)
General disorders and administration site conditions							
Chest pain	0 (0.00%)	2 (0.80%)	3 (2.42%)	0 (0.00%)	1 (0.81%)	1 (0.40%)	7 (0.72%)
Fatigue	2 (2.02%)	3 (1.20%)	2 (1.61%)	1 (0.79%)	0 (0.00%)	3 (1.20%)	11 (1.13%)
Infections and infestations							
Bronchitis	4 (4.04%)	6 (2.40%)	2 (1.61%)	0 (0.00%)	3 (2.42%)	2 (0.80%)	17 (1.75%)
COVID-19	0 (0.00%)	4 (1.60%)	1 (0.81%)	1 (0.79%)	6 (4.84%)	5 (1.99%)	17 (1.75%)
Cystitis	0 (0.00%)	2 (0.80%)	2 (1.61%)	3 (2.38%)	1 (0.81%)	1 (0.40%)	9 (0.92%)
Gastroenteritis	4 (4.04%)	2 (0.80%)	0 (0.00%)	1 (0.79%)	1 (0.81%)	1 (0.40%)	9 (0.92%)
Influenza	2 (2.02%)	4 (1.60%)	0 (0.00%)	1 (0.79%)	1 (0.81%)	2 (0.80%)	10 (1.03%)
Lower respiratory tract infection	3 (3.03%)	3 (1.20%)	3 (2.42%)	2 (1.59%)	4 (3.23%)	5 (1.99%)	20 (2.05%)
Nasopharyngitis	4 (4.04%)	12 (4.80%)	5 (4.03%)	10 (7.94%)	6 (4.84%)	10 (3.98%)	47 (4.83%)

Pharyngitis	2 (2.02%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	2 (1.61%)	3 (1.20%)	8 (0.82%)
Pneumonia	3 (3.03%)	5 (2.00%)	1 (0.81%)	1 (0.79%)	2 (1.61%)	2 (0.80%)	14 (1.44%)
Sinusitis	0 (0.00%)	1 (0.40%)	3 (2.42%)	1 (0.79%)	0 (0.00%)	2 (0.80%)	7 (0.72%)
Upper respiratory tract infection	3 (3.03%)	4 (1.60%)	5 (4.03%)	0 (0.00%)	0 (0.00%)	5 (1.99%)	17 (1.75%)
Upper respiratory tract infection bacterial	3 (3.03%)	12 (4.80%)	4 (3.23%)	4 (3.17%)	4 (3.23%)	9 (3.59%)	36 (3.70%)
Urinary tract infection	3 (3.03%)	8 (3.20%)	3 (2.42%)	5 (3.97%)	2 (1.61%)	5 (1.99%)	26 (2.67%)
Viral upper respiratory tract infection	3 (3.03%)	8 (3.20%)	3 (2.42%)	3 (2.38%)	3 (2.42%)	7 (2.79%)	27 (2.77%)
Injury, poisoning and procedural complications							
Contusion	0 (0.00%)	2 (0.80%)	0 (0.00%)	0 (0.00%)	3 (2.42%)	1 (0.40%)	6 (0.62%)
Investigations							
C-reactive protein increased	1 (1.01%)	8 (3.20%)	4 (3.23%)	0 (0.00%)	0 (0.00%)	2 (0.80%)	15 (1.54%)
Gamma-glutamyltransferase increased	4 (4.04%)	6 (2.40%)	4 (3.23%)	2 (1.59%)	0 (0.00%)	3 (1.20%)	19 (1.95%)
Haemoglobin decreased	2 (2.02%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	3 (0.31%)
Hepatic enzyme increased	2 (2.02%)	2 (0.80%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (0.80%)	6 (0.62%)
Metabolism and nutrition disorders							
Hypokalaemia	2 (2.02%)	1 (0.40%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	1 (0.40%)	5 (0.51%)
Musculoskeletal and connective tissue disorders							
Arthralgia	2 (2.02%)	2 (0.80%)	2 (1.61%)	1 (0.79%)	3 (2.42%)	6 (2.39%)	16 (1.64%)

Back pain	2 (2.02%)	7 (2.80%)	3 (2.42%)	3 (2.38%)	2 (1.61%)	7 (2.79%)	24 (2.46%)
Myalgia	1 (1.01%)	1 (0.40%)	4 (3.23%)	1 (0.79%)	0 (0.00%)	3 (1.20%)	10 (1.03%)
Nervous system disorders							
Dizziness	4 (4.04%)	5 (2.00%)	0 (0.00%)	1 (0.79%)	1 (0.81%)	1 (0.40%)	12 (1.23%)
Headache	4 (4.04%)	11 (4.40%)	4 (3.23%)	4 (3.17%)	4 (3.23%)	6 (2.39%)	33 (3.39%)
Respiratory, thoracic and mediastinal disorders							
Chronic obstructive pulmonary disease	16 (16.16%)	51 (20.40%)	32 (25.81%)	24 (19.05%)	34 (27.42%)	56 (22.31%)	213 (21.87%)
Cough	1 (1.01%)	4 (1.60%)	0 (0.00%)	1 (0.79%)	1 (0.81%)	6 (2.39%)	13 (1.33%)
Rhinitis allergic	2 (2.02%)	1 (0.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.31%)
Skin and subcutaneous tissue disorders							
Photosensitivity reaction	2 (2.02%)	0 (0.00%)	1 (0.81%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (0.31%)
Rash	3 (3.03%)	2 (0.80%)	2 (1.61%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	7 (0.72%)
Vascular disorders							
Hypertension	4 (4.04%)	8 (3.20%)	3 (2.42%)	3 (2.38%)	3 (2.42%)	4 (1.59%)	25 (2.57%)

Other Relevant Findings

Not Applicable

Conclusion:

- No dose-response was observed for trough FEV1 at Week 12 (primary endpoint of study). A clear dose-response was observed at Week 24 across five endpoints, including objective, symptomatic and biomarker measures: trough FEV1, E-RS cough and sputum subscale score, E-RS total score, rescue medication, and fibrinogen (validated biomarker for COPD exacerbations and mortality).
- The observed improvement in endpoints shown for QBW251 is on top of maximum available COPD therapy (inhaled triple therapy [LABA/LAMA/ICS]) which is considered to provide maximum bronchodilation and anti-inflammatory benefit.
- QBW251 demonstrated a favorable safety and tolerability profile.
- The QBW251 300mg dose demonstrated a positive benefit-risk profile supporting further investigation of its therapeutic potential in patients with COPD and chronic bronchitis.

Date of Clinical Trial Report

14 July 2022