



## 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     |
| <b>Arm title</b>             | 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

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | 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:<br>Placebo inhaled orally twice per day (BID) for 24 weeks |                     |
| Reporting group title   | GB002 (Seralutinib) |
| Reporting group description:<br>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:<br>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:<br>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 <sup>5</sup>                |                      |                         |  |  |
| 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                          |

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

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|                 |   |
|-----------------|---|
| 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

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| 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**

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | 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 %

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



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 18 June 2020    | <ul style="list-style-type: none"><li>• Updated serralutinib dose from 90 mg to 60 mg to reduce capsule burden.</li><li>• 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.</li><li>• Added dispensation and collection of an electronic handheld device to record daily dosing.</li><li>• Updated inclusion criterion to remove rheumatoid arthritis as a PAH-associated disease.</li><li>• Expanded exclusion criterion to exclude subjects with a condition limiting 6MWT assessment.</li><li>• Clarified male fertility assessment was optional, required 36 weeks of study participation.</li><li>• 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.</li></ul>  |
| 15 January 2021 | <ul style="list-style-type: none"><li>• 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.</li><li>• Updated serralutinib 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.</li><li>• Updated visit schedule to occur every 4 weeks through Week 12 for adverse event (AE) monitoring.</li><li>• Added monthly pregnancy testing for Women of childbearing potential (WOCBP) at-home testing when visits were less frequent.</li><li>• 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.</li><li>• Added functional respiratory imaging and heart rate monitoring substudies at select sites.</li><li>• Updated risk language to include embryo-fetal development as an identified risk.</li><li>• Reduced maximum age inclusion criterion from 80 years of age to 75 years.</li><li>• Reduced Left ventricular-end diastolic pressure (LVEDP) inclusion criterion from <math>\leq 15</math> mmHg to <math>\leq 12</math> mmHg.</li><li>• 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.</li><li>• Updated exclusion criteria to exclude subjects with documented uncontrolled symptomatic coronary disease and portopulmonary hypertension or Child-Pugh Class A or higher.</li><li>• Expanded estimated glomerular filtration rate (eGFR) exclusion criterion from <math>&lt; 30</math> mL/min/1.73m<sup>2</sup> to <math>&lt; 45</math> mL/min/1.73m<sup>2</sup>, including subjects with mild-moderate renal function impairment.</li></ul> |

|                  |  |
|------------------|--|
| 15 January 2021  | <p>(continued)</p> <ul style="list-style-type: none"> <li>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.</li> <li>Added stopping rules and in investigational product (IP) interruption instructions for fluid retention, neutropenia, thrombocytopenia, and electrocardiogram (ECG) abnormalities.</li> <li>Added criteria for clinical worsening and updated exploratory endpoint.</li> <li>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) &gt; 480 ms.</li> <li>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.</li> <li>Clarified that an open-label extension study was available. A 28-day safety follow up will not be required for subjects transitioning to OLE.</li> <li>Added subjects were encouraged to weigh themselves at home as part of standard of care in order to monitor for lower extremity edema.</li> <li>Updated biomarker collection schedule to remove assays.</li> </ul>  |
| 18 November 2021 | <ul style="list-style-type: none"> <li>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.</li> <li>Updated prohibited medications to clarify strong cytochrome P450 isoform 3A inhibitors and washout instructions for anticoagulants.</li> <li>Updated risk language to include potential risk of female reproductive organs based on nonclinical data and potential risk of bleeding to include hemoptysis.</li> <li>Updated AE assessments to include review of all system organ classes (SOCs), including reproductive system.</li> <li>Added clarification for the definition of Worsening Risk Score Category.</li> <li>Expanded inclusion criterion to include categories of connective tissue disease-associated pulmonary arterial hypertension (CTD-APAH).</li> <li>Updated inclusion criterion for pulmonary function test (PFTs) to be more informative of disease state.</li> <li>Clarified exclusion criterion to note portal hypertension due to cirrhosis.</li> <li>Updated exclusion criterion for alcohol use to align with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) definition.</li> <li>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).</li> <li>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.</li> </ul> |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported