



Clinical trial results:

A randomized, double blind placebo-controlled study to assess the safety, tolerability, pharmacokinetics, and preliminary pharmacodynamics of single and multiple ascending doses of QBW251 in healthy subjects and multiple doses in cystic fibrosis patients.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.novfor> complete trial results.

Summary

EudraCT number	2011-005085-37
Trial protocol	GB DE IE BE FR
Global end of trial date	30 November 2015

Results information

Result version number	v1 (current)
This version publication date	12 July 2018
First version publication date	12 July 2018

Trial information

Trial identification

Sponsor protocol code	CQBW251X2101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02190604
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of multiple ascending multiple oral doses in CF patients and to evaluate the preliminary efficacy of multiple doses of QBW251 on change from baseline in lung clearance index (LCI) in cystic fibrosis (CF) patients at Day 15.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 113
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	153
EEA total number of subjects	136

Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	153
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In parts 1 and 2, participants (Healthy Volunteers) were randomized 3:1 to receive QBW251X or placebo. In part 3, participants (cystic fibrosis (CF) patients) were randomized 3:1 to receive QBW251X or placebo.

Period 1

Period 1 title	Part 1 and 2 (Healthy Volunteers)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1 Cohort 1: QBW251

Arm description:

Single dose of QBW251 10 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251 10 mg,

Arm title	Part 1 Cohort 2: QBW251
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Arm description:

Single dose of QBW251 25 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251 25mg orally

Arm title	Part 1 Cohort 3: QBW251
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Arm description:

Single dose of QBW251 75 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 75mg orally

Arm title	Part 1 Cohort 4: QBW251
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Arm description:

Single dose of QBW251 150 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 150mg orally

Arm title	Part 1 Cohort 5: QBW251
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Arm description:

Single dose of QBW251 300 mg in healthy volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 300mg orally

Arm title	Part 1 Cohort 6: QBW251
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Arm description:

Single dose of QBW251 500 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 500mg orally

Arm title	Part 1 Cohort 7: QBW251
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Arm description:

Single dose of QBW251 750 mg in Healthy Volunteers. Each treatment period was comprised of a

baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 750mg orally

Arm title	Part 1 Cohort 8: QBW251
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Arm description:

Single dose of QBW251 1000 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 1000mg orally

Arm title	Part 1 Placebo
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Arm description:

Placebo to QBW251 in all cohorts of part 1 in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo, orally

Arm title	Part 2 Cohort 1: QBW251
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Arm description:

Multiple doses of QBW25 150 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 150 mg qd

Arm title	Part 2 Cohort 2: QBW251
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Arm description:
Multiple doses of QBW251 400 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 450mg qd

Arm title	Part 2 Cohort 3: QBW251
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Arm description:
Multiple doses of QBW251 750 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 750mg qd

Arm title	Part 2 Cohort 4: QBW251
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Arm description:
Multiple doses of QBW251 450 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 450mg bid

Arm title	Part 2 Cohort 5: QBW251
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Arm description:
Multiple doses of QBW251 750 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 750mg bid

Arm title	Part 2 Placebo
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Arm description:
Placebo to QBW251 in all cohorts of part 2 in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
Placebo	

Number of subjects in period 1^[1]	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1^[1]	Part 1 Cohort 4: QBW251	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1^[1]	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251	Part 1 Placebo
Started	6	6	16
Completed	6	6	16
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1^[1]	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1^[1]	Part 2 Cohort 4: QBW251	Part 2 Cohort 5: QBW251	Part 2 Placebo
Started	6	6	10
Completed	6	5	8
Not completed	0	1	2

Adverse event, non-fatal	-	-	2
Lost to follow-up	-	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: This is an adaptive design parts one and 2 were conducted first then part 3 conducted later . The total equals the ww number.

Period 2

Period 2 title	Part 3 (Patients)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 3 Cohort 1: QBW251

Arm description:

150 mg b.i.d. Multiple doses. Patients having a class III, IV, V, or VI mutation on one allele and any other CFTR mutation on the other allele in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 150mg bid

Arm title	Part 3 Cohort 2: QBW251
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Arm description:

450 mg b.i.d. Multiple doses. Patients having a class III, IV, V, or VI mutation on one allele and any other CFTR mutation on the other allele in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

QBW251, 450mg bid

Arm title	Part 3 Cohort 3: QBW251
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Arm description:

450 mg b.i.d. Multiple doses. Patients who are homozygous for the F508del mutation in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Arm type	Experimental
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Investigational medicinal product name	QBW251
Investigational medicinal product code	QBW251
Other name	QBW251
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: QBW251, 450mg bid	
Arm title	Part 3 Placebo

Arm description:

Placebo to QBW251 in all cohorts of part 3 in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	Placebo
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo

Number of subjects in period 2^[2]	Part 3 Cohort 1: QBW251	Part 3 Cohort 2: QBW251	Part 3 Cohort 3: QBW251
Started	6	12	19
Completed	6	12	19

Number of subjects in period 2^[2]	Part 3 Placebo
Started	12
Completed	12

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: group started after period one and 2 which were with healthy volunteers.

Baseline characteristics

Reporting groups

Reporting group title	Part 1 Cohort 1: QBW251
Reporting group description: Single dose of QBW251 10 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 2: QBW251
Reporting group description: Single dose of QBW251 25 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 3: QBW251
Reporting group description: Single dose of QBW251 75 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 4: QBW251
Reporting group description: Single dose of QBW251 150 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 5: QBW251
Reporting group description: Single dose of QBW251 300 mg in healthy volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 6: QBW251
Reporting group description: Single dose of QBW251 500 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 7: QBW251
Reporting group description: Single dose of QBW251 750 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 8: QBW251
Reporting group description: Single dose of QBW251 1000 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Placebo
Reporting group description: Placebo to QBW251 in all cohorts of part 1 in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 2 Cohort 1: QBW251

Reporting group description:

Multiple doses of QBW25 150 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 2: QBW251
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Reporting group description:

Multiple doses of QBW251 400 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 3: QBW251
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Reporting group description:

Multiple doses of QBW251 750 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 4: QBW251
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Reporting group description:

Multiple doses of QBW251 450 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 5: QBW251
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Reporting group description:

Multiple doses of QBW251 750 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Placebo
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Reporting group description:

Placebo to QBW251 in all cohorts of part 2 in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251
Number of subjects	6	6	6
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	36.3	35	43.5
standard deviation	± 8.69	± 14.25	± 3.39
Gender, Male/Female			
Units: Subjects			
Female	0	0	0
Male	6	6	6
Age Continuous Part 2, HV (n=40)			
Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999
Age Continuous Part 3, CF patients			

(n=49)			
Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999

Reporting group values	Part 1 Cohort 4: QBW251	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251
Number of subjects	6	6	6
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	33.3	32.7	44.2
standard deviation	± 9.61	± 5.85	± 8.23
Gender, Male/Female			
Units: Subjects			
Female	0	0	0
Male	6	6	6
Age Continuous Part 2, HV (n=40)			
Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999
Age Continuous Part 3, CF patients (n=49)			
Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999

Reporting group values	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251	Part 1 Placebo
Number of subjects	6	6	16
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	16
From 65-84 years	0	0	0

85 years and over	0	0	0
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Age Continuous Units: Years arithmetic mean standard deviation	28.2 ± 9.28	33.2 ± 9.47	30.3 ± 9.18
Gender, Male/Female Units: Subjects			
Female	0	0	0
Male	6	6	16
Age Continuous Part 2, HV (n=40) Units: Years arithmetic mean standard deviation	0.9999 ± 0.9999	0.9999 ± 0.9999	0.9999 ± 0.9999
Age Continuous Part 3, CF patients (n=49) Units: Years arithmetic mean standard deviation	0.9999 ± 0.9999	0.9999 ± 0.9999	0.9999 ± 0.9999

Reporting group values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251
Number of subjects	6	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years arithmetic mean standard deviation	0.9999 ± 0.9999	0.9999 ± 0.9999	0.9999 ± 0.9999
Gender, Male/Female Units: Subjects			
Female	0	0	0
Male	6	6	6
Age Continuous Part 2, HV (n=40) Units: Years arithmetic mean standard deviation	30.3 ± 5.13	30.5 ± 5.89	29.2 ± 11.62
Age Continuous Part 3, CF patients (n=49) Units: Years arithmetic mean	0.9999	0.9999	0.9999

standard deviation	± 0.9999	± 0.9999	± 0.9999
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Reporting group values	Part 2 Cohort 4: QBW251	Part 2 Cohort 5: QBW251	Part 2 Placebo
Number of subjects	6	6	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	10
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999
Gender, Male/Female Units: Subjects			
Female	0	0	0
Male	6	6	10
Age Continuous Part 2, HV (n=40) Units: Years			
arithmetic mean	31.7	27.8	29
standard deviation	± 13.22	± 5	± 6.22
Age Continuous Part 3, CF patients (n=49) Units: Years			
arithmetic mean	0.9999	0.9999	0.9999
standard deviation	± 0.9999	± 0.9999	± 0.9999

Reporting group values	Total		
Number of subjects	104		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	104		
From 65-84 years	0		
85 years and over	0		

Age Continuous Units: Years arithmetic mean standard deviation	-		
Gender, Male/Female Units: Subjects			
Female	0		
Male	104		
Age Continuous Part 2, HV (n=40) Units: Years arithmetic mean standard deviation	-		
Age Continuous Part 3, CF patients (n=49) Units: Years arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Part 1 Cohort 1: QBW251
Reporting group description: Single dose of QBW251 10 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 2: QBW251
Reporting group description: Single dose of QBW251 25 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 3: QBW251
Reporting group description: Single dose of QBW251 75 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 4: QBW251
Reporting group description: Single dose of QBW251 150 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 5: QBW251
Reporting group description: Single dose of QBW251 300 mg in healthy volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 6: QBW251
Reporting group description: Single dose of QBW251 500 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 7: QBW251
Reporting group description: Single dose of QBW251 750 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Cohort 8: QBW251
Reporting group description: Single dose of QBW251 1000 mg in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 1 Placebo
Reporting group description: Placebo to QBW251 in all cohorts of part 1 in Healthy Volunteers. Each treatment period was comprised of a baseline period (Day -1), an inpatient dosing period (Days 1 to 3), three follow-up visits (Days 4, 5, and 8), and one end-of-treatment-period evaluation performed 14 days after the dose of study drug (Day 15).	
Reporting group title	Part 2 Cohort 1: QBW251

Reporting group description:

Multiple doses of QBW25 150 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 2: QBW251
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Reporting group description:

Multiple doses of QBW251 400 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 3: QBW251
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Reporting group description:

Multiple doses of QBW251 750 mg qd in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 4: QBW251
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Reporting group description:

Multiple doses of QBW251 450 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Cohort 5: QBW251
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Reporting group description:

Multiple doses of QBW251 750 mg bid in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 2 Placebo
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Reporting group description:

Placebo to QBW251 in all cohorts of part 2 in Healthy Volunteers. 14-day treatment period, follow-up study visits (Days 18, 22 and 29) and one End-of-Study evaluation (Day 36).

Reporting group title	Part 3 Cohort 1: QBW251
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Reporting group description:

150 mg b.i.d. Multiple doses. Patients having a class III, IV, V, or VI mutation on one allele and any other CFTR mutation on the other allele in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Reporting group title	Part 3 Cohort 2: QBW251
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Reporting group description:

450 mg b.i.d. Multiple doses. Patients having a class III, IV, V, or VI mutation on one allele and any other CFTR mutation on the other allele in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Reporting group title	Part 3 Cohort 3: QBW251
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Reporting group description:

450 mg b.i.d. Multiple doses. Patients who are homozygous for the F508del mutation in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Reporting group title	Part 3 Placebo
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Reporting group description:

Placebo to QBW251 in all cohorts of part 3 in patients. treatment period (Day 1 to Day 14) with study visits on Days 1, 4, 7 and 14 with follow-up visits on Days 15, 28 and 42.

Subject analysis set title	Part 1 cohort 6 FED
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Subject analysis set type	Full analysis
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Subject analysis set description:

part 1 cohort 6 had testing done in fasting and fed stat....this data represents the Fed state

Primary: Part 1 and 2: Number of participants (Healthy Volunteers) with reported adverse events receiving QBW251

End point title	Part 1 and 2: Number of participants (Healthy Volunteers) with reported adverse events receiving QBW251 ^[1]
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End point description:

All adverse events (in healthy volunteers) reported. There were no reporting of serious adverse events or death in part 1 and 2. No statistical analysis was planned for this primary outcome

End point type	Primary
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End point timeframe:

Day 1 to Day 36

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants	1	0	0	0

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Participants	0	0	0	0

End point values	Part 1 Placebo	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	6	6	6
Units: Participants	2	0	1	0

End point values	Part 2 Cohort 4: QBW251	Part 2 Cohort 5: QBW251	Part 2 Placebo	Part 1 cohort 6 FED
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	6	10	5
Units: Participants	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Part 3: Change in Lung Clearance Index (LCI) from baseline to day 15

End point title	Part 3: Change in Lung Clearance Index (LCI) from baseline to day 15 ^[2]
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End point description:

Change in Lung Clearance Index (LCI) will be conducted according to international standards in cystic fibrosis patients. Lung clearance index (LCI) is a measure of ventilation inhomogeneity that is derived from a multiple-breath washout test. A reduction in mean change from baseline for LCI2.5 indicates improvement. No statistical analysis was planned for this primary outcome

End point type	Primary
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End point timeframe:

Baseline and Day 15

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: All end points are verified

Statistical analyses

No statistical analyses for this end point

Primary: Part 3: Number of participants (Patients) with reported adverse events receiving QBW251

End point title	Part 3: Number of participants (Patients) with reported adverse events receiving QBW251 ^[3]
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End point description:

All adverse events and serious adverse events (in patients) reported. There were no reporting of death in part 3. No statistical analysis was planned for this primary outcome

End point type	Primary
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End point timeframe:

Day 1 to Day 56

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: All end points are verified

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Change in Forced Expiratory Volume in 1 second (FEV1) at day 15

End point title	Part 3: Change in Forced Expiratory Volume in 1 second (FEV1) at day 15
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End point description:

Forced Expiratory Volume in 1 second (FEV1) will be measured via spirometer according to international standards. Forced Expiratory Volume in 1 second (FEV1) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation

End point type	Secondary
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End point timeframe:

Baseline and Day 15

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Change in Cystic Fibrosis Questionnaire-Revised reported outcomes

End point title	Part 3: Change in Cystic Fibrosis Questionnaire-Revised reported outcomes
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End point description:

Change in Cystic Fibrosis Questionnaire data will be obtained from patient reported outcomes (CFQ-R PRO). Respiratory Domain, cores range from 0 to 100, with higher scores indicating better health, a change of 4 is considered clinically relevant

End point type	Secondary
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End point timeframe:

Baseline and Day 14

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUC0-t in healthy volunteers

End point title	Part 1: AUC0-t in healthy volunteers ^[4]
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End point description:

Pharmacokinetics of QBW251 in plasma: area under the plasma concentration versus time curve from time zero to time of last measurable concentration (AUC0-t). In part one of the study a single dose was administered and samples were collected up to 5 days. As a result the AUC0-t goes from Day 1 to Day 5 (for some lower doses QBW251 concentrations were not measured up to Day 5 as the concentrations were low due to the low dose administered)

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 2-5)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	52.5 (± 28.1)	73.7 (± 51.8)	692 (± 389)	1650 (± 907)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	5470 (± 1070)	9450 (± 1740)	20200 (± 11500)	35900 (± 9100)

End point values	Part 1 Placebo			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: hr*ng/mL				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Maximum concentration (Cmax) in healthy volunteers

End point title	Part 1: Maximum concentration (Cmax) in healthy volunteers ^[5]
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End point description:

Pharmacokinetics of QBW251 in plasma: observed maximum plasma concentration following administration of QBW251. In this analysis Cmax will be reported using blood samples taken on Days 1-5 are from healthy volunteers

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ug/L				
arithmetic mean (standard deviation)	21.1 (± 11.9)	24.7 (± 15.9)	186 (± 82.3)	459 (± 267)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ug/L				
arithmetic mean (standard deviation)	1110 (± 330)	1910 (± 413)	2680 (± 1000)	4540 (± 930)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Time to maximum concentration (Tmax) in healthy volunteers

End point title	Part 1: Time to maximum concentration (Tmax) in healthy volunteers ^[6]
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End point description:

Pharmacokinetics of QBW251 in plasma: time to reach the maximum concentration after administration of QBW251. In this analysis Tmax will be reported using blood samples taken on Days 1 - 5 from healthy volunteers. In this part of the study a single dose was administered and samples were collected up to 5 days. As a result the Tmax is one value as the concentration-time curve goes to Day 5 (for some lower doses QBW251 concentrations were not measured up to Day 5 as the concentrations were low due to the low dose administered).

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)	0.756 (± 0.268)	1.25 (± 0.612)	1.33 (± 0.516)	1.5 (± 0.548)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)	1.5 (± 0.837)	2.17 (± 1.17)	2.52 (± 0.85)	1.83 (± 0.753)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: T1/2 in healthy volunteers

End point title	Part 1: T1/2 in healthy volunteers ^[7]
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End point description:

Pharmacokinetics of QBW251 in plasma: terminal elimination half-life. In this analysis T1/2 will be reported using blood samples taken on Days 1 - 5 from healthy volunteers. In part one of the study a single dose was administered and samples were collected up to 5 days. As a result the T1/2 goes from Day 1 to Day 5 (for some lower doses QBW251 concentrations were not measured up to Day 5 as the concentrations were low due to the low dose administered).

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)	0.9999 (± 0.9999)	10.3 (± 4.24)	10.1 (± 3.35)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)	12 (± 2.26)	12.7 (± 1.99)	12.8 (± 3.85)	10.7 (± 2.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: AUCinf in healthy volunteers

End point title	Part 1: AUCinf in healthy volunteers ^[8]
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End point description:

Pharmacokinetics of QBW251 in plasma: area under the plasma concentration time curve from time zero to infinity. In this analysis AUCinf will be reported using blood samples taken on Days 1 - 5 from healthy volunteers. In part one of the study a single dose was administered and samples were collected up to 5 days. As a result the AUCinf goes from Day 1 to Day 5 (for some lower doses QBW251 concentrations were not measured up to Day 5 as the concentrations were low due to the low dose administered)

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4 , 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)	0.9999 (± 0.9999)	731 (± 387)	1680 (± 903)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	5510 (± 1080)	9480 (± 1740)	20300 (± 11500)	36000 (± 9120)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: CL/F in healthy volunteers

End point title	Part 1: CL/F in healthy volunteers ^[9]
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End point description:

Pharmacokinetics of QBW251 in plasma: apparent systemic clearance from plasma following extravascular administration. In this analysis CL/F will be reported using blood samples taken on Days 1 - 5 from healthy volunteers. In part one of the study a single dose was administered and samples were collected up to 5 days. As a result the CL/F goes from Day 1 to Day 5 (for some lower doses QBW251 concentrations were not measured up to Day 5 as the concentrations were low due to the low dose administered)

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4 , 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: L/hr				
arithmetic mean (standard deviation)	0.9999 (\pm 0.9999)	0.9999 (\pm 0.9999)	123 (\pm 49)	114 (\pm 63.9)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: L/hr				
arithmetic mean (standard deviation)	56.2 (\pm 11)	54.5 (\pm 11.9)	45.9 (\pm 19.9)	29.7 (\pm 9)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Vz/F in healthy volunteers

End point title	Part 1: Vz/F in healthy volunteers ^[10]
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End point description:

Pharmacokinetics of QBW251 in plasma: apparent volume of distribution during the terminal elimination phase following extravascular administration. In this analysis Vz/F will be reported using blood samples taken on Days 1 - 5 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose (i.e. Days 1 - 5)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 1 Cohort 1: QBW251	Part 1 Cohort 2: QBW251	Part 1 Cohort 3: QBW251	Part 1 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Liters				
arithmetic mean (standard deviation)	0.9999 (\pm 0.9999)	0.9999 (\pm 0.9999)	1700 (\pm 772)	1490 (\pm 622)

End point values	Part 1 Cohort 5: QBW251	Part 1 Cohort 6: QBW251	Part 1 Cohort 7: QBW251	Part 1 Cohort 8: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6

Units: Liters				
arithmetic mean (standard deviation)	957 (± 151)	995 (± 235)	827 (± 375)	447 (± 112)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Ae0-t in healthy volunteers

End point title	Part 2: Ae0-t in healthy volunteers ^[11]
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End point description:

Pharmacokinetics of QBW251 in urine: amount of drug excreted in urine from time zero until last measurable concentration. In this analysis Ae0-t will be reported using urine samples taken on Day 1 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	5
Units: L/hr				
arithmetic mean (standard deviation)	2.36 (± 1.84)	2.2 (± 1.26)	1.21 (± 0.697)	0.419 (± 0.271)

End point values	Part 2 Cohort 5: QBW251	Part 2 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	10		
Units: L/hr				
arithmetic mean (standard deviation)	0.14 (± 0.0936)	0.9999 (± 0.9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: CLr in healthy volunteers

End point title	Part 2: CLr in healthy volunteers ^[12]
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End point description:

Pharmacokinetics of QBW251 in urine: renal clearance following drug administration. In this analysis CLr will be reported using urine samples taken on Day 1 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1; Day 14 was calculated as urine was only collected up to 12 hours on Day 1 thus CLr cannot be calculated.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: L/hr				
arithmetic mean (standard deviation)	2.36 (± 1.84)	2.2 (± 1.26)	1.21 (± 0.697)	0.419 (± 0.271)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: L/hr				
arithmetic mean (standard deviation)	0.14 (± 0.0936)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: AUCtau in healthy volunteers

End point title	Part 2: AUCtau in healthy volunteers ^[13]
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End point description:

Pharmacokinetics of QBW251 in plasma after multiple doses: the area under the plasma concentration-time curve from time zero to end of the dosing interval tau. In this analysis AUCtau will be reported. Samples taken on Days 1 and 14 from healthy volunteers

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1 and 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day1	1800 (± 794)	6170 (± 1250)	16100 (± 8170)	7160 (± 1960)
Day 14	2060 (± 708)	7620 (± 1470)	28300 (± 5570)	12100 (± 4930)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hr*ng/mL				
arithmetic mean (standard deviation)				
Day1	18800 (± 6360)			
Day 14	80300 (± 56300)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Maximum concentration (Cmax) in healthy volunteers

End point title	Part 2: Maximum concentration (Cmax) in healthy
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End point description:

Pharmacokinetics of QBW251 in plasma after multiple doses: observed maximum plasma concentration following QBW251 at steady state. In this analysis Cmax will be reported using blood samples taken on Days 1 and 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4 , 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1 and 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ug/L				
arithmetic mean (standard deviation)				
Day 1	541 (± 338)	1650 (± 343)	2790 (± 1040)	1650 (± 188)
Day 14	430 (± 145)	1500 (± 442)	3840 (± 868)	2190 (± 769)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ug/L				
arithmetic mean (standard deviation)				
Day 1	3720 (± 1530)			
Day 14	9420 (± 4330)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Time to maximum concentration (Tmax) in healthy volunteers

End point title	Part 2: Time to maximum concentration (Tmax) in healthy volunteers ^[15]
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End point description:

Pharmacokinetics of QBW251 in plasma after multiple doses: time to reach the maximum concentration after administration of QBW251. In this analysis Tmax will be reported using blood samples taken on Days 1 and 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1 and 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)				
Day 1	1.67 (± 0.816)	1.17 (± 0.408)	2.33 (± 1.21)	2.68 (± 0.813)
Day 2	2.17 (± 1.17)	2.17 (± 0.408)	2.33 (± 1.03)	3.25 (± 1.41)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hr				
arithmetic mean (standard deviation)				
Day 1	3.67 (± 0.516)			

Day 2	3.8 (\pm 0.447)			
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Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: AUC0-t

End point title	Part 2: AUC0-t ^[16]
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End point description:

Pharmacokinetics of QBW251 in plasma: area under the plasma concentration versus time curve from time zero to time of last measurable concentration. In this analysis AUC0-t will be reported using blood samples taken on Day 14 are from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr*ng/mL				
arithmetic mean (standard deviation)	2060 (\pm 708)	7620 (\pm 1470)	28300 (\pm 5570)	12100 (\pm 4930)

End point values	Part 2 Cohort 5: QBW251	Part 2 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	10		
Units: hr*ng/mL				
arithmetic mean (standard deviation)	80300 (\pm 56300)	0.9999 (\pm 0.9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Cav in healthy volunteers

End point title	Part 2: Cav in healthy volunteers ^[17]
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End point description:

The average drug concentration in plasma during multiple dosing. In this analysis Cav will be reported using blood samples taken on Days 1 and 14 are from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1 and 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ug/L				
arithmetic mean (standard deviation)	85.8 (± 29.5)	318 (± 61.1)	1180 (± 232)	0.9999 (± 0.9999)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ug/L				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: CL/F in healthy volunteers

End point title	Part 2: CL/F in healthy volunteers ^[18]
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End point description:

apparent systemic clearance from plasma following extravascular administration. In this analysis CL/F will be reported using blood samples taken on Day 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: L/hr				
arithmetic mean (standard deviation)	80.8 (± 29.7)	54 (± 9.4)	27.5 (± 5.98)	0.9999 (± 0.9999)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: L/hr				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Vz/F in healthy volunteers

End point title	Part 2: Vz/F in healthy volunteers ^[19]
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End point description:

Apparent volume of distribution during the terminal elimination phase following extravascular administration. In this analysis Vz/F will be reported using blood samples taken on Day 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4 , 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Liters				
arithmetic mean (standard deviation)	1330 (± 550)	1120 (± 395)	608 (± 255)	0.9999 (± 0.9999)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			

Units: Liters				
arithmetic mean (standard deviation)	0.9999 (\pm 0.9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: Racc in healthy volunteers

End point title	Part 2: Racc in healthy volunteers ^[20]
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End point description:

Accumulation ratio (Racc). In this analysis Racc will be reported using blood samples taken on Days 1 - 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 1 - 14; (If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Ratio				
arithmetic mean (standard deviation)	1.27 (\pm 0.425)	1.25 (\pm 0.199)	2.08 (\pm 0.913)	1.66 (\pm 0.386)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Ratio				
arithmetic mean (standard deviation)	3.88 (\pm 2.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2: T1/2 in healthy volunteers

End point title	Part 2: T1/2 in healthy volunteers ^[21]
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End point description:

terminal elimination half-life (T1/2). In this analysis T1/2 will be reported using blood samples taken on Day 14 from healthy volunteers.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose at Day 1; 24, 48, 72 and 96 hr post dose Day 14;
(If B ID dosing, 12 hours samples will be pre-dosed)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All end points are verified

End point values	Part 2 Cohort 1: QBW251	Part 2 Cohort 2: QBW251	Part 2 Cohort 3: QBW251	Part 2 Cohort 4: QBW251
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hr				
arithmetic mean (standard deviation)	11.3 (± 1.44)	14.1 (± 3.8)	15.1 (± 4.4)	0.9999 (± 0.9999)

End point values	Part 2 Cohort 5: QBW251			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: hr				
arithmetic mean (standard deviation)	0.9999 (± 0.9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of QBW251 in CF patients

End point title	Part 3: Area Under the Curve From Time Zero to Last Quantifiable Concentration (AUClast) of QBW251 in CF patients
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End point description:

Area under the plasma concentration time-curve from zero to the last measured concentration (AUClast)

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose in Day 1, Day 14

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Plasma Concentration at the Last Quantifiable Time Point (Clast) of QBW251 in CF patients

End point title	Part 3: Plasma Concentration at the Last Quantifiable Time Point (Clast) of QBW251 in CF patients
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End point description:

Blood samples were collected at timepoints prespecified in the study protocol. Tlast of QBW251 was the last time point when blood sample collected was quantifiable

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose in Day 1, Day2

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Maximum concentration (Cmax) in CF patients

End point title	Part 3: Maximum concentration (Cmax) in CF patients
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End point description:

Observed maximum plasma concentration following administration of QBW251. In this analysis Cmax will be reported using blood samples taken on Day 1 and day 14 from patients

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose in Day 1, Day 14

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Tlast in CF patients

End point title	Part 3: Tlast in CF patients
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End point description:

Blood samples were collected at timepoints prespecified in the study protocol. Tlast of QBW251 was the last time point when blood sample collected was quantifiable day 1 and day 14

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose in Day 1, Day 14

Statistical analyses

No statistical analyses for this end point

Secondary: Part 3: Time to maximum concentration (Tmax)

End point title	Part 3: Time to maximum concentration (Tmax)
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End point description:

Pharmacokinetics of QBW251 in plasma after multiple doses: time to reach the maximum concentration after administration of QBW251. In this analysis Tmax will be reported using blood samples taken on Days 1 and 14 in patients

End point type	Secondary
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End point timeframe:

Pre-dose (0 hr), 0.25, 0.5, 1, 2, 3, 4, 8 hr post-dose in Day 1, Day 14

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Part 1 QBW251 150 mg
Reporting group description: Part 1 QBW251 150 mg	
Reporting group title	Part 1 Placebo
Reporting group description: Part 1 Placebo	
Reporting group title	Part 1 QBW251 25 mg
Reporting group description: Part 1 QBW251 25 mg	
Reporting group title	Part 1 QBW251 10 mg
Reporting group description: Part 1 QBW251 10 mg	
Reporting group title	Part 1 QBW251 750 mg
Reporting group description: Part 1 QBW251 750 mg	
Reporting group title	Part 1 QBW251 1000 mg
Reporting group description: Part 1 QBW251 1000 mg	
Reporting group title	Part 1 QBW251 500 mg
Reporting group description: Part 1 QBW251 500 mg	
Reporting group title	Part 1 QBW251 500 mg (fed)
Reporting group description: Part 1 QBW251 500 mg (fed)	
Reporting group title	Part 1 QBW251 300 mg
Reporting group description: Part 1 QBW251 300 mg	
Reporting group title	Part 2 QBW251 150 mg
Reporting group description: Part 2 QBW251 150 mg	
Reporting group title	Part 2 QBW251 400 mg
Reporting group description: Part 2 QBW251 400 mg	
Reporting group title	Part 2 QBW251 750 mg
Reporting group description: Part 2 QBW251 750 mg	
Reporting group title	Part 2 Placebo

Reporting group description:

Part 2 Placebo

Reporting group title	Part 3 Placebo C1/C2/C3
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Reporting group description:

Part 3 Placebo C1/C2/C3

Reporting group title	Part 3 QBW251 150 mg b.i.d. C1
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Reporting group description:

Part 3 QBW251 150 mg b.i.d. C1

Reporting group title	Part 3 QBW251 450 mg b.i.d. C2
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Reporting group description:

Part 3 QBW251 450 mg b.i.d. C2

Reporting group title	Part 2 QBW251 450 mg bid
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Reporting group description:

Part 2 QBW251 450 mg bid

Reporting group title	Part 2 QBW251 750 mg bid
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Reporting group description:

Part 2 QBW251 750 mg bid

Reporting group title	Part 3 QBW251 450 mg b.i.d. C3
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Reporting group description:

Part 3 QBW251 450 mg b.i.d. C3

Serious adverse events	Part 1 QBW251 150 mg	Part 1 Placebo	Part 1 QBW251 25 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1 QBW251 10 mg	Part 1 QBW251 750 mg	Part 1 QBW251 1000 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1 QBW251 500 mg	Part 1 QBW251 500 mg (fed)	Part 1 QBW251 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 QBW251 150 mg	Part 2 QBW251 400 mg	Part 2 QBW251 750 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2 Placebo	Part 3 Placebo C1/C2/C3	Part 3 QBW251 150 mg b.i.d. C1
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 3 QBW251 450 mg b.i.d. C2	Part 2 QBW251 450 mg bid	Part 2 QBW251 750 mg bid
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 3 QBW251 450 mg b.i.d. C3		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part 1 QBW251 150 mg	Part 1 Placebo	Part 1 QBW251 25 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	8 / 16 (50.00%)	2 / 6 (33.33%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tonsillar disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Adenovirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	1 / 6 (16.67%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	3 / 16 (18.75%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 16 (12.50%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gingival disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary gland pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heat rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Photosensitivity reaction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus generalised subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1	0 / 6 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Rash pruritic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0	1 / 6 (16.67%) 1
Joint swelling			

subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1 QBW251 10 mg	Part 1 QBW251 750 mg	Part 1 QBW251 1000 mg
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	4 / 6 (66.67%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tonsillar disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Investigations			
Adenovirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Hyperaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Salivary gland pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders			
Erythema subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Heat rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Photosensitivity reaction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus generalised subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash pruritic subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Urticaria			

subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin d deficiency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Part 1 QBW251 500 mg	Part 1 QBW251 500 mg (fed)	Part 1 QBW251 300 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	2 / 6 (33.33%)
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Fatigue subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0

Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tonsillar disorder			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Adenovirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Skin wound subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Congenital, familial and genetic disorders Ichthyosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 5 (0.00%) 0	1 / 6 (16.67%) 1
Hyperaesthesia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Tremor			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary gland pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heat rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Pruritus generalised subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Rash pruritic subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Glycosuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Joint swelling subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 5 (20.00%) 1	0 / 6 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Pharyngitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin d deficiency subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 5 (0.00%) 0	0 / 6 (0.00%) 0

Non-serious adverse events	Part 2 QBW251 150 mg	Part 2 QBW251 400 mg	Part 2 QBW251 750 mg
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 6 (50.00%)	6 / 6 (100.00%)	3 / 6 (50.00%)
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Bronchial obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Painful respiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Sinus congestion subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Sneezing subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Sputum increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Throat irritation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Tonsillar disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Stress subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Investigations			
Adenovirus test positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood potassium decreased			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Breath sounds abnormal subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Coronavirus test positive subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin wound subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Congenital, familial and genetic disorders Ichthyosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0

Hyperaesthesia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Abdominal pain lower			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Aphthous stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Saliva altered			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary gland pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Heat rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2 Placebo	Part 3 Placebo C1/C2/C3	Part 3 QBW251 150 mg b.i.d. C1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	8 / 12 (66.67%)	5 / 6 (83.33%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thirst			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Painful respiration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 10 (0.00%)	2 / 12 (16.67%)	3 / 6 (50.00%)
occurrences (all)	0	2	3
Throat irritation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tonsillar disorder			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Insomnia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Stress			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Adenovirus test positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Coronavirus test positive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin wound			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 10 (40.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	4	0	1
Hyperaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tinnitus			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	2 / 10 (20.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gingival disorder			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Saliva altered			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary gland pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heat rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash pruritic			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	0 / 10 (0.00%)	3 / 12 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 12 (8.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	0 / 10 (0.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 12 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sinusitis			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin d deficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0

Non-serious adverse events	Part 3 QBW251 450 mg b.i.d. C2	Part 2 QBW251 450 mg bid	Part 2 QBW251 750 mg bid
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 12 (66.67%)	6 / 6 (100.00%)	4 / 6 (66.67%)
Vascular disorders			
Hot flush subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Fatigue			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Sensation of foreign body			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	1 / 12 (8.33%)	4 / 6 (66.67%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Epistaxis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Painful respiration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sputum increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat irritation			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tonsillar disorder subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Stress subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Investigations			
Adenovirus test positive subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood potassium decreased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Breath sounds abnormal subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Coronavirus test positive subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			

Arthropod bite subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin wound subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Congenital, familial and genetic disorders Ichthyosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4	1 / 6 (16.67%) 1	2 / 6 (33.33%) 2
Hyperaesthesia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Syncope subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ear and labyrinth disorders			
Ear discomfort subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Ear pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Aphthous stomatitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Faeces discoloured			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 12 (8.33%)	4 / 6 (66.67%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gingival disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 12 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Saliva altered			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Salivary gland pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heat rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infective pulmonary exacerbation of cystic fibrosis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vitamin d deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 3 QBW251 450 mg b.i.d. C3		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)		
Vascular disorders			

Hot flush			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Influenza like illness			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Peripheral swelling			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sensation of foreign body			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Thirst			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Vessel puncture site bruise			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	5		
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Haemoptysis			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Nasal discomfort			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Painful respiration			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Pulmonary congestion			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Sinus congestion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sneezing			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sputum increased			
subjects affected / exposed	5 / 19 (26.32%)		
occurrences (all)	5		
Throat irritation			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Tonsillar disorder			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Stress			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Investigations			
Adenovirus test positive			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Breath sounds abnormal			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Coronavirus test positive			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Skin wound			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		

Dizziness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	6		
Hyperaesthesia			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Abdominal distension			

subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Abdominal pain lower			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Aphthous stomatitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Faeces discoloured			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Gingival disorder			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Saliva altered			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Salivary gland pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Vomiting			

subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Heat rash			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Photosensitivity reaction			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Pruritus generalised			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Rash erythematous			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Chromaturia			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Glycosuria			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Proteinuria			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Infective pulmonary exacerbation of cystic fibrosis			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypoglycaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Vitamin d deficiency			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2012	<p>The purpose of this amendment was to respond to the MHRA response received on 07-Jun-2012 regarding 'Discontinuation of study treatment and premature subject withdrawal', which states the following: Discontinuation of study treatment and subject withdrawal was at the discretion of the Investigator, under the following circumstances:</p> <ul style="list-style-type: none">• An SAE that was suspected of being related to study drug• An AE which was severe (Grade 3 or greater) and suspected of being related to study drug <p>MHRA stated the above was unacceptable; if either of the situation under 2 bullets occurred the subject was required to be discontinued from the study medication. Minor typographical errors have been addressed throughout the protocol</p>
10 October 2012	<p>The purpose of this amendment was to address discrepancies in the assessment schedule with the urine and blood logs in addition to minor clarifications for Parts 1 and Parts 2.</p>
17 July 2013	<p>The rationale for this amendment was based on the preliminary PK data from the food effect study performed in Part 1, which demonstrated an approximate 21% and 43% reduction in total (AUCinf) and maximal (Cmax) systemic exposure to QBW251, respectively, as compared to the fasted stated. Having demonstrated the impact of food on the PK of QBW251, it was recognized the need to modify protocol language to allow for dose and dosing frequency under food effect conditions to better represent a real-world clinical situation in Parts 2, 3, and 4. Thus this amendment was provided language that was to allow adaptive dose and dosing frequency in order to achieve optimal exposure below the imposed exposure cap.</p>
12 August 2013	<p>Since the last amendment of this protocol two issues have occurred to justify changes, as follows: 1) The protocol underwent review by both the EU and US Cystic Fibrosis networks, and on the basis of these reviews, the protocol was amended to meet their proposed suggestions. 2) New scientific findings now support the rationale for using specific genotypes of CF patients in the current protocol. The new evidence supported that QBW251 would only benefit CF patients that have a mutation in CFTR that allows trafficking of CFTR to the cell membrane (e.g., class III, IV, V, VI CFTR mutations), but require potentiation of the receptor to repair function. On the basis of the above issues, this amendment implemented these changes relevant to Parts 3 and 4 of the protocol related to CF patients. Furthermore, while Part 2 was ongoing per protocol, the study had completed Part 1 of the study</p>

15 April 2014	<p>The purpose of this amendment was to address requests from FDA received on 01Apr 2014 regarding:</p> <ul style="list-style-type: none"> •The maximum clinical exposure (exposure cap) supported by nonclinical data was based on the NOEL in monkeys (i.e., AUC0-24 = 47850 ng.hr/mL) instead of those observed at the rat no-observed-adverse-effect-level (i.e., AUC0-24 = 78850 ng×hr/mL). Healthy Volunteer data demonstrated that the exposure at 450 mg b.i.d. (AUC_{tau}=12,100 ng×hr/mL or AUC0-24 = 24 200 ng×hr/mL), which was the highest dose planned in the study in CF patients, were approximately 2- and 3- fold below the exposures from monkeys and rats, respectively that produced no adverse findings. Based on this data, the highest planned dose in CF patients at 450 mg b.i.d. was still expected to result in exposures less than the new exposure cap of 47 850 ng×hr/mL. •Use of hyperpolarized helium-3 MRI (exploratory objective). This assessment was removed from Part 4 as the 3He MRI methodology is available only at limited number of centers globally. For the type of CF patient population targeted in this protocol, only three 3He MRI centers could potentially be utilized such that the number of subjects receiving the assessment would not be statistically meaningful. Hence this technology was not deployed in this trial. •Dose-escalation stopping rules •Other minor administrative aspects are clarified. <p>A copy of this amended protocol was sent to the IRBs / IECs and Health Authorities for approval prior to implementation</p>
15 September 2014	<p>The purpose of this amendment was to address requests from the Irish Health Authorities regarding the Screening period that was changed from Day –28 to Day –2 to Day –28 to Day –7. This was done in order to minimize risks of early pregnancy by the urine pregnancy test at Baseline (Day –1) in case Screening visit (formal latest start of contraception) was done less than 7 days prior to Baseline (Day –1). The seven days between end of Screening and first study treatment was sufficient for newly started contraception to be effective, and an early pregnancy would not be missed by a negative hCG at baseline visit (Day –1) one day prior to dosing.</p> <p>This amendment also stipulated that patients that were included in Part 3 could not be enrolled in Part 4. At that time, only 28 days of toxicology data was available which was not a sufficient coverage for patients to participate in both, Parts 3 and 4 (total 6 weeks duration).</p> <p>The assessment of effect of QBW251 on height was removed from the exploratory objective.</p> <p>The effect of QBW251 was evaluated on weight and BMI only as we don't expect to see a change in height in the short period of the study.</p>

16 February 2015	<p>The purpose of this amendment was to include the assessment of safety, tolerability and efficacy of QBW251 in adult CF patients who are homozygous for the F508del mutation (F508del/F508del). These patients were previously not included in the study due to insufficient pre-clinical data. QBW251 was developed and optimized to potentiate the F508del-CFTR in vitro. Pre-clinical studies had demonstrated that QBW251, as compared to a competitor drug, does not have the same negative effect on cell surface expression and potentiation of human bronchial epithelial cells that express F508del/F508del CFTR (Veit et al 2014 and Cholon et al 2014). In addition, PK studies had showed that QBW251 had an excellent PK profile with lower plasma protein binding and increased free fraction, which supports the notion that a larger proportion of the administered dose may reach the target. Therefore, the inclusion of F508del homozygous patients was based on the rationale that through providing sustained potentiation of F508del-CFTR, QBW251 as monotherapy may provide a clinical benefit to the F508del homozygous patient population without the need to co-administer a corrector to improve surface trafficking of F508del-CFTR. These F508del homozygous patients (n=32) were included in Cohort 3 of Part 3 of the study. Cohort 2 and Cohort 3 of Part 3 of the study were conducted in parallel. In addition to the above rationale for this amendment, this amendment increased the age range for inclusion in Part 3 for Cohort 2 and Cohort 3 from 18 - 55 years to 18 - 65 years. Based on good safety/tolerability profile in 18-55 year olds, and because there was no mechanistic reason to expect a different safety profile in individuals between 55 - 65 years, the upper age limit had been increased to 65 years.</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 November 2015	An interim analysis was conducted during Part 3 of the study, which demonstrated evidence of efficacy in Cohorts 1 and 2, but futility in cohort 3; hence the study was terminated in Nov 2015 before Cohort 3 was completed.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com/CtrdWeb/home.novfor> complete trial results.

Notes:

