



## Clinical trial results:

### A Phase 2b, Randomized, Controlled Trial Evaluating GS-5806 in Lung Transplant (LT) Recipients with Respiratory Syncytial Virus (RSV) Infection

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-002287-16    |
| Trial protocol           | BE GB AT NL       |
| Global end of trial date | 27 September 2017 |

#### Results information

|                                |                                                                                                                                        |
|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Result version number          | v3 (current)                                                                                                                           |
| This version publication date  | 18 May 2019                                                                                                                            |
| First version publication date | 04 October 2018                                                                                                                        |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>Adding text to "Limitations and Caveats" section</li></ul> |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-218-1797 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02534350 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                               |
|------------------------------|-----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Gilead Sciences                                                                               |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404                                     |
| Public contact               | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.com |
| Scientific contact           | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.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                       | 27 September 2017 |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 20 February 2017  |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 27 September 2017 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of presatovir on nasal respiratory syncytial virus (RSV) viral load in RSV-positive lung transplant (LT) recipients with acute respiratory symptoms.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 31 December 2015 |
| 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 | Netherlands: 1    |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Belgium: 4        |
| Country: Number of subjects enrolled | France: 2         |
| Country: Number of subjects enrolled | Germany: 11       |
| Country: Number of subjects enrolled | United States: 38 |
| Country: Number of subjects enrolled | Australia: 3      |
| Country: Number of subjects enrolled | Canada: 1         |
| Worldwide total number of subjects   | 61                |
| EEA total number of subjects         | 19                |

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)                      | 41 |
| From 65 to 84 years                       | 20 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at sites in Europe, North America and Australia. The first participant was screened on 31 December 2015 and the last study visit occurred on 27 September 2017.

### Pre-assignment

Screening details:

111 participants were screened.

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

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

Arm description:

Administered orally or via nasogastric (NG) tube once daily for 14 days

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Experimental               |
| Investigational medicinal product name | Presatovir                 |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Nasogastric use , Oral use |

Dosage and administration details:

200 mg (4 x 50 mg) on Day1/Baseline followed by 100 mg (2 x 50 mg) on Days 2 through 14

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

Arm description:

Tablets administered orally or via NG tube once daily for 14 days

|                                        |                            |
|----------------------------------------|----------------------------|
| Arm type                               | Placebo                    |
| Investigational medicinal product name | Placebo                    |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Nasogastric use , Oral use |

Dosage and administration details:

Administered orally or via NG tube once daily for 14 days

| Number of subjects in period<br>1 <sup>[1]</sup> | Presatovir | Placebo |
|--------------------------------------------------|------------|---------|
|                                                  |            |         |
| Started                                          | 40         | 20      |
| Completed                                        | 37         | 20      |
| Not completed                                    | 3          | 0       |
| Withdrew Consent                                 | 2          | -       |
| Protocol deviation                               | 1          | -       |

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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: 1 participant who was randomized but not treated was not included.

## Baseline characteristics

### Reporting groups

|                                                                         |            |
|-------------------------------------------------------------------------|------------|
| Reporting group title                                                   | Presatovir |
| Reporting group description:                                            |            |
| Administered orally or via nasogastric (NG) tube once daily for 14 days |            |
| Reporting group title                                                   | Placebo    |
| Reporting group description:                                            |            |
| Tablets administered orally or via NG tube once daily for 14 days       |            |

| Reporting group values | Presatovir | Placebo | Total |
|------------------------|------------|---------|-------|
| Number of subjects     | 40         | 20      | 60    |
| Age categorical        |            |         |       |
| Units: Subjects        |            |         |       |

|                                     |         |         |    |
|-------------------------------------|---------|---------|----|
| Age continuous                      |         |         |    |
| Units: years                        |         |         |    |
| arithmetic mean                     | 56.4    | 55.1    |    |
| standard deviation                  | ± 12.54 | ± 14.23 | -  |
| Gender categorical                  |         |         |    |
| Units: Subjects                     |         |         |    |
| Female                              | 19      | 10      | 29 |
| Male                                | 21      | 10      | 31 |
| Ethnicity                           |         |         |    |
| Units: Subjects                     |         |         |    |
| Hispanic or Latino                  | 2       | 1       | 3  |
| Not Hispanic or Latino              | 36      | 19      | 55 |
| Unknown or Not Reported             | 2       | 0       | 2  |
| Race                                |         |         |    |
| Units: Subjects                     |         |         |    |
| Asian                               | 0       | 1       | 1  |
| Black or African American           | 0       | 2       | 2  |
| Native Hawaiian or Pacific Islander | 1       | 0       | 1  |
| White                               | 36      | 16      | 52 |
| Other                               | 1       | 1       | 2  |
| Not Permitted                       | 2       | 0       | 2  |

|                  |  |  |  |
|------------------|--|--|--|
| Nasal Viral Load |  |  |  |
|------------------|--|--|--|

Measure Analysis Population Description: Participants in the Safety Analysis Set with available data were analyzed (Presatovir: N = 37; Placebo: N = 20).

|                        |         |         |   |
|------------------------|---------|---------|---|
| Units: log10 copies/mL |         |         |   |
| arithmetic mean        | 5.88    | 6.59    |   |
| standard deviation     | ± 2.088 | ± 2.092 | - |

|                                                     |  |  |  |
|-----------------------------------------------------|--|--|--|
| inFLUenza Patient- Reported Outcome (FLU-PRO) Score |  |  |  |
|-----------------------------------------------------|--|--|--|

Participants in the Safety Analysis Set with available data were analyzed (Presatovir: N = 37; Placebo: N = 18). Flu-PRO Score was calculated as the mean of 38 individual scores. Individual scores ranged from 0 (no symptoms) to 4 (worst symptoms) for the 5-point severity scale and 0 (never) to 4 or more times (always) for the 5-point frequency scale.

|                         |      |      |  |
|-------------------------|------|------|--|
| Units: units on a scale |      |      |  |
| arithmetic mean         | 2.05 | 2.11 |  |

|                                                                                                                                                           |          |          |   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----------|---|
| standard deviation                                                                                                                                        | ± 0.607  | ± 0.684  | - |
| The Forced Expiratory Volume in One Second (FEV1) % Predicted                                                                                             |          |          |   |
| Measure Analysis Population Description: Participants in the Safety Analysis Set with available data were analyzed (Presatovir: N = 40; Placebo: N = 19). |          |          |   |
| Units: percent FEV1                                                                                                                                       |          |          |   |
| arithmetic mean                                                                                                                                           | 63.64    | 61.95    |   |
| standard deviation                                                                                                                                        | ± 24.787 | ± 18.625 | - |

## End points

### End points reporting groups

|                                                                         |            |
|-------------------------------------------------------------------------|------------|
| Reporting group title                                                   | Presatovir |
| Reporting group description:                                            |            |
| Administered orally or via nasogastric (NG) tube once daily for 14 days |            |
| Reporting group title                                                   | Placebo    |
| Reporting group description:                                            |            |
| Tablets administered orally or via NG tube once daily for 14 days       |            |

### Primary: Time-Weighted Average Change in Viral Load From Day 1/Baseline Through Day 7 in Participants in the Full Analysis Set

|                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                               | Time-Weighted Average Change in Viral Load From Day 1/Baseline Through Day 7 in Participants in the Full Analysis Set |
| End point description:                                                                                                                                                                                                                                                                                                                                        |                                                                                                                       |
| Participants in the Full Analysis Set (participants who received at least 1 full dose of study drug and had an RSV viral load $\geq$ lower limit of quantification (LLOQ) of the real-time quantitative polymerase chain reaction (RT-qPCR) assay in the Day 1 nasal sample, as determined by RT-qPCR at the central lab) with available data were analyzed . |                                                                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                                                | Primary                                                                                                               |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                          |                                                                                                                       |
| Up to 7 days                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                       |

| End point values                     | Presatovir           | Placebo              |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 35                   | 19                   |  |  |
| Units: log10 copies/mL               |                      |                      |  |  |
| arithmetic mean (standard deviation) | -0.73 ( $\pm$ 0.938) | -0.90 ( $\pm$ 0.815) |  |  |

### Statistical analyses

|                                         |                        |
|-----------------------------------------|------------------------|
| Statistical analysis title              | Presatovir vs. Placebo |
| Comparison groups                       | Presatovir v Placebo   |
| Number of subjects included in analysis | 54                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.72                 |
| Method                                  | ANCOVA                 |
| Parameter estimate                      | Treatment Difference   |
| Point estimate                          | 0.1                    |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.43   |
| upper limit         | 0.63    |

**Primary: Time-Weighted Average Change in Viral Load From Day 1/Baseline Through Day 7 in a Subset of Participants in the Full Analysis Set Whose Duration of RSV Symptoms Prior to the First Dose of Study Drug is ≤ Median**

|                 |                                                                                                                                                                                                                    |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Time-Weighted Average Change in Viral Load From Day 1/Baseline Through Day 7 in a Subset of Participants in the Full Analysis Set Whose Duration of RSV Symptoms Prior to the First Dose of Study Drug is ≤ Median |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Participants in the Full Analysis Set with available data were analyzed.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 7 days

| End point values                     | Presatovir      | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 16              | 11              |  |  |
| Units: log10 copies/mL               |                 |                 |  |  |
| arithmetic mean (standard deviation) | -0.83 (± 1.013) | -0.83 (± 0.757) |  |  |

**Statistical analyses**

|                                         |                        |
|-----------------------------------------|------------------------|
| <b>Statistical analysis title</b>       | Presatovir vs. Placebo |
| Comparison groups                       | Presatovir v Placebo   |
| Number of subjects included in analysis | 27                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.76                 |
| Method                                  | ANCOVA                 |
| Parameter estimate                      | Treatment Difference   |
| Point estimate                          | -0.12                  |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -0.94                  |
| upper limit                             | 0.69                   |

**Secondary: Time-Weighted Average Change in FLU-PRO Score From Day 1/Baseline Through Day 7**

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Time-Weighted Average Change in FLU-PRO Score From Day 1/Baseline Through Day 7 |
|-----------------|---------------------------------------------------------------------------------|

End point description:

The Flu-PRO is a patient-reported outcome questionnaire utilized as a standardized method for evaluating symptoms of influenza. Flu-PRO Score was calculated as the mean of 38 individual scores. Individual scores ranged from 0 (no symptoms) to 4 (worst symptoms) for the 5-point severity scale and 0 (never) to 4 or more times (always) for the 5-point frequency scale. The mean values presented were calculated using the ANCOVA model and are adjusted for baseline value and stratification factor. Participants in the Full Analysis Set with available data were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 7 days

| End point values                     | Presatovir           | Placebo              |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed          | 33                   | 17                   |  |  |
| Units: units on a scale              |                      |                      |  |  |
| arithmetic mean (standard deviation) | -0.27 ( $\pm$ 0.313) | -0.31 ( $\pm$ 0.298) |  |  |

**Statistical analyses**

|                                         |                        |
|-----------------------------------------|------------------------|
| <b>Statistical analysis title</b>       | Presatovir vs. Placebo |
| Comparison groups                       | Presatovir v Placebo   |
| Number of subjects included in analysis | 50                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.86                 |
| Method                                  | ANCOVA                 |
| Parameter estimate                      | Treatment Difference   |
| Point estimate                          | 0.01                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -0.12                  |
| upper limit                             | 0.15                   |

**Secondary: Percent Change From Study Baseline in FEV1% Predicted Value**

|                 |                                                             |
|-----------------|-------------------------------------------------------------|
| End point title | Percent Change From Study Baseline in FEV1% Predicted Value |
|-----------------|-------------------------------------------------------------|

End point description:

FEV1 is defined as forced expiratory volume in the first second. Participants in the Full Analysis Set with available data were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline; Day 28

| <b>End point values</b>              | Presatovir       | Placebo          |  |  |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed          | 30               | 17               |  |  |
| Units: percent change                |                  |                  |  |  |
| arithmetic mean (standard deviation) | 22.69 (± 27.437) | 26.36 (± 23.312) |  |  |

### Statistical analyses

| <b>Statistical analysis title</b>       | Presatovir vs. Placebo |
|-----------------------------------------|------------------------|
| Comparison groups                       | Presatovir v Placebo   |
| Number of subjects included in analysis | 47                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.6                  |
| Method                                  | ANCOVA                 |
| Parameter estimate                      | Treatment Difference   |
| Point estimate                          | -3.25                  |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -15.58                 |
| upper limit                             | 9.08                   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 28

Adverse event reporting additional description:

Safety Analysis Set

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Tablets administered orally or via NG tube once daily for 14 days

|                       |            |
|-----------------------|------------|
| Reporting group title | Presatovir |
|-----------------------|------------|

Reporting group description:

Administered orally or via nasogastric (NG) tube once daily for 14 days

| Serious adverse events                               | Placebo         | Presatovir     |  |
|------------------------------------------------------|-----------------|----------------|--|
| Total subjects affected by serious adverse events    |                 |                |  |
| subjects affected / exposed                          | 4 / 20 (20.00%) | 2 / 40 (5.00%) |  |
| number of deaths (all causes)                        | 0               | 0              |  |
| number of deaths resulting from adverse events       |                 |                |  |
| Vascular disorders                                   |                 |                |  |
| Deep vein thrombosis                                 |                 |                |  |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypotension                                          |                 |                |  |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders                 |                 |                |  |
| Anaemia                                              |                 |                |  |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| General disorders and administration site conditions |                 |                |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| Non-cardiac chest pain                          |                 |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| Hypoxia                                         |                 |                |  |
| subjects affected / exposed                     | 2 / 20 (10.00%) | 0 / 40 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Psychiatric disorders                           |                 |                |  |
| Mental status changes                           |                 |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 1 / 40 (2.50%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| Sepsis                                          |                 |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 40 (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          | Presatovir       |  |
|---------------------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events               |                  |                  |  |
| subjects affected / exposed                                         | 17 / 20 (85.00%) | 24 / 40 (60.00%) |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |  |
| Seborrhoeic keratosis                                               |                  |                  |  |
| subjects affected / exposed                                         | 1 / 20 (5.00%)   | 0 / 40 (0.00%)   |  |
| occurrences (all)                                                   | 1                | 0                |  |
| Squamous cell carcinoma                                             |                  |                  |  |
| subjects affected / exposed                                         | 1 / 20 (5.00%)   | 0 / 40 (0.00%)   |  |
| occurrences (all)                                                   | 1                | 0                |  |
| Vascular disorders                                                  |                  |                  |  |
| Deep vein thrombosis                                                |                  |                  |  |

|                                                         |                     |                     |  |
|---------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| General disorders and administration<br>site conditions |                     |                     |  |
| Fatigue                                                 |                     |                     |  |
| subjects affected / exposed                             | 3 / 20 (15.00%)     | 4 / 40 (10.00%)     |  |
| occurrences (all)                                       | 3                   | 4                   |  |
| Non-cardiac chest pain                                  |                     |                     |  |
| subjects affected / exposed                             | 1 / 20 (5.00%)      | 0 / 40 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                   |  |
| Respiratory, thoracic and mediastinal<br>disorders      |                     |                     |  |
| Cough                                                   |                     |                     |  |
| subjects affected / exposed                             | 0 / 20 (0.00%)      | 4 / 40 (10.00%)     |  |
| occurrences (all)                                       | 0                   | 4                   |  |
| Productive cough                                        |                     |                     |  |
| subjects affected / exposed                             | 2 / 20 (10.00%)     | 2 / 40 (5.00%)      |  |
| occurrences (all)                                       | 2                   | 2                   |  |
| Epistaxis                                               |                     |                     |  |
| subjects affected / exposed                             | 2 / 20 (10.00%)     | 0 / 40 (0.00%)      |  |
| occurrences (all)                                       | 2                   | 0                   |  |
| Sputum discoloured                                      |                     |                     |  |
| subjects affected / exposed                             | 0 / 20 (0.00%)      | 2 / 40 (5.00%)      |  |
| occurrences (all)                                       | 0                   | 2                   |  |
| Paranasal sinus discomfort                              |                     |                     |  |
| subjects affected / exposed                             | 1 / 20 (5.00%)      | 0 / 40 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                   |  |
| Psychiatric disorders                                   |                     |                     |  |
| Confusional state                                       |                     |                     |  |
| subjects affected / exposed                             | 1 / 20 (5.00%)      | 1 / 40 (2.50%)      |  |
| occurrences (all)                                       | 1                   | 1                   |  |
| Insomnia                                                |                     |                     |  |
| subjects affected / exposed                             | 0 / 20 (0.00%)      | 2 / 40 (5.00%)      |  |
| occurrences (all)                                       | 0                   | 2                   |  |
| Agitation                                               |                     |                     |  |
| subjects affected / exposed                             | 1 / 20 (5.00%)      | 0 / 40 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                   |  |
| Investigations                                          |                     |                     |  |

|                                                                                           |                      |                      |  |
|-------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Forced expiratory volume decreased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 20 (5.00%)<br>1  | 2 / 40 (5.00%)<br>2  |  |
| Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)           | 2 / 20 (10.00%)<br>2 | 0 / 40 (0.00%)<br>0  |  |
| Haemoglobin decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 20 (0.00%)<br>0  | 2 / 40 (5.00%)<br>2  |  |
| Chest X-ray abnormal<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 20 (5.00%)<br>1  | 0 / 40 (0.00%)<br>0  |  |
| Forced expiratory flow decreased<br>subjects affected / exposed<br>occurrences (all)      | 1 / 20 (5.00%)<br>1  | 0 / 40 (0.00%)<br>0  |  |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 20 (5.00%)<br>1  | 0 / 40 (0.00%)<br>0  |  |
| Cardiac disorders<br>Palpitations<br>subjects affected / exposed<br>occurrences (all)     | 0 / 20 (0.00%)<br>0  | 2 / 40 (5.00%)<br>2  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all) | 5 / 20 (25.00%)<br>6 | 4 / 40 (10.00%)<br>4 |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                              | 4 / 20 (20.00%)<br>4 | 5 / 40 (12.50%)<br>5 |  |
| Tremor<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 20 (5.00%)<br>1  | 2 / 40 (5.00%)<br>2  |  |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 20 (5.00%)<br>1  | 0 / 40 (0.00%)<br>0  |  |
| Blood and lymphatic system disorders                                                      |                      |                      |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Anaemia                     |                 |                 |  |
| subjects affected / exposed | 3 / 20 (15.00%) | 2 / 40 (5.00%)  |  |
| occurrences (all)           | 3               | 2               |  |
| Leukopenia                  |                 |                 |  |
| subjects affected / exposed | 0 / 20 (0.00%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)           | 0               | 4               |  |
| Eye disorders               |                 |                 |  |
| Lacrimation increased       |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 40 (0.00%)  |  |
| occurrences (all)           | 1               | 0               |  |
| Ocular hyperaemia           |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 40 (0.00%)  |  |
| occurrences (all)           | 1               | 0               |  |
| Vision blurred              |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 40 (0.00%)  |  |
| occurrences (all)           | 1               | 0               |  |
| Visual impairment           |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 40 (0.00%)  |  |
| occurrences (all)           | 1               | 0               |  |
| Gastrointestinal disorders  |                 |                 |  |
| Nausea                      |                 |                 |  |
| subjects affected / exposed | 3 / 20 (15.00%) | 5 / 40 (12.50%) |  |
| occurrences (all)           | 4               | 5               |  |
| Diarrhoea                   |                 |                 |  |
| subjects affected / exposed | 4 / 20 (20.00%) | 2 / 40 (5.00%)  |  |
| occurrences (all)           | 4               | 2               |  |
| Vomiting                    |                 |                 |  |
| subjects affected / exposed | 3 / 20 (15.00%) | 3 / 40 (7.50%)  |  |
| occurrences (all)           | 4               | 4               |  |
| Flatulence                  |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 2 / 40 (5.00%)  |  |
| occurrences (all)           | 1               | 2               |  |
| Abdominal pain upper        |                 |                 |  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 1 / 40 (2.50%)  |  |
| occurrences (all)           | 1               | 1               |  |
| Abdominal pain              |                 |                 |  |



|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Gastrooesophageal reflux disease                |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Glossodynia                                     |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Mouth ulceration                                |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Pneumatosis intestinalis                        |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Skin and subcutaneous tissue disorders          |                |                |  |
| Pruritus                                        |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 1 / 40 (2.50%) |  |
| occurrences (all)                               | 1              | 1              |  |
| Renal and urinary disorders                     |                |                |  |
| Pollakiuria                                     |                |                |  |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 2 / 40 (5.00%) |  |
| occurrences (all)                               | 0              | 2              |  |
| Chronic kidney disease                          |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Arthralgia                                      |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Flank pain                                      |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 40 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Infections and infestations                     |                |                |  |
| Urinary tract infection                         |                |                |  |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 1 / 40 (2.50%) |  |
| occurrences (all)                               | 1              | 1              |  |

|                                                                                 |                     |                     |  |
|---------------------------------------------------------------------------------|---------------------|---------------------|--|
| Candida infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| Nasal herpes<br>subjects affected / exposed<br>occurrences (all)                | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| Metabolism and nutrition disorders                                              |                     |                     |  |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 20 (5.00%)<br>1 | 1 / 40 (2.50%)<br>1 |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)          | 1 / 20 (5.00%)<br>2 | 0 / 40 (0.00%)<br>0 |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)               | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |
| Increased appetite<br>subjects affected / exposed<br>occurrences (all)          | 1 / 20 (5.00%)<br>1 | 0 / 40 (0.00%)<br>0 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 02 December 2015  | <ul style="list-style-type: none"><li>• Added electrocardiograms (ECGs), troponin testing, and collection of standard of care clinical data for central review</li><li>• Additional spirometry measurements collected via handheld devices</li><li>• Study Endpoint and statistical analysis revisions</li><li>• Inclusion criteria updated to allow subjects <math>\geq 18</math> to enroll and to allow PCR positive subjects to be enrolled using an upper or lower respiratory tract sample</li><li>• Exclusion criteria updated to state that viral co-infection and systemic infection may be allowed if discussed with the medical monitor and deemed acceptable; additional restrictions added as related to sulfa drug response</li><li>• iADL, ADL, and SF-12 assessments for the Optional Registry will begin at Day 1/Baseline</li><li>• Edits throughout for clarity and administrative changes were made</li></ul>                                                                                                                                  |
| 12 September 2016 | <ul style="list-style-type: none"><li>• Renumbering as appropriate due to the addition of new sections</li><li>• Addition of a window for Day 1/Baseline spirometry and the addition of information and clarification on historical spirometry data that should be collected</li><li>• Updates to pregnancy testing and requirements</li><li>• Updates to the Study Design schema to include the spirometry window and PK lab draws</li><li>• Removal of the requirement for safety labs to be collected during the optional registry</li><li>• Clarification that only procedure-related AEs need to be collected during the optional Extended Viral Monitoring and Optional Registry portions of the study</li><li>• Clarification that the Day 21 local RSV PCR testing, as required for the optional extended viral monitoring, does not need to be redone if completed for clinical purposes prior to Day 21 with a negative result</li><li>• Addition of new Phase 1 data</li><li>• Consolidation of the Prior and Concomitant Medication section</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

An unplanned review of unblinded clinical trial data was performed in this study that was not prospectively specified in the protocol. There was no impact on the overall integrity or conclusions of the study.

Notes: