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	• Correction of full data set Adding text to "Limitations and Caveats" section

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, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, 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
Arm title	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

Arm title	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 1[1]	Presatovir	Placebo
Started	40	20
Completed	37	20
Not completed	3	0
Withdrew Consent	2	-
Protocol deviation	1	-

Notes:

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

Justification: 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 ≥ 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 (± 0.938)	-0.90 (± 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

Statistical analysis title	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 (± 0.313)	-0.31 (± 0.298)		

Statistical analyses

Statistical analysis title	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

End point values	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

Statistical analysis title	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 %

Non-serious adverse events	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	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
General disorders and administration 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 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			
subjects affected / exposed	1 / 20 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Blood bicarbonate decreased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Chest X-ray abnormal			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Forced expiratory flow decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 20 (25.00%)	4 / 40 (10.00%)	
occurrences (all)	6	4	
Headache			
subjects affected / exposed	4 / 20 (20.00%)	5 / 40 (12.50%)	
occurrences (all)	4	5	
Tremor			
subjects affected / exposed	1 / 20 (5.00%)	2 / 40 (5.00%)	
occurrences (all)	1	2	
Hypoaesthesia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	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			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Nasal herpes			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 20 (5.00%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Decreased appetite			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Hyperglycaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	1 / 20 (5.00%)	0 / 40 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2015	• Added electrocardiograms (ECGs), troponin testing, and collection of standard of care clinical data for central review • Additional spirometry measurements collected via handheld devices Study Endpoint and statistical analysis revisions • Inclusion criteria updated to allow subjects ≥ 18 to enroll and to allow PCR positive subjects to be enrolled using an upper or lower respiratory tract sample • 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 • iADL, ADL, and SF-12 assessments for the Optional Registry will begin at Day 1/Baseline • Edits throughout for clarity and administrative changes were made
12 September 2016	• Renumbering as appropriate due to the addition of new sections • Addition of a window for Day 1/Baseline spirometry and the addition of information and clarification on historical spirometry data that should be collected • Updates to pregnancy testing and requirements • Updates to the Study Design schema to include the spirometry window and PK lab draws • Removal of the requirement for safety labs to be collected during the optional registry • Clarification that only procedure-related AEs need to be collected during the optional Extended Viral Monitoring and Optional Registry portions of the study • 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 •Addition of new Phase 1 data •Consolidation of the Prior and Concomitant Medication section

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: