Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Clinical Study to Evaluate the Efficacy and Safety of Oral Inhalation of GB002 for the Treatment of WHO Group 1 Pulmonary Arterial Hypertension (PAH)

Summary

EudraCT number	2019-002669-37
Trial protocol	GB FR DE AT CZ BE
Global end of trial date	01 November 2022

Results information

Result version number	v1 (current)
This version publication date	10 November 2023
First version publication date	10 November 2023

Trial information

Trial identification

Sponsor protocol code	GB002-2101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04456998
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GB002 Inc., a wholly owned subsidiary of Gossamer Bio, Inc.
Sponsor organisation address	3013 Science Park Road, San Diego, United States, 92121
Public contact	Study Director, GB002, Inc., wholly owned subsidiary of Gossamer Bio Inc., GB002, Inc., +1 866 668-4083, ClinicalTrials@gossamerbio.com
Scientific contact	Study Director, GB002, Inc., wholly owned subsidiary of Gossamer Bio Inc., GB002, Inc., +1 866 668-4083, ClinicalTrials@gossamerbio.com

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 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine the effect of GB002 on improving pulmonary hemodynamics in subjects with World Health Organization (WHO) Group 1 PAH who are WHO Functional Class (FC) II or III

Protection of trial subjects:

This study was conducted in accordance with consensus ethical principles derived from international guidelines including the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines and International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All applicable local laws and regulations regarding patient safety were also followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2020
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	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	United States: 59
Worldwide total number of subjects	86
EEA total number of subjects	20

Notes:

Subjects enrolled per age group

In utero	0
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)	73
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After signing an informed consent form (ICF), subjects were screened for study eligibility for up to a 5-week screening period. 151 participants were screened, 86 of whom were randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo inhaled orally twice per day (BID) for 24 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo inhaled orally BID for 24 weeks

Arm title	GB002 (Seralutinib)

Arm description:

GB002 (seralutinib) inhaled orally BID for 24 weeks

Arm type	Experimental
Investigational medicinal product name	GB002
Investigational medicinal product code	GB002
Other name	Seralutinib
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

GB002 (seralutinib) inhaled orally BID for 24 weeks

Number of subjects in period 1	Placebo	GB002 (Seralutinib)
Started	42	44
Completed	42	38
Not completed	0	6
Adverse event	-	4

Protocol deviation	-	1
Withdrawal by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo inhaled orally twice per day (BID) for 24 weeks	
Reporting group title	GB002 (Seralutinib)
Reporting group description:	
GB002 (seralutinib) inhaled orally BID for 24 weeks	

Reporting group values	Placebo	GB002 (Seralutinib)	Total
Number of subjects	42	44	86
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	49.5	48.3	
standard deviation	± 11.81	± 12.70	-
Gender categorical Units: Subjects			
Female	38	40	78
Male	4	4	8
Race Units: Subjects			
White	37	37	74
Black or African American	1	0	1
Asian	2	4	6
Other, Not Specified	2	3	5
Ethnicity Units: Subjects			
Hispanic or Latino	6	8	14
Not Hispanic or Latino	34	36	70
Not Reported	2	0	2

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo inhaled orally twice per day (BID) for 24 weeks	
Reporting group title	GB002 (Seralutinib)
Reporting group description: GB002 (seralutinib) inhaled orally BID for 24 weeks	

Primary: Change From Baseline to Week 24 in Pulmonary Vascular Resistance (PVR)

End point title	Change From Baseline to Week 24 in Pulmonary Vascular Resistance (PVR)
End point description: PVR was evaluated using right heart catheterization (RHC). Intent-to-Treat (ITT) Population: all participants who were randomized.	
End point type	Primary
End point timeframe: Baseline, Week 24	

End point values	Placebo	GB002 (Seralutinib)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	44		
Units: dyne•s/cm^5				
least squares mean (confidence interval 95%)	21.2 (-37.4 to 79.8)	-74.9 (-139.7 to -10.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GB002 (Seralutinib)
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-96.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-183.5
upper limit	-8.8

Secondary: Change From Baseline to Week 24 in Distance Achieved on the Six-Minute Walk Test (6MWT)

End point title	Change From Baseline to Week 24 in Distance Achieved on the Six-Minute Walk Test (6MWT)

End point description:

The 6MWT measures the distance a subject is able to walk quickly on a flat, hard surface in a period of 6 minutes.

ITT Population: all participants who were randomized. Participants with a baseline and post-baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	GB002 (Seralutinib)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	38		
Units: meters				
least squares mean (confidence interval 95%)	7.4 (-11.2 to 25.9)	13.9 (-5.1 to 32.8)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v GB002 (Seralutinib)
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5972
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	30.9

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug through Week 28	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo inhaled orally twice per day (BID) for 24 weeks	
Reporting group title	GB002 (Seralutinib)
Reporting group description:	
GB002 (seralutinib) inhaled orally BID for 24 weeks	

Serious adverse events	Placebo	GB002 (Seralutinib)	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 42 (14.29%)	10 / 44 (22.73%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			

subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Right ventricular failure			
subjects affected / exposed	3 / 42 (7.14%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
subjects affected / exposed	0 / 42 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	GB002 (Seralutinib)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 42 (66.67%)	31 / 44 (70.45%)	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 42 (19.05%)	6 / 44 (13.64%)	
occurrences (all)	12	7	
Dizziness			
subjects affected / exposed	2 / 42 (4.76%)	5 / 44 (11.36%)	
occurrences (all)	2	7	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 42 (7.14%)	5 / 44 (11.36%)	
occurrences (all)	3	5	
Chest discomfort			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 42 (7.14%)	6 / 44 (13.64%)	
occurrences (all)	3	6	
Nausea			
subjects affected / exposed	6 / 42 (14.29%)	5 / 44 (11.36%)	
occurrences (all)	6	5	
Abdominal pain lower			
subjects affected / exposed	0 / 42 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	3 / 42 (7.14%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 42 (38.10%)	19 / 44 (43.18%)	
occurrences (all)	16	19	
Dyspnoea			

subjects affected / exposed	4 / 42 (9.52%)	4 / 44 (9.09%)	
occurrences (all)	4	5	
Nasal congestion			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Throat irritation			
subjects affected / exposed	0 / 42 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	3	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	
occurrences (all)	1	4	
Psychiatric disorders			
Nightmare			
subjects affected / exposed	1 / 42 (2.38%)	4 / 44 (9.09%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Back pain			
subjects affected / exposed	2 / 42 (4.76%)	3 / 44 (6.82%)	
occurrences (all)	2	3	
Pain in extremity			
subjects affected / exposed	3 / 42 (7.14%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 42 (16.67%)	6 / 44 (13.64%)	
occurrences (all)	7	6	
Nasopharyngitis			
subjects affected / exposed	0 / 42 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	3 / 42 (7.14%)	1 / 44 (2.27%)	
occurrences (all)	3	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2020	• Updated seralutinib dose from 90 mg to 60 mg to reduce capsule burden. • Updated visit schedule to occur every 6 weeks (instead of 4 weeks), increased visit windows, changed Week 8 visit to telephone contact, and clarified home-health visit options to reduce patient burden. • Added dispensation and collection of an electronic handheld device to record daily dosing. • Updated inclusion criterion to remove rheumatoid arthritis as a PAH-associated disease. • Expanded exclusion criterion to exclude subjects with a condition limiting 6MWT assessment. • Clarified male fertility assessment was optional, required 36 weeks of study participation. • Added language related to photosafety to match language in Version 5 of the Investigator's Brochure and to align with a United Kingdom specific amendment.
15 January 2021	• Version 3.0.1 was issued to correct a typographical error in v3.0.0. Protocol v3.0.1 replaced v3.0.0 and no patients were enrolled under v3.0.0. • Updated seralutinib dose from 60 mg to up to 90 mg (dose range of 45 mg to 90 mg BID) based on on-going safety in Phase 1 studies and projected efficacious exposure range. • Updated visit schedule to occur every 4 weeks through Week 12 for adverse event (AE) monitoring. • Added monthly pregnancy testing for Women of childbearing potential (WOCBP) at-home testing when visits were less frequent. • Added clarification that morning doses of oral PAH disease-specific background medications should be taken immediately prior to GB002 dosing in clinic on pharmacokinetic (PK) sampling days. • Added functional respiratory imaging and heart rate monitoring substudies at select sites. • Updated risk language to include embryo-fetal development as an identified risk. • Reduced maximum age inclusion criterion from 80 years of age to 75 years. • Reduced Left ventricular-end diastolic pressure (LVEDP) inclusion criterion from ≤ 15 mmHg to ≤ 12 mmHg. • Updated to indicate that if historical echocardiogram (ECHO) not available, screening ECHO may be used to establish this criterion. Expanded exclusion criterion to exclude subjects with left-sided heart disease. • Updated exclusion criteria to exclude subjects with documented uncontrolled symptomatic coronary disease and portopulmonary hypertension or Child-Pugh Class A or higher. • Expanded estimated glomerular filtration rate (eGFR) exclusion criterion from < 30 mL/min/1.73m^2 to < 45 mL/min/1.73m^2, including subjects with mild-moderate renal function impairment.

15 January 2021	(continued) • Updated exclusion criteria to exclude inhaled marijuana product use, subjects with history of alcohol abuse and/or a positive test for drugs of abuse, subjects with milk allergy, and subjects that have any other condition or reason that (in the opinion of the Investigator or Sponsor's Medical Monitor) would prohibit study participation. • Added stopping rules and in investigational product (IP) interruption instructions for fluid retention, neutropenia, thrombocytopenia, and electrocardiogram (ECG) abnormalities. • Added criteria for clinical worsening and updated exploratory endpoint. • Updated prohibited medications to prohibit use of medications associated with QT interval prolongation, as a cautionary measure, and added exclusionary criterion for subjects with QT corrected for heart rate by Fridericia's cube root formula (QTcF) > 480 ms. • Increased window for Week 24 RHC to up to 8 weeks beyond the Week 24 visit for subjects remaining on IP, to allow for impact of pandemic/global emergencies. • Clarified that an open-label extension study was available. A 28-day safety follow up will not be required for subjects transitioning to OLE. • Added subjects were encouraged to weigh themselves at home as part of standard of care in order to monitor for lower extremity edema. • Updated biomarker collection schedule to remove assays.
18 November 2021	• Updated prohibited medications due to new data indicating seralutinib was not expected to have clinically significant drug-drug interactions with medications which are inhibitors of P-glycoprotein, Breast Cancer Resistance Protein, or moderate or weak cytochrome P450 isoform 3A inhibitors. • Updated prohibited medications to clarify strong cytochrome P450 isoform 3A inhibitors and washout instructions for anticoagulants. • Updated risk language to include potential risk of female reproductive organs based on nonclinical data and potential risk of bleeding to include hemoptysis. • Updated AE assessments to include review of all system organ classes (SOCs), including reproductive system. • Added clarification for the definition of Worsening Risk Score Category. • Expanded inclusion criterion to include categories of connective tissue disease-associated pulmonary arterial hypertension (CTD-APAH). • Updated inclusion criterion for pulmonary function test (PFTs) to be more informative of disease state. • Clarified exclusion criterion to note portal hypertension due to cirrhosis. • Updated exclusion criterion for alcohol use to align with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) definition. • Removed collection of nasal mucosal fluid samples (protocol clarification letter 12APR2021); based on standard laboratory practices, added assessment of urate and activated partial thromboplastin time (APTT). • Replace measure of forced expiratory volume in 1 second (FEV1) with ratio of FEV1 to forced vital capacity (FVC). Replace requirement for carbon monoxide diffusing capacity (DLCO) with FVC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported