



## Clinical trial results:

### A Phase 3, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Lumacaftor in Combination With Ivacaftor in Subjects Aged 6 Through 11 Years With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2015-000543-16    |
| Trial protocol           | GB DE SE DK BE FR |
| Global end of trial date | 20 September 2016 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 19 April 2017 |
| First version publication date | 19 April 2017 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | VX14-809-109 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02514473 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Vertex Pharmaceuticals Incorporated  |
| Sponsor organisation address | 50 Northern Avenue, Boston, Massachusetts, United States, 022101862                        |
| Public contact               | Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com |
| Scientific contact           | Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001582-PIP01-13 |
| 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? | Yes                 |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 11 October 2016   |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 20 September 2016 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 20 September 2016 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of lumacaftor (LUM) in combination with ivacaftor (IVA) in subjects aged 6 through 11 years with cystic fibrosis (CF), homozygous for the F508del CF transmembrane conductance regulator (CFTR) mutation.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Council on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 23 July 2015 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 103 |
| Country: Number of subjects enrolled | Canada: 17         |
| Country: Number of subjects enrolled | Belgium: 15        |
| Country: Number of subjects enrolled | Germany: 11        |
| Country: Number of subjects enrolled | France: 14         |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Denmark: 7         |
| Country: Number of subjects enrolled | Sweden: 1          |
| Country: Number of subjects enrolled | Australia: 28      |
| Worldwide total number of subjects   | 206                |
| EEA total number of subjects         | 58                 |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|  |     |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 206 |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 0   |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 206 subjects were randomized in the study, of which 204 subjects were exposed to study treatment (101 subjects received 'Placebo' and 103 subjects received 'LUM/IVA').

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Subjects received placebo matched to lumacaftor (LUM, VX-809) in combination with ivacaftor (IVA, VX-770) fixed-dose combination (FDC) tablet orally every 12 hours (q12h) for 24 weeks.

|  |          |
|--|----------|
| 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:

Placebo matched to LUM in combination with IVA FDC tablet q12h for 24 weeks.

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

Arm description:

Subjects received LUM 200 milligram (mg) in combination with IVA 250 mg FDC tablet orally q12h for 24 weeks.

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Lumacaftor/Ivacaftor FDC |
| Investigational medicinal product code | VX-809/VX-770            |
| Other name                             |                          |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

LUM 200 mg in combination with IVA 250 mg tablet orally q12h for 24 weeks.

| Number of subjects in period<br>1[1] | Placebo | LUM/IVA |
|--------------------------------------|---------|---------|
|                                      |         |         |
| Started                              | 101     | 103     |
| Completed                            | 98      | 98      |
| Not completed                        | 3       | 5       |
| Consent withdrawn by subject         | 2       | 1       |
| Adverse event                        | -       | 2       |
| Unspecified                          | 1       | 1       |
| Lost to follow-up                    | -       | 1       |

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Notes:

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

Justification: A total of 206 subjects were randomized in the study, of which 204 subjects were exposed to study drug (101 subjects received 'Placebo' and 103 subjects received 'LUM/IVA'). Subject Disposition and Baseline Characteristics are presented for the 204 subjects who received the study treatment.

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Subjects received placebo matched to lumacaftor (LUM, VX-809) in combination with ivacaftor (IVA, VX-770) fixed-dose combination (FDC) tablet orally every 12 hours (q12h) for 24 weeks.

|                       |         |
|-----------------------|---------|
| Reporting group title | LUM/IVA |
|-----------------------|---------|

Reporting group description:

Subjects received LUM 200 milligram (mg) in combination with IVA 250 mg FDC tablet orally q12h for 24 weeks.

| Reporting group values             | Placebo | LUM/IVA | Total |
|------------------------------------|---------|---------|-------|
| Number of subjects                 | 101     | 103     | 204   |
| Age categorical<br>Units: Subjects |         |         |       |

|   |               |              |     |
|---|---------------|--------------|-----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 8.9<br>± 1.59 | 8.7<br>± 1.6 | -   |
| Gender categorical<br>Units: Subjects                                   |               |              |     |
| Female  | 58            | 63           | 121 |
| Male  | 43            | 40           | 83  |

## End points

### End points reporting groups

|  |         |
|--|---------|
| Reporting group title  | Placebo |
| Reporting group description:<br>Subjects received placebo matched to lumacaftor (LUM, VX-809) in combination with ivacaftor (IVA, VX-770) fixed-dose combination (FDC) tablet orally every 12 hours (q12h) for 24 weeks. |         |
| Reporting group title  | LUM/IVA |
| Reporting group description:<br>Subjects received LUM 200 milligram (mg) in combination with IVA 250 mg FDC tablet orally q12h for 24 weeks.   |         |

### Primary: Absolute Change From Baseline in Lung Clearance Index 2.5 (LCI2.5) Through Week 24

|   |  |
|---|--|
| End point title   | Absolute Change From Baseline in Lung Clearance Index 2.5 (LCI2.5) Through Week 24 |
| End point description:<br>Lung clearance index (LCI) is a measure of ventilation inhomogeneity that is derived from a multiple breath washout test using Nitrogen (N <sub>2</sub> ). LCI2.5 represents the number of lung turnovers required to reduce the end tidal inert gas concentration to 1/40th of its starting value. Analysis was performed on the Full Analysis Set (FAS), which included all randomized subjects who received any amount of study drug. Here, number of subjects analyzed signifies subjects who were evaluable for this endpoint. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline through Week 24  |  |

| End point values                    | Placebo         | LUM/IVA         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 99              | 99              |  |  |
| Units: Ratio                        |                 |                 |  |  |
| least squares mean (standard error) | 0.08 (± 0.13)   | -1.01 (± 0.13)  |  |  |

### Statistical analyses

|   |                        |
|---|------------------------|
| Statistical analysis title  | Statistical Analysis 1 |
| Statistical analysis description:<br>Analysis was performed using mixed-effects model for repeated measures (MMRM). The model included treatment, visit and treatment-by-visit interaction as fixed effects; and subject as a random effect with adjustments for weight (less than [ $<$ ] 25 kilogram [kg] versus greater than or equal to [ $\geq$ ] 25 kg) and percent predicted forced expiratory volume in 1 second (FEV1) severity ( $<90$ versus $\geq 90$ ) at screening. |                        |
| Comparison groups   | LUM/IVA v Placebo      |

|   |                    |
|---|--------------------|
| Number of subjects included in analysis | 198                |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | superiority        |
| P-value                                 | < 0.0001           |
| Method                                  | MMRM               |
| Parameter estimate                      | LS Mean Difference |
| Point estimate                          | -1.09              |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | -1.43              |
| upper limit                             | -0.75              |



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 28

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Subjects received placebo matched to LUM in combination with IVA FDC tablet orally q12h for 24 weeks.

|                       |         |
|-----------------------|---------|
| Reporting group title | LUM/IVA |
|-----------------------|---------|

Reporting group description:

Subjects received LUM 200 mg in combination with IVA 250 mg FDC tablet orally q12h for 24 weeks.

| Serious adverse events                            | Placebo           | LUM/IVA           |  |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events |                   |                   |  |
| subjects affected / exposed                       | 11 / 101 (10.89%) | 13 / 103 (12.62%) |  |
| number of deaths (all causes)                     | 0                 | 0                 |  |
| number of deaths resulting from adverse events    |                   |                   |  |
| Investigations                                    |                   |                   |  |
| Bacterial test positive                           |                   |                   |  |
| subjects affected / exposed                       | 0 / 101 (0.00%)   | 1 / 103 (0.97%)   |  |
| occurrences causally related to treatment / all   | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Alanine aminotransferase increased                |                   |                   |  |
| subjects affected / exposed                       | 1 / 101 (0.99%)   | 0 / 103 (0.00%)   |  |
| occurrences causally related to treatment / all   | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Aspartate aminotransferase increased              |                   |                   |  |
| subjects affected / exposed                       | 1 / 101 (0.99%)   | 0 / 103 (0.00%)   |  |
| occurrences causally related to treatment / all   | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0             | 0 / 0             |  |
| Transaminases increased                           |                   |                   |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 103 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications       |                 |                 |  |
| Procedural anxiety                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                   |                 |                 |  |
| Poor venous access                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Drug interaction                                     |                 |                 |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Device related thrombosis                            |                 |                 |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 103 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders                 |                 |                 |  |
| Lymphadenitis  |                 |                 |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 103 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                           |                 |                 |  |
| Constipation   |                 |                 |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 103 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Distal intestinal obstruction syndrome               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                         | 2 / 101 (1.98%) | 0 / 103 (0.00%) |  |
| occurrences causally related to treatment / all     | 1 / 6           | 0 / 0           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders     |                 |                 |  |
| Obstructive airways disorder                        |                 |                 |  |
| subjects affected / exposed                         | 0 / 101 (0.00%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all     | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Infections and infestations                         |                 |                 |  |
| Infective pulmonary exacerbation of cystic fibrosis |                 |                 |  |
| subjects affected / exposed                         | 5 / 101 (4.95%) | 8 / 103 (7.77%) |  |
| occurrences causally related to treatment / all     | 0 / 6           | 0 / 8           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Bronchopulmonary aspergillosis allergic             |                 |                 |  |
| subjects affected / exposed                         | 0 / 101 (0.00%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |
| Pneumonia   |                 |                 |  |
| subjects affected / exposed                         | 1 / 101 (0.99%) | 1 / 103 (0.97%) |  |
| occurrences causally related to treatment / all     | 0 / 3           | 0 / 1           |  |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Placebo           | LUM/IVA           |  |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 98 / 101 (97.03%) | 98 / 103 (95.15%) |  |
| Investigations  |                   |                   |  |
| Alanine aminotransferase increased                    |                   |                   |  |
| subjects affected / exposed                           | 8 / 101 (7.92%)   | 8 / 103 (7.77%)   |  |
| occurrences (all)                                     | 10                | 10                |  |
| Bacterial test positive                               |                   |                   |  |

|  |                         |                         |  |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 8 / 101 (7.92%)<br>8    | 7 / 103 (6.80%)<br>7    |  |
| Aspartate aminotransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)                            | 6 / 101 (5.94%)<br>6    | 6 / 103 (5.83%)<br>7    |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                               | 9 / 101 (8.91%)<br>10   | 13 / 103 (12.62%)<br>19 |  |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 20 / 101 (19.80%)<br>25 | 15 / 103 (14.56%)<br>16 |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 11 / 101 (10.89%)<br>14 | 9 / 103 (8.74%)<br>9    |  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                 | 7 / 101 (6.93%)<br>7    | 13 / 103 (12.62%)<br>13 |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)   | 10 / 101 (9.90%)<br>12  | 10 / 103 (9.71%)<br>12  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 9 / 101 (8.91%)<br>11   | 10 / 103 (9.71%)<br>11  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 10 / 101 (9.90%)<br>11  | 10 / 103 (9.71%)<br>11  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 4 / 101 (3.96%)<br>4    | 6 / 103 (5.83%)<br>6    |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 8 / 101 (7.92%)<br>8    | 5 / 103 (4.85%)<br>5    |  |
| Respiratory, thoracic and mediastinal  |                         |                         |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| disorders   |                   |                   |  |
| Cough   |                   |                   |  |
| subjects affected / exposed                         | 47 / 101 (46.53%) | 46 / 103 (44.66%) |  |
| occurrences (all)                                   | 71                | 64                |  |
| Productive cough                                    |                   |                   |  |
| subjects affected / exposed                         | 6 / 101 (5.94%)   | 18 / 103 (17.48%) |  |
| occurrences (all)                                   | 7                 | 21                |  |
| Nasal congestion                                    |                   |                   |  |
| subjects affected / exposed                         | 8 / 101 (7.92%)   | 17 / 103 (16.50%) |  |
| occurrences (all)                                   | 9                 | 20                |  |
| Oropharyngeal pain                                  |                   |                   |  |
| subjects affected / exposed                         | 10 / 101 (9.90%)  | 15 / 103 (14.56%) |  |
| occurrences (all)                                   | 12                | 20                |  |
| Sputum increased                                    |                   |                   |  |
| subjects affected / exposed                         | 2 / 101 (1.98%)   | 11 / 103 (10.68%) |  |
| occurrences (all)                                   | 2                 | 11                |  |
| Rhinorrhoea   |                   |                   |  |
| subjects affected / exposed                         | 5 / 101 (4.95%)   | 10 / 103 (9.71%)  |  |
| occurrences (all)                                   | 6                 | 14                |  |
| Respiration abnormal                                |                   |                   |  |
| subjects affected / exposed                         | 4 / 101 (3.96%)   | 6 / 103 (5.83%)   |  |
| occurrences (all)                                   | 4                 | 8                 |  |
| Skin and subcutaneous tissue disorders              |                   |                   |  |
| Rash  |                   |                   |  |
| subjects affected / exposed                         | 1 / 101 (0.99%)   | 6 / 103 (5.83%)   |  |
| occurrences (all)                                   | 1                 | 6                 |  |
| Infections and infestations                         |                   |                   |  |
| Infective pulmonary exacerbation of cystic fibrosis |                   |                   |  |
| subjects affected / exposed                         | 16 / 101 (15.84%) | 13 / 103 (12.62%) |  |
| occurrences (all)                                   | 23                | 16                |  |
| Upper respiratory tract infection                   |                   |                   |  |
| subjects affected / exposed                         | 10 / 101 (9.90%)  | 13 / 103 (12.62%) |  |
| occurrences (all)                                   | 13                | 15                |  |
| Rhinitis  |                   |                   |  |
| subjects affected / exposed                         | 5 / 101 (4.95%)   | 6 / 103 (5.83%)   |  |
| occurrences (all)                                   | 7                 | 7                 |  |

|  |                       |                      |  |
|--|-----------------------|----------------------|--|
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 8 / 101 (7.92%)<br>13 | 5 / 103 (4.85%)<br>7 |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                  | 8 / 101 (7.92%)<br>9  | 5 / 103 (4.85%)<br>6 |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)  | 6 / 101 (5.94%)<br>6  | 4 / 103 (3.88%)<br>4 |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 6 / 101 (5.94%)<br>7  | 3 / 103 (2.91%)<br>3 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 01 September 2015 | Added serial post-dose spirometry assessments; added an additional PK sample. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported