Clinical trial results:
A Phase 2a, randomized, double-blind, placebo-controlled, multi-center study to evaluate the effect of GB001 in patients with chronic rhinosinusitis with or without nasal polyps

Summary

EudraCT number	2019-001682-33
Trial protocol	CZ
Global end of trial date	05 August 2020

Results information

Result version number	v1 (current)
This version publication date	27 August 2021
First version publication date	27 August 2021

Trial information

Trial identification

Sponsor protocol code	GB001-2101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03956862
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GB001 Inc., a wholly owned subsidiary of Gossamer Bio, Inc.
Sponsor organisation address	3013 Science Park Road, San Diego, United States, 92121
Public contact	GB001, Inc. Study Director, GB001, Inc., wholly owned subsidiary of Gossamer Bio Inc., 866 668-4083, ClinicalTrials@gossamerbio.com
Scientific contact	GB001, Inc. Study Director, GB001, Inc., wholly owned subsidiary of Gossamer Bio Inc., 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	05 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 July 2020
Global end of trial reached?	Yes
Global end of trial date	05 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To evaluate the effect of GB001 on the Sino-Nasal Outcome Test-22 (SNOT-22)

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	16 May 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Ukraine: 42
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	97
EEA total number of subjects	7

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)	88
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the Czechia, Ukraine, and United States.

Pre-assignment

Screening details:

The study included a run-in period, during which eligibility for randomization was determined. 192 participants entered the run-in period, 97 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 QD for 16 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo QD for 16 weeks

Arm title	GB001

Arm description:

GB001 40 mg QD for 16 weeks

Arm type	Experimental
Investigational medicinal product name	GB001
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

GB001 40 mg QD for 16 weeks

Number of subjects in period 1	Placebo	GB001
Started	50	47
Completed	48	45
Not completed	2	2
Consent withdrawn by subject	1	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo QD for 16 weeks	

Reporting group title	GB001
Reporting group description:	
GB001 40 mg QD for 16 weeks	

Reporting group values	Placebo	GB001	Total
Number of subjects	50	47	97
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.6	51.7	
standard deviation	± 10.34	± 11.81	-
Gender categorical Units: Subjects			
Female	21	28	49
Male	29	19	48

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo QD for 16 weeks	

Reporting group title	GB001
Reporting group description: GB001 40 mg QD for 16 weeks	

Primary: Change From Baseline to Week 16 in Sino-Nasal Outcome Test (SNOT) 22 Total Score

End point title	Change From Baseline to Week 16 in Sino-Nasal Outcome Test (SNOT) 22 Total Score

End point description:

The SNOT-22 is a validated questionnaire to assess the impact of chronic rhinosinusitis (CRS) on quality of life and utilizes a 2-week recall period. It is a 22-item outcome measure on a 5-point category scale applicable to sinonasal conditions and surgical treatments. The total scores range from 0 to 110 with higher total scores implying greater impact of CRS on quality of life.

Analysis Population Description
Intent-to-treat (ITT) population: all participants who were randomized and received at least 1 dose of study treatment. Participants with a baseline and a post-baseline value.

End point type	Primary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	45		
Units: score on a scale				
least squares mean (confidence interval 95%)	-18.1 (-23.1 to -13.0)	-18.3 (-23.5 to -13.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9499
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	7.1

Secondary: Change From Baseline to Week 16 in Lund-Mackay Score

End point title	Change From Baseline to Week 16 in Lund-Mackay Score

End point description:

Lund-Mackay scores are based on centralized imaging data assessments and are scored by blinded central reading at the imaging core laboratory. The Lund-Mackay system is based on localization with points given for degree of opacification: 0=normal, 1=partial opacification, 2=total opacification. These points are then applied to each sinus (maxillary, anterior ethmoid, posterior ethmoid, sphenoid, and frontal sinus) on each side. The osteomeatal complex on each side is graded as 0=not occluded, or 2=occluded. The maximum score is 12 per side, for a total score ranging from 0 to 24.

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	47		
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.6 (-1.6 to 0.4)	-0.9 (-2.0 to 0.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6778
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.2

Secondary: Change From Baseline to Week 16 in Nasal Polyp Score (NPS)

End point title	Change From Baseline to Week 16 in Nasal Polyp Score (NPS)

End point description:

The bilateral endoscopic NPS is the sum of the right and left nostril scores, as evaluated by means of blinded, centrally read nasal endoscopy and ranges from 0 to 8. NP is graded based on polyp size: 0 = No polyps, 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate, 2 = Polyps reaching below the lower border of the middle turbinate, 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate, and 4 = Large polyps causing complete obstruction of the inferior nasal cavity.

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment. Participants with nasal polyps with a baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	30		
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.8 (-1.4 to -0.3)	-0.7 (-1.3 to -0.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7914
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.9

Secondary: Time to First Response in NPS

End point title	Time to First Response in NPS

End point description:

Response was defined as ≥ 1-point improvement from baseline. The bilateral endoscopic NPS is the sum of the right and left nostril scores, as evaluated by means of blinded, centrally read nasal endoscopy and ranges from 0-8. NP is graded based on polyp size: 0 = No polyps, 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle turbinate, 2 = Polyps reaching below the lower border of the middle turbinate, 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate, and 4 = Large polyps causing complete obstruction of the inferior nasal cavity.

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment. Participants with nasal polyps.

'99999' indicates the value is not estimable due to an insufficient number of observed events.

End point type	Secondary

End point timeframe:

up to Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	32		
Units: weeks				
median (confidence interval 95%)	16.43 (8.571 to 99999)	16.14 (8.143 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8916
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.944
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	2.173

Secondary: Change From Baseline to Week 16 in Morning (AM) Nasal Congestion (NC) Score

End point title	Change From Baseline to Week 16 in Morning (AM) Nasal Congestion (NC) Score

End point description:

AM NC score was assessed using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild

symptoms, 2 = moderate symptoms and 3 = severe symptoms).

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment. Participants with a baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	46		
Units: score on a scale				
least squares mean (confidence interval 95%)	-0.733 (-0.917 to -0.549)	-0.543 (-0.738 to -0.347)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1635
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.191
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.077
upper limit	0.459

Secondary: Change From Baseline to Week 16 in AM Total Symptom Score (TSS)

End point title	Change From Baseline to Week 16 in AM Total Symptom Score (TSS)

End point description:

AM TSS is the sum of the scores from the 4 AM symptom categories (congestion and/or obstruction, anterior rhinorrhea, posterior rhinorrhea, loss of sense of smell) and ranges from 0–12. Each symptom category was assessed using a 0 to 3 categorical scale (where 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms).

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment. Participants with a baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	46		
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.499 (-3.130 to -1.869)	-1.867 (-2.526 to -1.209)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1742
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.632
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	1.544

Secondary: Change From Baseline to Week 16 in University of Pennsylvania Smell Identification Test (UPSIT) Score

End point title	Change From Baseline to Week 16 in University of Pennsylvania Smell Identification Test (UPSIT) Score

End point description:

The UPSIT test consists of four booklets, each containing 10 odorants with one odorant per page. The test-time is about 15 minutes. The stimuli are embedded in 10–50 µm diameter plastic microcapsules on brown strips at the bottom of each page. Above each odorant strip is a multiple-choice question with four alternative words to describe the odor. The participant is asked to release the odorant by rubbing the brown-strip with the tip of a pencil and to indicate which of 4 words best describes the odor. An UPSIT result is scored from 0 to 40 where a higher score indicates better olfaction.

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment. Participants with a baseline value.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	47		
Units: score on a scale				
least squares mean (confidence interval 95%)	1.5 (-0.3 to 3.2)	2.3 (0.5 to 4.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4851
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	3.4

Secondary: Time to First Chronic Rhinosinusitis (CRS) Exacerbation

End point title	Time to First Chronic Rhinosinusitis (CRS) Exacerbation

End point description:

Chronic rhinosinusitis exacerbation is defined as deterioration of CRS symptoms requiring treatment with an antibiotic, an anti-inflammatory drug, or a symptom reliever; an Emergency Department visit; or hospitalization.

Analysis Population Description
ITT population: all participants who were randomized and received at least 1 dose of study treatment.

'-99999' and '99999' indicate the value is not estimable due to an insufficient number of observed events.

End point type	Secondary

End point timeframe:

up to Week 16

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	47		
Units: weeks				
median (confidence interval 95%)	99999 (-99999 to 99999)	99999 (-99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	GB001 v Placebo
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3898
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.544
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.136
upper limit	2.178

Secondary: Incidence of Treatment-Emergent Adverse Events (TEAEs)

End point title	Incidence of Treatment-Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant, whether or not considered related to study drug. Abnormal laboratory test results or other safety assessments, including those that worsened from baseline, that were considered clinically significant in the medical and scientific judgment of the investigator were to be reported as AEs.

Analysis Population Description
Safety Population: all participants who received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose of study drug through Week 20

End point values	Placebo	GB001		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	47		
Units: percentage of participants				
number (not applicable)	36.0	44.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug through Week 20	
Adverse event reporting additional description:	
[Not specified]	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	GB001
Reporting group description: -	

Serious adverse events	Placebo	GB001	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	GB001	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 50 (20.00%)	12 / 47 (25.53%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 50 (6.00%)	5 / 47 (10.64%)	
occurrences (all)	5	5	
Respiratory, thoracic and mediastinal disorders			

Asthma subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	3 / 47 (6.38%) 3	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	3 / 47 (6.38%) 3	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	0 / 47 (0.00%) 0	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	2 / 47 (4.26%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2019	Amendment 1 (v2.0.0)
02 May 2019	Amendment 2 (v2.1)
28 August 2019	Amendment 3 (v3.0)
18 February 2020	Amendment 4 (v4.0)
16 April 2020	Amendment 5 (v5.0)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported