



## Clinical trial results:

### A Phase 2b, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Antiviral Activity, Clinical Outcomes, Safety, Tolerability, and Pharmacokinetics of Orally Administered ALS-008176 Regimens in Adult Subjects Hospitalized with Respiratory Syncytial Virus

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2016-001653-40       |
| Trial protocol           | GB BE ES PL SE NL BG |
| Global end of trial date | 17 October 2018      |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 28 October 2019 |
| First version publication date | 28 October 2019 |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | 64041575RSV2003 |
|-----------------------|-----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02935673 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Janssen Research & Development, LLC   |
| Sponsor organisation address | 920 Route 202, Raritan, United States, NJ 08869   |
| Public contact               | Clinical Registry Group, Janssen Research and Development LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen Research and Development LLC, ClinicalTrialsEU@its.jnj.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                       | 17 October 2018 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 17 October 2018 |
| Was the trial ended prematurely?                     | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

The main objectives of this study were to characterize the pharmacokinetics (PK) and to confirm the population PK (popPK) model derived from healthy volunteers in hospitalized adults infected with respiratory syncytial virus (RSV) (Part 1) and to determine in hospitalized adults infected with RSV the dose response relationship of multiple regimens of lumicitabine on antiviral activity based on nasal RSV shedding using quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) assay (Part 2).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety was evaluated throughout the study and included monitoring of adverse events (AEs), clinical laboratory tests, vital signs/peripheral capillary oxygen saturation (SpO2) measurements, physical examinations, and electrocardiograms (ECGs).

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 08 November 2016 |
| 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 | Argentina: 2          |
| Country: Number of subjects enrolled | Australia: 7          |
| Country: Number of subjects enrolled | Spain: 3              |
| Country: Number of subjects enrolled | France: 7             |
| Country: Number of subjects enrolled | United Kingdom: 1     |
| Country: Number of subjects enrolled | Japan: 9              |
| Country: Number of subjects enrolled | Korea, Republic of: 4 |
| Country: Number of subjects enrolled | Malaysia: 2           |
| Country: Number of subjects enrolled | Poland: 2             |
| Country: Number of subjects enrolled | Sweden: 7             |
| Country: Number of subjects enrolled | Taiwan: 3             |
| Country: Number of subjects enrolled | United States: 2      |
| Worldwide total number of subjects   | 49                    |
| EEA total number of subjects         | 20                    |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 20 |
| From 65 to 84 years                       | 22 |
| 85 years and over                         | 7  |

## Subject disposition

### Recruitment

Recruitment details:

Sponsor halted screening and enrollment in study on 22 June 2018 due to emerging lumicitabine nonclinical data. On 17 October 2018, study was stopped prematurely by Sponsor as a precautionary measure, to allow further evaluation of new nonclinical pharmacokinetic (PK) and safety findings and determine their relevance to human studies.

### Pre-assignment

Screening details:

A total of 49 subjects were randomized and treated (2 subjects in Part 0, 36 subjects in Part 1 and 11 subjects in Part 2). Analyses were conducted on pooled groups across the 3 study parts.

### 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>             | Placebo |

Arm description:

Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

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

Dosage and administration details:

Subjects received a single LD followed by nine MDs (Doses 2 to 10) of matched placebo bid.

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | 750 mg LD / 250 mg MD Lumicitabine |
|------------------|------------------------------------|

Arm description:

Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Lumicitabine 250 mg      |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-64041575, ALS-008176 |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Subjects received nine 250 mg MDs (Doses 2 to 10) of lumicitabine bid.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Lumicitabine 750 mg      |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-64041575, ALS-008176 |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Subjects received a single 750 mg LD of lumicitabine.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | 1000 mg LD / 500 mg MD Lumicitabine |
|------------------|-------------------------------------|

Arm description:

Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Lumicitabine 1000 mg     |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-64041575, ALS-008176 |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Subjects received a single 1000 mg LD of lumicitabine.

|  |                          |
|--|--------------------------|
| Investigational medicinal product name | Lumicitabine 500 mg      |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-64041575, ALS-008176 |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Subjects received nine 500 mg MDs (Doses 2 to 10) of lumicitabine bid.

| <b>Number of subjects in period 1</b> | Placebo | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |
|---------------------------------------|---------|------------------------------------|-------------------------------------|
| Started                               | 16      | 27                                 | 6                                   |
| Completed                             | 15      | 24                                 | 6                                   |
| Not completed                         | 1       | 3                                  | 0                                   |
| Adverse event, non-fatal              | -       | 1                                  | -                                   |
| Withdrawal by subject                 | 1       | 2                                  | -                                   |

## Baseline characteristics

### Reporting groups

|   |                                     |
|---|-------------------------------------|
| Reporting group title   | Placebo                             |
| Reporting group description:  |                                     |
| Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration). |                                     |
| Reporting group title   | 750 mg LD / 250 mg MD Lumicitabine  |
| Reporting group description:  |                                     |
| Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).   |                                     |
| Reporting group title   | 1000 mg LD / 500 mg MD Lumicitabine |
| Reporting group description:  |                                     |
| Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).  |                                     |

| Reporting group values                      | Placebo | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |
|---|---------|------------------------------------|-------------------------------------|
| Number of subjects                          | 16      | 27                                 | 6                                   |
| Title for AgeCategorical<br>Units: subjects |         |                                    |                                     |
| Adults (18-64 years)                        | 8       | 10                                 | 2                                   |
| From 65 to 84 years                         | 5       | 13                                 | 4                                   |
| 85 years and over                           | 3       | 4                                  | 0                                   |
| Title for AgeContinuous<br>Units: months    |         |                                    |                                     |
| arithmetic mean                             | 65.5    | 66.3                               | 68.7                                |
| standard deviation                          | ± 17.94 | ± 17.75                            | ± 18.46                             |
| Title for Gender<br>Units: subjects         |         |                                    |                                     |
| Female                                      | 5       | 9                                  | 5                                   |
| Male  | 11      | 18                                 | 1                                   |

| Reporting group values                      | Total |  |  |
|---|-------|--|--|
| Number of subjects                          | 49    |  |  |
| Title for AgeCategorical<br>Units: subjects |       |  |  |
| Adults (18-64 years)                        | 20    |  |  |
| From 65 to 84 years                         | 22    |  |  |
| 85 years and over                           | 7     |  |  |
| Title for AgeContinuous<br>Units: months    |       |  |  |
| arithmetic mean                             |       |  |  |
| standard deviation                          | -     |  |  |
| Title for Gender<br>Units: subjects         |       |  |  |
| Female                                      | 19    |  |  |
| Male  | 30    |  |  |



## End points

### End points reporting groups

|   |                                     |
|---|-------------------------------------|
| Reporting group title   | Placebo                             |
| Reporting group description:<br>Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration). |                                     |
| Reporting group title   | 750 mg LD / 250 mg MD Lumicitabine  |
| Reporting group description:<br>Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).   |                                     |
| Reporting group title   | 1000 mg LD / 500 mg MD Lumicitabine |
| Reporting group description:<br>Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).  |                                     |

### Primary: Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 at Day 1

|   |   |
|---|---|
| End point title   | Maximum Observed Plasma Concentration (Cmax) of JNJ-63549109 at Day 1 <sup>[1][2]</sup> |
| End point description:<br>Cmax is the maximum observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. Pharmacokinetic (PK) analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type  | Primary   |
| End point timeframe:<br>Day 1   |   |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                       | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |  |
|--|------------------------------------|-------------------------------------|--|--|
| Subject group type                     | Reporting group                    | Reporting group                     |  |  |
| Number of subjects analysed            | 26                                 | 4                                   |  |  |
| Units: nanogram per milliliter (ng/mL) |                                    |                                     |  |  |
| arithmetic mean (standard deviation)   | 1845 (± 545.2)                     | 2801 (± 1509)                       |  |  |

## Statistical analyses



No statistical analyses for this end point

### Primary: Maximum Observed Plasma Concentration of JNJ-63549109 at Day 5

|                 |  |
|-----------------|--|
| End point title | Maximum Observed Plasma Concentration of JNJ-63549109 at Day 5 <sup>[3][4]</sup> |
|-----------------|--|

End point description:

C<sub>max</sub> is the maximum observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Day 5

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                     | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed          | 22                                       | 2   |  |  |
| Units: ng/mL                         |  |   |  |  |
| arithmetic mean (standard deviation) | 745.4 (±<br>164.2)                       | 1145 (± 440.8)                            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 1

|                 |   |
|-----------------|---|
| End point title | Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 1 <sup>[5][6]</sup> |
|-----------------|---|

End point description:

AUC (0-24h) is the area under the plasma concentration-time curve from time 0 to 24 hours after dosing of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Day 1

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                                 | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |  |
|--|--|---|--|--|
| Subject group type                               | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed                      | 26                                       | 4   |  |  |
| Units: nanogram*hour per milliliter<br>(ng*h/mL) |  |   |  |  |
| arithmetic mean (standard deviation)             | 9936 ( $\pm$ 2090)                       | 17120 ( $\pm$ 4330)                       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 5

|                 |   |
|-----------------|---|
| End point title | Area Under the Plasma Concentration-time Curve from Time 0 to 24 Hours After Dosing (AUC[0-24h]) of JNJ-63549109 at Day 5 <sup>[7][8]</sup> |
|-----------------|---|

End point description:

AUC(0-24h) is the area under the plasma concentration-time curve from time 0 to 24 hours after dosing of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Day 5

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                     | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed          | 22                                       | 2   |  |  |
| Units: ng*h/mL                       |  |   |  |  |
| arithmetic mean (standard deviation) | 7557 ( $\pm$ 1525)                       | 13300 ( $\pm$ 4603)                       |  |  |

## Statistical analyses

**Primary: Trough Observed Plasma Concentration (C<sub>trough</sub>) of JNJ-63549109 at Day 1**

|                 |   |
|-----------------|---|
| End point title | Trough Observed Plasma Concentration (C <sub>trough</sub> ) of JNJ-63549109 at Day 1 <sup>[9][10]</sup> |
|-----------------|---|

## End point description:

C<sub>trough</sub> is the trough observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

## End point timeframe:

Day 1

## Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                     | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           |  |  |
| Number of subjects analysed          | 26                                       | 4   |  |  |
| Units: ng/mL                         |  |   |  |  |
| arithmetic mean (standard deviation) | 93.7 (± 44.16)                           | 184.4 (± 184.4)                           |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Trough Observed Plasma Concentration of JNJ-63549109 at Day 5**

|                 |   |
|-----------------|---|
| End point title | Trough Observed Plasma Concentration of JNJ-63549109 at Day 5 <sup>[11][12]</sup> |
|-----------------|---|

## End point description:

C<sub>trough</sub> is the trough observed plasma concentration of JNJ-63549109. JNJ-63549109 is the metabolized product of lumicitabine. PK analysis was performed on safety population which included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

## End point timeframe:

Day 5

## Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                     | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |  |
|--------------------------------------|------------------------------------|-------------------------------------|--|--|
| Subject group type                   | Reporting group                    | Reporting group                     |  |  |
| Number of subjects analysed          | 22                                 | 2                                   |  |  |
| Units: ng/mL                         |                                    |                                     |  |  |
| arithmetic mean (standard deviation) | 148.3 (± 60.41)                    | 281.3 (± 156.6)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Least Square Mean Difference (Low and High Dose Lumicitabine Versus Placebo) of Respiratory Syncytial Virus (RSV) Ribonucleic Acid (RNA) Viral Load Area Under the Concentration-time Curve From Day 0 to 7 (AUC[0-7])

|                 |  |
|-----------------|--|
| End point title | Least Square Mean Difference (Low and High Dose Lumicitabine Versus Placebo) of Respiratory Syncytial Virus (RSV) Ribonucleic Acid (RNA) Viral Load Area Under the Concentration-time Curve From Day 0 to 7 (AUC[0-7])[13][14] |
|-----------------|--|

End point description:

RSV RNA viral load in log10 copies/milliliter/day (log10 copies/mL/day) was measured in mid-turbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling methods) using quantitative reverse transcription-polymerase chain reaction (qRT-PCR). Intent-to-treat-infected (ITT-i) set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Day 0 to 7

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint was planned to be analyzed for specified arm only.

| End point values                             | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |  |
|--|------------------------------------|-------------------------------------|--|--|
| Subject group type                           | Reporting group                    | Reporting group                     |  |  |
| Number of subjects analysed                  | 21                                 | 5                                   |  |  |
| Units: log10 copies/mL/day                   |                                    |                                     |  |  |
| least squares mean (confidence interval 95%) | -0.32 (-0.89 to 0.24)              | -0.36 (-1.33 to 0.62)               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Adverse Events (AEs)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects with Adverse Events (AEs) |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non-investigational) product, whether or not related to that medicinal (investigational or non-investigational) product. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 16              | 27                                       | 6   |  |
| Units: Subjects             | 7               | 22                                       | 5   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Vital Sign Abnormalities

|                 |  |
|-----------------|--|
| End point title | Number of Subjects with Vital Sign Abnormalities |
|-----------------|--|

End point description:

Number of subjects with vital sign (systolic and diastolic blood pressure [BP], pulse rate, respiratory rate, temperature and oxygen saturation) abnormalities were reported. For systolic BP: abnormally low refers to less than or equal to ( $\leq$ ) 90 millimeter of mercury (mmHg); for diastolic BP: abnormally low refers to  $\leq$  50 mmHg; for pulse rate abnormally low refers to less than ( $<$ ) 45 beats per minutes (bpm) and abnormally high refers to greater than or equal to ( $\geq$ ) 120 bpm; for temperature in degree Celsius abnormally high refers to greater than ( $>$ ) 37.8 (tympanic),  $>38.0$  (forehead),  $>38.0$  (oral),  $>37.2$  (rectal),  $>38.0$  (axillary); for oxygen saturation in % abnormally low refers to  $<95$ . Grade 1=mild; grade 2=moderate; grade 3=severe. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'n' (number analyzed) signifies number of subjects evaluable for specified categories. Analyses were conducted on pooled groups across 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                                      | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|---|-----------------|--|---|--|
| Subject group type                                    | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed                           | 16              | 27                                       | 6   |  |
| Units: Subjects                                       |                 |  |   |  |
| Systolic BP (Abnormally Low)<br>(n=16,27,6)           | 1               | 0  | 0   |  |
| Systolic BP (Grade 1 or mild)<br>(n=16,27,6)          | 2               | 6  | 2   |  |
| Systolic BP (Grade 2 or moderate)<br>(n=16,27,6)      | 5               | 4  | 0   |  |
| Systolic BP (Grade 3 or severe)<br>(n=16,27,6)        | 1               | 1  | 1   |  |
| Diastolic BP (Abnormally low)<br>(n=16,27,6)          | 2               | 2  | 1   |  |
| Diastolic BP (Grade 1 or mild)<br>(n=16,27,6)         | 5               | 8  | 1   |  |
| Diastolic BP (Grade 2 or moderate)<br>(n=16,27,6)     | 3               | 1  | 0   |  |
| Diastolic BP (Grade 3 or severe)<br>(n=16,27,6)       | 0               | 1  | 0   |  |
| Pulse Rate (Abnormally high<br>(n=16,27,6)            | 2               | 1  | 0   |  |
| Respiratory Rate (Grade 1 or mild)<br>(n=16,26,6)     | 2               | 0  | 1   |  |
| Respiratory Rate (Grade 2 or moderate)<br>(n=16,26,6) | 4               | 6  | 1   |  |
| Respiratory Rate (Grade 3 or severe)<br>(n=16,26,6)   | 3               | 2  | 0   |  |
| Temperature (Abnormally high)<br>(n=16,27,6)          | 4               | 2  | 0   |  |
| Oxygen Saturation (Abnormally low)<br>(n=16,27,6)     | 7               | 9  | 2   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with QT Interval Abnormalities

|  |   |
|--|---|
| End point title  | Number of Subjects with QT Interval Abnormalities |
| End point description:<br>Number of subjects with QT interval abnormalities (prolonged) were reported. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Up to 28 Days  |   |

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 24                                       | 5   |  |
| Units: Subjects             | 0               | 1  | 0   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Clinical Laboratory Abnormalities

|   |   |
|---|---|
| End point title   | Number of Subjects with Clinical Laboratory Abnormalities |
| End point description:  |   |
| Number of subjects with clinical laboratory (serum chemistry and hematology) abnormalities were reported. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Here 'n' (number analyzed) signifies number of subjects evaluable for specified categories. Analyses were conducted on pooled groups across the 3 study parts. Abbreviations; Erythrocyte MCHC = Erythrocyte Mean Corpuscular Hemoglobin Concentration; Erythrocyte MCH = Erythrocyte Mean Corpuscular Hemoglobin; Ery. = Erythrocyte |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Up to 28 Days   |   |

| End point values                    | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-------------------------------------|-----------------|--|---|--|
| Subject group type                  | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed         | 16              | 27                                       | 6   |  |
| Units: Subjects                     |                 |  |   |  |
| Bicarbonate : Low (n=9,17,2)        | 0               | 2  | 0   |  |
| Bicarbonate: High (n=9,17,2)        | 3               | 5  | 0   |  |
| Chloride : Low (n=15,25,6)          | 0               | 3  | 0   |  |
| Chloride : High (n=15,25,6)         | 0               | 2  | 0   |  |
| Creatine Kinase : Low (n=13,19,6)   | 4               | 2  | 3   |  |
| Creatine Kinase ; High (n=13,19,6)  | 0               | 0  | 1   |  |
| Direct Bilirubin : High (n=7,15,4)  | 0               | 1  | 0   |  |
| Indirect Bilirubin : Low (n=7,12,4) | 1               | 0  | 2   |  |
| Basophils : High (n=16,27,6)        | 0               | 0  | 1   |  |
| Eosinophils : High (n=16,27,6)      | 3               | 1  | 1   |  |
| Erythrocyte MCHC : Low (n=16,27,6)  | 1               | 1  | 0   |  |
| Erythrocyte MCH : Low (n=16,27,6)   | 1               | 0  | 0   |  |
| Erythrocyte MCH : High (n=16,27,6)  | 0               | 3  | 1   |  |
| Erythrocytes : Low (n=16,27,6)      | 5               | 3  | 1   |  |

|  |   |   |   |  |
|--|---|---|---|--|
| Ery. Distribution Width : Low (n=11,20,4)    | 0 | 1 | 0 |  |
| Ery. Distribution Width : High (n=11,20,4)   | 2 | 5 | 3 |  |
| Hematocrit : Low (n=16,26,6)                 | 4 | 5 | 0 |  |
| Hematocrit : High (n=16,26,6)                | 1 | 0 | 0 |  |
| Lymphocytes : Low (n=16,27,6)                | 0 | 4 | 0 |  |
| Lymphocytes : High (n=16,27,6)               | 4 | 3 | 2 |  |
| Monocyte : Low (n=16,27,6)                   | 0 | 2 | 1 |  |
| Monocyte : High (n=16,27,6)                  | 5 | 5 | 3 |  |
| Reticulocytes : Low (n=8,11,6)               | 0 | 1 | 2 |  |
| Reticulocytes : High (n=8,11,6)              | 4 | 2 | 4 |  |
| Reticulocytes/Erythrocytes : Low (n=6,14,4)  | 1 | 0 | 1 |  |
| Reticulocytes/Erythrocytes : High (n=6,14,4) | 4 | 9 | 3 |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time of Hospital Stay From Study Treatment Initiation to Discharge

|                 |  |
|-----------------|--|
| End point title | Time of Hospital Stay From Study Treatment Initiation to Discharge |
|-----------------|--|

End point description:

It is the time from treatment initiation to hospital discharge in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

From study treatment initiation to discharge (Up to 28 Days)

| End point values                     | Placebo                 | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |
|--------------------------------------|-------------------------|------------------------------------|-------------------------------------|--|
| Subject group type                   | Reporting group         | Reporting group                    | Reporting group                     |  |
| Number of subjects analysed          | 15                      | 21                                 | 5                                   |  |
| Units: Hours                         |                         |                                    |                                     |  |
| arithmetic mean (standard deviation) | 183.91 ( $\pm$ 217.020) | 146.72 ( $\pm$ 94.910)             | 405.24 ( $\pm$ 294.771)             |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time of Hospital Stay From Admission to Discharge



|  |   |
|--|---|
| End point title  | Time of Hospital Stay From Admission to Discharge |
| End point description:   |   |
| It is the time from hospital admission to hospital discharge in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| From admission to discharge (Up to 28 days)  |   |

| End point values                     | Placebo               | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-----------------------|--|---|--|
| Subject group type                   | Reporting group       | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 10                    | 17                                       | 3   |  |
| Units: Hours                         |                       |  |   |  |
| arithmetic mean (standard deviation) | 192.40 (±<br>199.363) | 181.97 (±<br>107.938)                    | 297.53 (±<br>348.729)                     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time of Hospital Stay from Study Treatment Initiation to Readiness for Discharge

|  |  |
|--|--|
| End point title  | Time of Hospital Stay from Study Treatment Initiation to Readiness for Discharge |
| End point description:   |  |
| It is the time from study treatment initiation to readiness for discharge in hours, with readiness for discharge defined by the investigator. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| From study treatment initiation to readiness for discharge on Day 2 or up to Day 6 if hospitalization is prolonged   |  |

| End point values                     | Placebo              | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|----------------------|--|---|--|
| Subject group type                   | Reporting group      | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 15                   | 21                                       | 5   |  |
| Units: Hours                         |                      |  |   |  |
| arithmetic mean (standard deviation) | 111.05 (±<br>78.237) | 144.17 (±<br>96.019)                     | 197.60 (±<br>256.702)                     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time of Hospital Stay from Admission to Readiness for Discharge

|                 |   |
|-----------------|---|
| End point title | Time of Hospital Stay from Admission to Readiness for Discharge |
|-----------------|---|

End point description:

It is the time from hospital admission to readiness for discharge in hours, with readiness for discharge defined by the investigator. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo              | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|----------------------|--|---|--|
| Subject group type                   | Reporting group      | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 10                   | 17                                       | 3   |  |
| Units: Hours                         |                      |  |   |  |
| arithmetic mean (standard deviation) | 133.41 (±<br>83.057) | 178.82 (±<br>108.522)                    | 297.13 (±<br>349.159)                     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Required to be Admitted to the Intensive Care Unit (ICU) Since Initiation of Treatment

|                 |   |
|-----------------|---|
| End point title | Number of Subjects Who Required to be Admitted to the Intensive Care Unit (ICU) Since Initiation of Treatment |
|-----------------|---|

End point description:

Number of subjects who required to be admitted to the ICU after the initiation of treatment were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 0               | 0  | 0   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Intensive Care Unit Stay

|   |                                      |
|---|--------------------------------------|
| End point title   | Duration of Intensive Care Unit Stay |
| End point description:  |                                      |
| In the event that a subject required ICU since initiation of treatment, the duration for how long the subject remained in the ICU was measured. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. |                                      |
| End point type  | Secondary                            |
| End point timeframe:  |                                      |
| Up to 28 Days   |                                      |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[15]</sup> | 0 <sup>[16]</sup>                        | 0 <sup>[17]</sup>                         |  |
| Units: Hours                         |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[15] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

[16] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

[17] - Overall subjects analyzed is 0 as none of subjects admitted to ICU since initiation of treatment.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Required Supplemental Oxygen

|   |   |
|---|---|
| End point title   | Number of Subjects Who Required Supplemental Oxygen |
| End point description:  |   |
| Number of subjects who required supplemental oxygen were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type  | Secondary   |

End point timeframe:

Up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 14              | 18                                       | 4   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to End of Oxygen Supplementation

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Time to End of Oxygen Supplementation |
|-----------------|---------------------------------------|

End point description:

It is the time from first dose of study drug to the last end date and time of any oxygen supplementation in hours. Population included ITT-i set who required supplemental oxygen. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                 | Placebo              | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|----------------------------------|----------------------|--|---|--|
| Subject group type               | Reporting group      | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed      | 14                   | 18                                       | 4   |  |
| Units: Hours                     |                      |  |   |  |
| arithmetic mean (standard error) | 83.92 (±<br>168.125) | 139.38 (±<br>237.584)                    | 132.40 (±<br>288.568)                     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time (Number of Hours) Until Peripheral Capillary Oxygen Saturation (SpO2) Greater Than or Equal to (≥) 93 Percent (%) on Room Air Among Subjects Who Were Not on Supplemental Oxygen Prior to the Onset of Respiratory Symptoms

|                 |  |
|-----------------|--|
| End point title | Time (Number of Hours) Until Peripheral Capillary Oxygen Saturation (SpO2) Greater Than or Equal to (≥) 93 Percent (%) on Room Air Among Subjects Who Were Not on Supplemental Oxygen Prior to the Onset of Respiratory Symptoms |
|-----------------|--|

End point description:

Time (number of hours) until SpO2  $\geq$  93% on room air among subjects who were not on supplemental oxygen prior to the onset of respiratory symptoms was reported.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[18]</sup> | 0 <sup>[19]</sup>                        | 0 <sup>[20]</sup>                         |  |
| Units: Hours                         |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[18] - Data was not collected and analyzed because this study was stopped prematurely.

[19] - Data was not collected and analyzed because this study was stopped prematurely.

[20] - Data was not collected and analyzed because this study was stopped prematurely.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Return to Pre-respiratory Syncytial Virus (Pre-RSV) Disease Level for Respiratory Rate

|                 |  |
|-----------------|--|
| End point title | Time to Return to Pre-respiratory Syncytial Virus (Pre-RSV) Disease Level for Respiratory Rate |
|-----------------|--|

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for respiratory rate. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo                   | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|---------------------------|--|---|--|
| Subject group type                   | Reporting group           | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 15                        | 21                                       | 5   |  |
| Units: Hours                         |                           |  |   |  |
| arithmetic mean (standard deviation) | 64.72 ( $\pm$<br>180.542) | 47.75 ( $\pm$<br>153.293)                | 196.96 ( $\pm$<br>290.694)                |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Return to Pre-RSV Disease Level for Oxygen Saturation

|                 |   |
|-----------------|---|
| End point title | Time to Return to Pre-RSV Disease Level for Oxygen Saturation |
|-----------------|---|

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for oxygen saturation. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo             | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|---------------------|--|---|--|
| Subject group type                   | Reporting group     | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 15                  | 21                                       | 5   |  |
| Units: Hours                         |                     |  |   |  |
| arithmetic mean (standard deviation) | 55.55 (±<br>85.915) | 33.85 (±<br>57.703)                      | 47.56 (±<br>106.347)                      |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Return to Pre-RSV Disease Level for Body Temperature

|                 |  |
|-----------------|--|
| End point title | Time to Return to Pre-RSV Disease Level for Body Temperature |
|-----------------|--|

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV disease level for body temperature. The return to pre-RSV disease level occurred when the observed value of the parameter was indicated by the investigator as normal, and no later observed values were indicated by the investigator as abnormal.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[21]</sup> | 0 <sup>[22]</sup>                        | 0 <sup>[23]</sup>                         |  |
| Units: Degree Celsius                |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[21] - Data was not collected and analyzed because this study was stopped prematurely.

[22] - Data was not collected and analyzed because this study was stopped prematurely.

[23] - Data was not collected and analyzed because this study was stopped prematurely.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Who Required Noninvasive Mechanical Ventilation Support

|                 |  |
|-----------------|--|
| End point title | Number of Subjects Who Required Noninvasive Mechanical Ventilation Support |
|-----------------|--|

End point description:

Number of subjects who required noninvasive mechanical ventilation support (that is supplemental oxygen [excluding mechanical ventilation]) were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 14              | 18                                       | 4   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to End of Noninvasive Mechanical Ventilation Support

|                 |   |
|-----------------|---|
| End point title | Time to End of Noninvasive Mechanical Ventilation Support |
|-----------------|---|

End point description:

It is the time from first dose of study drug to the last end date and time of noninvasive mechanical ventilation in hours. Population included ITT-i set who required noninvasive mechanical ventilation support. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values                     | Placebo              | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|----------------------|--|---|--|
| Subject group type                   | Reporting group      | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 14                   | 18                                       | 4   |  |
| Units: Hours                         |                      |  |   |  |
| arithmetic mean (standard deviation) | 83.92 (±<br>168.125) | 139.38 (±<br>237.584)                    | 132.40 (±<br>288.568)                     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Required Invasive Mechanical Ventilation Support

|                 |   |
|-----------------|---|
| End point title | Number of Subjects Who Required Invasive Mechanical Ventilation Support |
|-----------------|---|

End point description:

Number of subjects who required invasive mechanical ventilation support were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 0               | 0  | 0   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to End of Invasive Mechanical Ventilation Support

|                 |  |
|-----------------|--|
| End point title | Time to End of Invasive Mechanical Ventilation Support |
|-----------------|--|

End point description:

It is the time from first dose of study drug to the last end date and time of invasive mechanical ventilation support in hours. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Zero subjects were analysed for this endpoint as none



of subjects required invasive ventilation support. Analyses were conducted on pooled groups across the 3 study parts.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 28 Days        |           |

| End point values                     | Placebo           | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |
|--------------------------------------|-------------------|------------------------------------|-------------------------------------|--|
| Subject group type                   | Reporting group   | Reporting group                    | Reporting group                     |  |
| Number of subjects analysed          | 0 <sup>[24]</sup> | 0 <sup>[25]</sup>                  | 0 <sup>[26]</sup>                   |  |
| Units: Hours                         |                   |                                    |                                     |  |
| arithmetic mean (standard deviation) | ()                | ()                                 | ()                                  |  |

Notes:

[24] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

[25] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

[26] - 0 subjects analysed for this endpoint as none of subjects required invasive ventilation support.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Return to Pre-RSV Functional Status as Assessed by KATZ Activities of Daily Living (ADL) Score

|                 |  |
|-----------------|--|
| End point title | Time to Return to Pre-RSV Functional Status as Assessed by KATZ Activities of Daily Living (ADL) Score |
|-----------------|--|

End point description:

It is the time from first dose of study drug until the time to return to pre-RSV functional status. Functional status is total points on KATZ index of independence in activities of daily living (KATZ ADL score). Katz activities of daily living assessed questions related to bathing, dressing, toileting, transferring, continence and feeding components. Total score was calculated by adding scores for all 6 activities which ranges from 0 high (subject independent) to 6 low (subject very dependent). Return to pre-RSV functional status occurs at timepoint where for first time KATZ ADL score is equal or higher than pre-RSV KATZ ADL score and after which no scores lower than pre-RSV KATZ ADL score occur anymore. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 28 Days        |           |

| End point values                     | Placebo         | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |
|--------------------------------------|-----------------|------------------------------------|-------------------------------------|--|
| Subject group type                   | Reporting group | Reporting group                    | Reporting group                     |  |
| Number of subjects analysed          | 15              | 21                                 | 5                                   |  |
| Units: Days                          |                 |                                    |                                     |  |
| arithmetic mean (standard deviation) | 3.60 (± 7.434)  | 4.48 (± 6.961)                     | 6.00 (± 11.203)                     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Required Hydration or Feeding by Intravenous (IV) Catheter or Nasogastric Tube

|                 |   |
|-----------------|---|
| End point title | Number of Subjects Who Required Hydration or Feeding by Intravenous (IV) Catheter or Nasogastric Tube |
|-----------------|---|

End point description:

Number of subjects who required hydration or feeding by IV catheter or nasogastric tube were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 3               | 5  | 1   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Clinical Stability

|                 |                            |
|-----------------|----------------------------|
| End point title | Time to Clinical Stability |
|-----------------|----------------------------|

End point description:

Time to clinical stability is defined as the time from first dose of study drug until the time at which the following criteria were all met: normalization of blood oxygen level (return to baseline; by pulse oximetry) without requirement of supplemental oxygen beyond baseline level, normalization of oral feeding, normalization of respiratory rate and normalization of heart rate. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Up to 28 Days

| <b>End point values</b>              | Placebo               | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-----------------------|--|---|--|
| Subject group type                   | Reporting group       | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 15                    | 21                                       | 5   |  |
| Units: Hours                         |                       |  |   |  |
| arithmetic mean (standard deviation) | 151.21 (±<br>266.460) | 171.74 (±<br>261.384)                    | 207.00 (±<br>282.955)                     |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects in Each Ordinal Scale Category

|  |   |
|--|---|
| End point title  | Number of Subjects in Each Ordinal Scale Category |
| End point description:   |   |
| Number of subjects in each ordinal scale category were reported. Ordinal scale consists of 6 categories or clinical states that are exhaustive, mutually exclusive, and ordered: category 1) death; category 2) admitted to ICU; category 3) non-ICU hospitalization requiring supplemental oxygen; category 4) non-ICU hospitalization not requiring supplemental oxygen; category 5) not hospitalized, unable to resume normal activities; category 6) not hospitalized, resumption of normal activities. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Day 5/6 (Day of last study treatment)  |   |

| <b>End point values</b>     | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             |                 |  |   |  |
| Category 1                  | 0               | 0  | 0   |  |
| Category 2                  | 0               | 1  | 0   |  |
| Category 3                  | 2               | 5  | 1   |  |
| Category 4                  | 6               | 8  | 1   |  |
| Category 5                  | 5               | 2  | 1   |  |
| Category 6                  | 2               | 5  | 2   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with All-Cause Mortality

|  |   |
|--|---|
| End point title  | Number of Subjects with All-Cause Mortality |
| End point description:<br>All-cause mortality included all deaths of subjects due to any cause. Safety set included all subjects who received at least 1 dose of study drug, analyzed as treated. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type   | Secondary                                   |
| End point timeframe:<br>Up to 28 Days  |   |

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 16              | 27                                       | 6   |  |
| Units: Subjects             | 0               | 0  | 0   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: RSV RNA Viral Load Over Time

|   |                              |
|---|------------------------------|
| End point title   | RSV RNA Viral Load Over Time |
| End point description:<br>Antiviral activity RSV RNA viral load was measured in mid-turbinate nasal swabs (obtained from non-intubated subjects) or in mid-turbinate nasal swabs and endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling methods) using qRT-PCR performed at the central laboratory. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'n' (number analyzed) signifies number of subjects evaluable for each time point. Analyses were conducted on pooled groups across the 3 study parts. |                              |
| End point type  | Secondary                    |
| End point timeframe:<br>Days 2, 3, 4, 5, 6, 7, 10, 14 and 28  |                              |

| End point values                     | Placebo               | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-----------------------|--|---|--|
| Subject group type                   | Reporting group       | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 15                    | 21                                       | 5   |  |
| Units: log10 copies/mL               |                       |  |   |  |
| arithmetic mean (standard deviation) |                       |  |   |  |
| Day 2 (n=15,21,4)                    | 5.9257 (±<br>1.95951) | 4.7208 (±<br>1.60154)                    | 3.4242 (±<br>1.10867)                     |  |

|                    |                    |                    |                    |  |
|--------------------|--------------------|--------------------|--------------------|--|
| Day 3 (n=15,19,3)  | 4.8255 (± 1.84651) | 4.3515 (± 1.97633) | 4.3129 (± 0.99078) |  |
| Day 4 (n=15,21,3)  | 4.0608 (± 1.57493) | 3.9345 (± 1.64600) | 4.0729 (± 1.15419) |  |
| Day 5 (n=15,20,3)  | 3.6463 (± 1.44056) | 3.6206 (± 1.71515) | 4.5344 (± 0.97473) |  |
| Day 6 (n=15,19,3)  | 3.6996 (± 1.98383) | 3.4313 (± 1.57700) | 3.2163 (± 1.30083) |  |
| Day 7 (n=15,19,5)  | 3.4044 (± 1.75773) | 3.2306 (± 1.58432) | 2.6147 (± 0.89779) |  |
| Day 10 (n=15,15,4) | 2.5966 (± 1.04644) | 2.7516 (± 1.72825) | 2.5792 (± 1.00954) |  |
| Day 14 (n=15,21,4) | 2.3605 (± 1.00220) | 2.3010 (± 1.03732) | 2.1512 (± 0.50236) |  |
| Day 28 (n=14,21,4) | 1.9179 (± 0.06682) | 1.9714 (± 0.22559) | 1.9000 (± 0.00000) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Peak Viral Load

|   |                 |
|---|-----------------|
| End point title   | Peak Viral Load |
| End point description:<br>Peak Viral load is the highest value of log10 viral load at or after the baseline measurement. Peak viral load over time was measured by qRT-PCR. |                 |
| End point type  | Secondary       |
| End point timeframe:<br>Up to 28 Days   |                 |

| End point values                     | Placebo           | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |  |
|--------------------------------------|-------------------|------------------------------------|-------------------------------------|--|
| Subject group type                   | Reporting group   | Reporting group                    | Reporting group                     |  |
| Number of subjects analysed          | 0 <sup>[27]</sup> | 0 <sup>[28]</sup>                  | 0 <sup>[29]</sup>                   |  |
| Units: Copies/mL                     |                   |                                    |                                     |  |
| arithmetic mean (standard deviation) | ()                | ()                                 | ()                                  |  |

Notes:

[27] - Data was not collected and analyzed because this study was stopped prematurely.

[28] - Data was not collected and analyzed because this study was stopped prematurely.

[29] - Data was not collected and analyzed because this study was stopped prematurely.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Peak Viral Load

|  |                         |
|--|-------------------------|
| End point title  | Time to Peak Viral Load |
| End point description:<br>Time to peak viral load is the time from initiation of study treatment until the first time point with the |                         |

peak viral load.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 28 Days        |           |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[30]</sup> | 0 <sup>[31]</sup>                        | 0 <sup>[32]</sup>                         |  |
| Units: Hours                         |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[30] - Data was not collected and analyzed because this study was stopped prematurely.

[31] - Data was not collected and analyzed because this study was stopped prematurely.

[32] - Data was not collected and analyzed because this study was stopped prematurely.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Rate of Decline of Viral Load

|   |                               |
|---|-------------------------------|
| End point title   | Rate of Decline of Viral Load |
| End point description:  |                               |
| Rate of decline of viral load over the first 24 hours calculated as a log decline/24 hours defined as: 24-hour log viral load after first dose of study drug minus (-) log viral load at baseline divided by (/) date/time of 24-hour viral load sample – date/time of baseline viral load. |                               |
| End point type  | Secondary                     |
| End point timeframe:  |                               |
| Up to 28 Days   |                               |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[33]</sup> | 0 <sup>[34]</sup>                        | 0 <sup>[35]</sup>                         |  |
| Units: copies/ml                     |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[33] - Data was not collected and analyzed because this study was stopped prematurely.

[34] - Data was not collected and analyzed because this study was stopped prematurely.

[35] - Data was not collected and analyzed because this study was stopped prematurely.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to RSV RNA Viral Load Being Undetectable

|   |   |
|---|---|
| End point title   | Time to RSV RNA Viral Load Being Undetectable |
| End point description:<br>It is the time in hours from initiation of study treatment until the first post baseline time point at which the virus is undetectable in an assessment and after which time no detectable virus assessment follows as measured by qRT-PCR. |   |
| End point type  | Secondary                                     |
| End point timeframe:<br>Up to 28 Days   |   |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[36]</sup> | 0 <sup>[37]</sup>                        | 0 <sup>[38]</sup>                         |  |
| Units: Hours                         |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[36] - Data was not collected and analyzed because this study was stopped prematurely.

[37] - Data was not collected and analyzed because this study was stopped prematurely.

[38] - Data was not collected and analyzed because this study was stopped prematurely.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Undetectable Viral Load

|   |   |
|---|---|
| End point title   | Number of Subjects with Undetectable Viral Load |
| End point description:<br>Number of subjects with undetectable viral load up to 28 days were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Analyses were conducted on pooled groups across the 3 study parts. |   |
| End point type  | Secondary                                       |
| End point timeframe:<br>Up to 28 Days   |   |

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 15              | 21                                       | 5   |  |
| Units: Subjects             | 14              | 19                                       | 5   |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: RSV RNA Viral Load AUC up to Day 14**

|   |                                     |
|---|-------------------------------------|
| End point title   | RSV RNA Viral Load AUC up to Day 14 |
| End point description:<br>RSV RNA viral load was measured in midturbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling). |                                     |
| End point type  | Secondary                           |
| End point timeframe:<br>Up to Day 14  |                                     |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[39]</sup> | 0 <sup>[40]</sup>                        | 0 <sup>[41]</sup>                         |  |
| Units: Log10 copies/mL/day           |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[39] - Data was not collected and analyzed because this study was stopped prematurely.

[40] - Data was not collected and analyzed because this study was stopped prematurely.

[41] - Data was not collected and analyzed because this study was stopped prematurely.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: RSV RNA Viral Load AUC in Subjects Assigned to a Longer Dosing Duration**

|   |   |
|---|---|
| End point title   | RSV RNA Viral Load AUC in Subjects Assigned to a Longer Dosing Duration |
| End point description:<br>RSV RNA viral load was measured in midturbinate nasal swabs and in endotracheal samples (obtained from intubated subjects or via suction through tracheostomy or other sampling. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized). |   |
| End point type  | Secondary   |
| End point timeframe:<br>Up to 1 Day after the last dose of study drug   |   |

| End point values                     | Placebo           | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|--------------------------------------|-------------------|--|---|--|
| Subject group type                   | Reporting group   | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed          | 0 <sup>[42]</sup> | 0 <sup>[43]</sup>                        | 0 <sup>[44]</sup>                         |  |
| Units: log10 copies/mL/day           |                   |  |   |  |
| arithmetic mean (standard deviation) | ()                | ()                                       | ()  |  |

Notes:

[42] - No subject received extended treatment, therefore data was not analyzed.

[43] - No subject received extended treatment, therefore data was not analyzed.



## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Postbaseline Changes in the RSV Polymerase L Gene and Other Regions of the RSV Genome Compared with Baseline Sequences

|                 |  |
|-----------------|--|
| End point title | Number of Subjects with Postbaseline Changes in the RSV Polymerase L Gene and Other Regions of the RSV Genome Compared with Baseline Sequences |
|-----------------|--|

End point description:

Number of subjects with postbaseline changes in the RSV polymerase L gene and other regions of the RSV genome compared with baseline sequences were reported. ITT-i set included all randomly assigned subjects who received at least 1 dose of study drug and who had an RSV infection confirmed by a PCR-based assay at the central laboratory at baseline, analyzed as randomized. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint. Analyses were conducted on pooled groups across the 3 study parts.

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

End point timeframe:

Baseline up to 28 Days

| End point values            | Placebo         | 750 mg LD /<br>250 mg MD<br>Lumicitabine | 1000 mg LD /<br>500 mg MD<br>Lumicitabine |  |
|-----------------------------|-----------------|--|---|--|
| Subject group type          | Reporting group | Reporting group                          | Reporting group                           |  |
| Number of subjects analysed | 10              | 12                                       | 4   |  |
| Units: Subjects             | 0               | 0  | 0   |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 28 Days

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

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

### Reporting groups

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

Reporting group description:

Subjects received a single loading dose (LD) (Dose 1) of matching placebo tablet orally on Day 1 followed by nine maintenance doses (MD) (Doses 2 to 10) of matching placebo tablets orally twice daily (bid) from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | 750 mg LD / 250 mg MD Lumicitabine |
|-----------------------|------------------------------------|

Reporting group description:

Subjects received a single 750 milligram (mg) LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 250 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

|                       |                                     |
|-----------------------|-------------------------------------|
| Reporting group title | 1000 mg LD / 500 mg MD Lumicitabine |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects received a single 1000 mg LD (Dose 1) of lumicitabine tablet orally followed by nine MD (Doses 2 to 10) of 500 mg lumicitabine tablets orally bid from Day 1/2 to Day 5/6 (depending on the timing of the LD administration).

| Serious adverse events                            | Placebo         | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |
|---|-----------------|------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events |                 |                                    |                                     |
| subjects affected / exposed                       | 2 / 16 (12.50%) | 4 / 27 (14.81%)                    | 1 / 6 (16.67%)                      |
| number of deaths (all causes)                     | 0               | 0                                  | 0                                   |
| number of deaths resulting from adverse events    |                 |                                    |                                     |
| Injury, poisoning and procedural complications    |                 |                                    |                                     |
| Thermal Burn                                      |                 |                                    |                                     |
| subjects affected / exposed                       | 1 / 16 (6.25%)  | 0 / 27 (0.00%)                     | 0 / 6 (0.00%)                       |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0                              | 0 / 0                               |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0                              | 0 / 0                               |
| Cardiac disorders                                 |                 |                                    |                                     |
| Cardiac Failure                                   |                 |                                    |                                     |
| subjects affected / exposed                       | 1 / 16 (6.25%)  | 0 / 27 (0.00%)                     | 0 / 6 (0.00%)                       |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0                              | 0 / 0                               |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0                              | 0 / 0                               |
| Blood and lymphatic system disorders              |                 |                                    |                                     |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Pancytopenia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 27 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Intestinal Obstruction                          |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 27 (3.70%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic Obstructive Pulmonary Disease           |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 27 (3.70%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Rash  |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 27 (3.70%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Influenza                                       |                |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 27 (3.70%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 27 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                           | Placebo         | 750 mg LD / 250 mg MD Lumicitabine | 1000 mg LD / 500 mg MD Lumicitabine |
|---|-----------------|------------------------------------|-------------------------------------|
| Total subjects affected by non-serious adverse events       |                 |                                    |                                     |
| subjects affected / exposed                                 | 6 / 16 (37.50%) | 17 / 27 (62.96%)                   | 5 / 6 (83.33%)                      |
| <b>Vascular disorders</b>                                   |                 |                                    |                                     |
| Deep Vein Thrombosis  |                 |                                    |                                     |
| subjects affected / exposed                                 | 0 / 16 (0.00%)  | 0 / 27 (0.00%)                     | 1 / 6 (16.67%)                      |
| occurrences (all)   | 0               | 0                                  | 1                                   |
| Hypertension  |                 |                                    |                                     |
| subjects affected / exposed                                 | 1 / 16 (6.25%)  | 1 / 27 (3.70%)                     | 0 / 6 (0.00%)                       |
| occurrences (all)   | 4               | 1                                  | 0                                   |
| <b>General disorders and administration site conditions</b> |                 |                                    |                                     |
| Asthenia  |                 |                                    |                                     |
| subjects affected / exposed                                 | 1 / 16 (6.25%)  | 0 / 27 (0.00%)                     | 0 / 6 (0.00%)                       |
| occurrences (all)   | 1               | 0                                  | 0                                   |
| Chest Pain  |                 |                                    |                                     |
| subjects affected / exposed                                 | 2 / 16 (12.50%) | 2 / 27 (7.41%)                     | 0 / 6 (0.00%)                       |
| occurrences (all)   | 3               | 2                                  | 0                                   |
| Oedema Peripheral   |                 |                                    |                                     |
| subjects affected / exposed                                 | 1 / 16 (6.25%)  | 0 / 27 (0.00%)                     | 0 / 6 (0.00%)                       |
| occurrences (all)   | 1               | 0                                  | 0                                   |
| Pyrexia   |                 |                                    |                                     |
| subjects affected / exposed                                 | 0 / 16 (0.00%)  | 0 / 27 (0.00%)                     | 1 / 6 (16.67%)                      |
| occurrences (all)   | 0               | 0                                  | 1                                   |
| <b>Respiratory, thoracic and mediastinal disorders</b>      |                 |                                    |                                     |
| Asthma  |                 |                                    |                                     |
| subjects affected / exposed                                 | 0 / 16 (0.00%)  | 2 / 27 (7.41%)                     | 0 / 6 (0.00%)                       |
| occurrences (all)   | 0               | 2                                  | 0                                   |
| Chronic Obstructive Pulmonary Disease                       |                 |                                    |                                     |
| subjects affected / exposed                                 | 0 / 16 (0.00%)  | 0 / 27 (0.00%)                     | 1 / 6 (16.67%)                      |
| occurrences (all)   | 0               | 0                                  | 1                                   |
| Haemoptysis   |                 |                                    |                                     |
| subjects affected / exposed                                 | 0 / 16 (0.00%)  | 0 / 27 (0.00%)                     | 1 / 6 (16.67%)                      |
| occurrences (all)   | 0               | 0                                  | 2                                   |
| <b>Psychiatric disorders</b>                                |                 |                                    |                                     |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 16 (12.50%)<br>2 | 0 / 27 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Investigations   |                      |                     |                     |
| Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)     | 1 / 16 (6.25%)<br>1  | 2 / 27 (7.41%)<br>2 | 1 / 6 (16.67%)<br>1 |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0  | 1 / 27 (3.70%)<br>1 | 1 / 6 (16.67%)<br>1 |
| Blood Creatine Phosphokinase Increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0  | 2 / 27 (7.41%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Blood Fibrinogen Increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 16 (6.25%)<br>1  | 0 / 27 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| C-Reactive Protein Increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 16 (6.25%)<br>1  | 0 / 27 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Eosinophil Count Increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 16 (6.25%)<br>1  | 0 / 27 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Gamma-Glutamyltransferase Increased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 16 (6.25%)<br>1  | 1 / 27 (3.70%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Hepatic Enzyme Increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 16 (0.00%)<br>0  | 0 / 27 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Occult Blood Positive<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 16 (0.00%)<br>0  | 0 / 27 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Injury, poisoning and procedural complications<br>Overdose                                 |                      |                     |                     |

|  |                     |                      |                    |
|--|---------------------|----------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 16 (6.25%)<br>1 | 3 / 27 (11.11%)<br>3 | 0 / 6 (0.00%)<br>0 |
| Nervous system disorders                         |                     |                      |                    |
| Headache   |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 2 / 27 (7.41%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 2                    | 0                  |
| Somnolence                                       |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 27 (0.00%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 0                    | 1                  |
| Blood and lymphatic system disorders             |                     |                      |                    |
| Eosinophilia                                     |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 27 (0.00%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 0                    | 1                  |
| Febrile Neutropenia                              |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 27 (0.00%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 0                    | 1                  |
| Gastrointestinal disorders                       |                     |                      |                    |
| Abdominal Pain Upper                             |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 2 / 27 (7.41%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 2                    | 1                  |
| Diarrhoea  |                     |                      |                    |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 1 / 27 (3.70%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 1                    | 0                  |
| Gastritis  |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 27 (0.00%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 0                    | 1                  |
| Hepatobiliary disorders                          |                     |                      |                    |
| Hepatic Function Abnormal                        |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 2 / 27 (7.41%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 2                    | 0                  |
| Skin and subcutaneous tissue disorders           |                     |                      |                    |
| Acne   |                     |                      |                    |
| subjects affected / exposed                      | 1 / 16 (6.25%)      | 0 / 27 (0.00%)       | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 0                    | 0                  |
| Alopecia   |                     |                      |                    |
| subjects affected / exposed                      | 0 / 16 (0.00%)      | 0 / 27 (0.00%)       | 1 / 6 (16.67%)     |
| occurrences (all)                                | 0                   | 0                    | 1                  |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Erythema  |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 27 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Haemorrhage Subcutaneous                        |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 27 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Hyperhidrosis                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 2 / 27 (7.41%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 2               | 0              |
| Rash  |                |                 |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 3 / 27 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 1              | 3               | 1              |
| Renal and urinary disorders                     |                |                 |                |
| Nephrolithiasis                                 |                |                 |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 27 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0              |
| Renal Impairment                                |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 27 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| Myalgia   |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 2 / 27 (7.41%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 2               | 0              |
| Infections and infestations                     |                |                 |                |
| Acarodermatitis                                 |                |                 |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 27 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0              |
| Respiratory Tract Infection Bacterial           |                |                 |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 27 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0              |
| Urinary Tract Infection                         |                |                 |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 27 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Metabolism and nutrition disorders              |                |                 |                |
| Hyperglycaemia                                  |                |                 |                |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 27 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 2              | 0              | 0             |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 19 July 2016      | The overall reason for the amendment 1 was to add an inclusion criteria for female subjects to assure that woman agree not to donate eggs, and to add a section on rash management.  |
| 13 January 2017   | The overall reason for the amendment 2 was to create a new Part 1 of the study protocol to characterize the pharmacokinetics (PK), to confirm the population pharmacokinetic (popPK) model derived from healthy volunteers in hospitalized adults with respiratory syncytial virus (RSV) infection, and to more clearly define the study eligibility criteria to ensure subject safety. Furthermore, changes requested by health authorities were made: women of childbearing potential were allowed to participate in the study, the age limit for subjects was lowered, the endpoints of the study were updated, subjects on extracorporeal membrane oxygenation were excluded, the guidelines concerning corticosteroid use were adjusted, clarifications regarding the use of the electronic clinical outcome assessment (eCOA) device were added single electrocardiogram (ECG) measurements were changed to triplicate ECGs and the dose dispensing instructions were deleted. |
| 05 September 2017 | The overall reason for the amendment 3 was to remove furosemide, ibuprofen, and trimethoprim/sulfamethoxazole from the list of prohibited moderate/strong inhibitors of organic anion transporter (OAT) 3.   |
| 20 March 2018     | The overall reason for the amendment 4 was for Part 2 of the study (1) to include additional safety samples for biochemistry, (2) to lift the requirement for triplicate electrocardiograms (ECGs) and reduce the ECG timepoints, (3) to prohibit the use of P-glycoprotein (P-gp) inhibitors and inducers, and (4) to optimize the PK sampling scheme.  |

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.

As the study was stopped prematurely the planned final analyses were adapted. Due to small number of subjects in Part 2, it was decided to pool the data from the 3 parts of the study to perform an evaluation of selected planned analyses only.

Notes: