



## Clinical trial results:

### Protocol TRO19622CLEQ1275-1 (WN29836) Phase II, Multicenter, Randomized, Adaptive, Double-Blind, Placebo Controlled Study to Assess Safety and Efficacy of Olesoxime (TRO19622) in 3-25 Year Old Spinal Muscular Atrophy (SMA) Patients

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2010-020386-24    |
| Trial protocol           | FR NL BE DE IT GB |
| Global end of trial date | 09 October 2013   |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 25 January 2018 |
| First version publication date | 25 January 2018 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | WN29836 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01302600 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                    |
|------------------------------|----------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | F. Hoffmann-La Roche AG                                                                            |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070                                                 |
| Public contact               | Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact           | Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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                       | 09 October 2013 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 09 October 2013 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 09 October 2013 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The main objectives of this study were to assess the efficacy and safety of olesoxime 10 milligrams per kilogram (mg/kg) once daily liquid suspension formulation in spinal muscular atrophy (SMA) Type 2 or Type 3 non-ambulant subjects, aged 3 - 25 years.

Protection of trial subjects:

Each subject, or the subject's representative, signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 18 November 2011 |
| 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 | Belgium: 16        |
| Country: Number of subjects enrolled | France: 29         |
| Country: Number of subjects enrolled | Germany: 20        |
| Country: Number of subjects enrolled | Italy: 52          |
| Country: Number of subjects enrolled | Netherlands: 9     |
| Country: Number of subjects enrolled | Poland: 20         |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Worldwide total number of subjects   | 165                |
| EEA total number of subjects         | 165                |

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)                     | 108 |

|                           |    |
|---------------------------|----|
| Adolescents (12-17 years) | 36 |
| Adults (18-64 years)      | 21 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Eligible subjects included 3 to 25 year-old patients with Type 2 or non-ambulant Type 3 SMA.

### 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                | Investigator, Subject          |

### Arms

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

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

Arm description:

Matching placebo, once a day for 104 weeks.

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

Dosage and administration details:

Matching placebo, once a day for 104 weeks.

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

Arm description:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Olesoxime       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

Dosage and administration details:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

| Number of subjects in period 1 | Placebo | Olesoxime |
|--------------------------------|---------|-----------|
| Started                        | 57      | 108       |
| Completed                      | 50      | 98        |
| Not completed                  | 7       | 10        |
| Consent withdrawn by subject   | 1       | 3         |
| Adverse event, non-fatal       | 2       | 4         |

|                                |   |   |
|--------------------------------|---|---|
| Death                          | 1 | 1 |
| Non-compliance with study drug | 1 | - |
| Reason not specified           | 2 | 2 |

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Matching placebo, once a day for 104 weeks.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Olesoxime |
|-----------------------|-----------|

Reporting group description:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

| Reporting group values                                | Placebo | Olesoxime | Total |
|-------------------------------------------------------|---------|-----------|-------|
| Number of subjects                                    | 57      | 108       | 165   |
| Age Categorical<br>Units: Subjects                    |         |           |       |
| In utero                                              | 0       | 0         | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0       | 0         | 0     |
| Newborns (0-27 days)                                  | 0       | 0         | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0       | 0         | 0     |
| Children (2-11 years)                                 | 30      | 78        | 108   |
| Adolescents (12-17 years)                             | 20      | 16        | 36    |
| Adults (18-64 years)                                  | 7       | 14        | 21    |
| From 65-84 years                                      | 0       | 0         | 0     |
| 85 years and over                                     | 0       | 0         | 0     |
| Age Continuous<br>Units: years                        |         |           |       |
| arithmetic mean                                       | 11.2    | 9.3       | -     |
| standard deviation                                    | ± 6.0   | ± 5.7     | -     |
| Gender Categorical<br>Units: Subjects                 |         |           |       |
| Female                                                | 32      | 51        | 83    |
| Male                                                  | 25      | 57        | 82    |

## End points

### End points reporting groups

|                                                                                           |           |
|-------------------------------------------------------------------------------------------|-----------|
| Reporting group title                                                                     | Placebo   |
| Reporting group description:<br>Matching placebo, once a day for 104 weeks.               |           |
| Reporting group title                                                                     | Olesoxime |
| Reporting group description:<br>Olesoxime, 10 mg/kg body weight once a day for 104 weeks. |           |

### Primary: Mean Change from Baseline to Week 104 in the Motor Function Measure (MFM) Dimensions 1 and 2 (D1+D2) Score

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Mean Change from Baseline to Week 104 in the Motor Function Measure (MFM) Dimensions 1 and 2 (D1+D2) Score |
| End point description:<br>The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. |                                                                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Primary                                                                                                    |
| End point timeframe:<br>Baseline to Week 104                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                            |

| End point values                    | Placebo              | Olesoxime           |  |  |
|-------------------------------------|----------------------|---------------------|--|--|
| Subject group type                  | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed         | 57                   | 103                 |  |  |
| Units: score                        |                      |                     |  |  |
| least squares mean (standard error) | -1.82 ( $\pm$ 0.901) | 0.18 ( $\pm$ 0.717) |  |  |

### Statistical analyses

|                                         |                       |
|-----------------------------------------|-----------------------|
| Statistical analysis title              | Statistical Analysis  |
| Comparison groups                       | Placebo v Olesoxime   |
| Number of subjects included in analysis | 160                   |
| Analysis specification                  | Pre-specified         |
| Analysis type                           | superiority           |
| P-value                                 | = 0.0676              |
| Method                                  | Mixed models analysis |

### Secondary: Change from Baseline in MFM Total Score at Week 104

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Change from Baseline in MFM Total Score at Week 104 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                     |
| The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. |                                                     |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Secondary                                           |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                     |
| Baseline to Week 104                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                     |

|                                     |                 |                 |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>             | Placebo         | Olesoxime       |  |  |
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 57              | 103             |  |  |
| Units: score                        |                 |                 |  |  |
| least squares mean (standard error) | -1.45 (± 0.943) | 0.59 (± 0.751)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Hammersmith Functional Motor Scale (HFMS) at Week 91

|                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                             | Change from Baseline in Hammersmith Functional Motor Scale (HFMS) at Week 91 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                      |                                                                              |
| The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. |                                                                              |
| End point type                                                                                                                                                                                                                                                                                                                                                                                              | Secondary                                                                    |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                        |                                                                              |
| Baseline to Week 91                                                                                                                                                                                                                                                                                                                                                                                         |                                                                              |

|                                     |                 |                 |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>             | Placebo         | Olesoxime       |  |  |
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 57              | 103             |  |  |
| Units: score                        |                 |                 |  |  |
| least squares mean (standard error) | -1.72 (± 0.515) | -0.78 (± 0.416) |  |  |

### Statistical analyses



No statistical analyses for this end point

### Secondary: Time to 4-Point Decrease on the HFMS Score

|                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                           | Time to 4-Point Decrease on the HFMS Score |
| End point description:<br>The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. 9999=not estimable. |                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                            | Secondary                                  |
| End point timeframe:<br>Up to Week 104                                                                                                                                                                                                                                                                                                                                                                                                                    |                                            |

| End point values                 | Placebo             | Olesoxime           |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 57                  | 103                 |  |  |
| Units: weeks                     |                     |                     |  |  |
| median (confidence interval 95%) | 9999 (91.4 to 9999) | 9999 (9999 to 9999) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Response for MFM D1+D2 Score at Week 104

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Percentage of Subjects with Response for MFM D1+D2 Score at Week 104 |
| End point description:<br>The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available. |                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                                                            |
| End point timeframe:<br>Baseline to Week 104                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                      |

| End point values              | Placebo         | Olesoxime       |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 57              | 103             |  |  |
| Units: percentage of subjects |                 |                 |  |  |
| number (not applicable)       | 38.6            | 54.4            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Response for MFM Total Score at Week 104

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | Percentage of Subjects with Response for MFM Total Score at Week 104 |
|-----------------|----------------------------------------------------------------------|

End point description:

The MFM is an assessment of functional motor abilities of subjects with neuromuscular disease comprising items rated on a 4-point scale (0 to 3). The MFM items are grouped into three functional dimensions D1, D2 and D3. Patient MFM scores were normalized to the maximum achievable score. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Baseline to Week 104

| End point values              | Placebo         | Olesoxime       |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 57              | 103             |  |  |
| Units: percentage of subjects |                 |                 |  |  |
| number (not applicable)       | 38.6            | 56.3            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects with Response for HFMS Score at Week 91

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Percentage of Subjects with Response for HFMS Score at Week 91 |
|-----------------|----------------------------------------------------------------|

End point description:

The HFMS consists of 20 items, assessing the subject's ability to perform various activities. Each activity is scored on a 3-point scoring system, with a score of 2 for unaided, 1 for assistance, and 0 for inability. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Baseline to Week 91

| End point values              | Placebo         | Olesoxime       |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 57              | 103             |  |  |
| Units: percentage of subjects |                 |                 |  |  |
| number (not applicable)       | 28.1            | 49.5            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104

|                 |                                                                             |
|-----------------|-----------------------------------------------------------------------------|
| End point title | Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104 |
|-----------------|-----------------------------------------------------------------------------|

End point description:

CMAP is an electromyography investigation (electrical study of muscle function). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Change from Baseline in Compound Muscle Action Potential (CMAP) at Week 104

| End point values                    | Placebo         | Olesoxime       |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 57              | 103             |  |  |
| Units: millivolts (mV)              |                 |                 |  |  |
| least squares mean (standard error) | -0.16 (± 0.294) | -0.07 (± 0.214) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Motor Unit Number Estimation (MUNE) at Week 104

|                 |                                                                         |
|-----------------|-------------------------------------------------------------------------|
| End point title | Change from Baseline in Motor Unit Number Estimation (MUNE) at Week 104 |
|-----------------|-------------------------------------------------------------------------|

End point description:

MUNE is a technique that can be used to determine the approximate number of motor neurons in a muscle or group of muscles. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Baseline to Week 104

| End point values                    | Placebo              | Olesoxime            |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed         | 57                   | 103                  |  |  |
| Units: mune                         |                      |                      |  |  |
| least squares mean (standard error) | -6.69 ( $\pm$ 5.106) | -4.51 ( $\pm$ 3.867) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Pediatric Quality of Life Inventory (PedsQL) Neuromuscular Module Score - Patient Report

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Pediatric Quality of Life Inventory (PedsQL) Neuromuscular Module Score - Patient Report |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

The PedsQL Neuromuscular Module Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5-18 years, and a parent proxy-report format for children ages 2-4 years. The PedsQL scale assess: the disease process and associated symptoms; the subject's ability to communicate with healthcare providers and others about his/her illness; and items related to family financial and social support systems. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Baseline to Week 104

| End point values                    | Placebo              | Olesoxime            |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed         | 47                   | 80                   |  |  |
| Units: score                        |                      |                      |  |  |
| least squares mean (standard error) | -3.49 ( $\pm$ 2.061) | -3.24 ( $\pm$ 1.729) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in PedsQL Neuromuscular Module Score - Parent/Caregiver Report at Week 104

|                 |                                                                                                 |
|-----------------|-------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in PedsQL Neuromuscular Module Score - Parent/Caregiver Report at Week 104 |
|-----------------|-------------------------------------------------------------------------------------------------|

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**End point description:**

The PedsQL Neuromuscular Module Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5-18 years, and a parent proxy-report format for children ages 2-4 years. The PedsQL scale assesses: the disease process and associated symptoms; the subject's ability to communicate with healthcare providers and others about his/her illness; and items related to family financial and social support systems. The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

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End point timeframe:

Baseline to Week 104

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| End point values                    | Placebo              | Olesoxime            |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed         | 57                   | 103                  |  |  |
| Units: score                        |                      |                      |  |  |
| least squares mean (standard error) | -5.67 ( $\pm$ 1.954) | -2.06 ( $\pm$ 1.564) |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change from Baseline in Forced Expiratory Vital Capacity (FVC)/Theoretical Capacity (TC) at Week 104**

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|                 |                                                                                                      |
|-----------------|------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline in Forced Expiratory Vital Capacity (FVC)/Theoretical Capacity (TC) at Week 104 |
|-----------------|------------------------------------------------------------------------------------------------------|

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**End point description:**

Pulmonary Function was assessed in subjects 5 years or older by measuring FVC (as percent predicted for age and height). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

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End point timeframe:

Baseline to Week 104

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| End point values                    | Placebo             | Olesoxime           |  |  |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type                  | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed         | 47                  | 80                  |  |  |
| Units: percent                      |                     |                     |  |  |
| least squares mean (standard error) | 6.16 ( $\pm$ 2.601) | 4.28 ( $\pm$ 2.316) |  |  |

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**Statistical analyses**

No statistical analyses for this end point

### Secondary: Clinical Global Impression of Change - Patient/Caregiver Assessment at Week 104

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Clinical Global Impression of Change - Patient/Caregiver Assessment at Week 104 |
|-----------------|---------------------------------------------------------------------------------|

End point description:

The CGI-C measures global improvement or change and is rated on a 7-point scale, with scores ranging from 1 (very much improved) through to 7 (very much worse). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Week 104

| End point values              | Placebo         | Olesoxime       |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 57              | 103             |  |  |
| Units: percentage of subjects |                 |                 |  |  |
| number (not applicable)       |                 |                 |  |  |
| Very much improved            | 0.0             | 1.0             |  |  |
| Much improved                 | 6.1             | 3.1             |  |  |
| Minimally improved            | 16.3            | 20.8            |  |  |
| No change                     | 59.2            | 66.7            |  |  |
| Minimally worse               | 12.2            | 7.3             |  |  |
| Much worse                    | 6.1             | 1.0             |  |  |
| Very much worse               | 0.0             | 0.0             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical Global Impression of Change at Week 104 - Physician Assessment

|                 |                                                                         |
|-----------------|-------------------------------------------------------------------------|
| End point title | Clinical Global Impression of Change at Week 104 - Physician Assessment |
|-----------------|-------------------------------------------------------------------------|

End point description:

The CGI-C measures global improvement or change and is rated on a 7-point scale, with scores ranging from 1 (very much improved) through to 7 (very much worse). The full analysis set (FAS) included all randomized subjects who received at least one dose of study drug and who had at least one post-randomization assessment of MFM available.

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

End point timeframe:

Week 104

| <b>End point values</b>       | Placebo         | Olesoxime       |  |  |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type            | Reporting group | Reporting group |  |  |
| Number of subjects analysed   | 57              | 103             |  |  |
| Units: percentage of subjects |                 |                 |  |  |
| number (not applicable)       |                 |                 |  |  |
| Very much improved            | 0.0             | 0.0             |  |  |
| Much improved                 | 6.0             | 1.0             |  |  |
| Minimally improved            | 8.0             | 16.7            |  |  |
| No change                     | 66.0            | 75.0            |  |  |
| Minimally worse               | 18.0            | 7.3             |  |  |
| Much worse                    | 2.0             | 0.0             |  |  |
| Very much worse               | 0.0             | 0.0             |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 2 years.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Matching placebo, once a day for 104 weeks.

|                       |           |
|-----------------------|-----------|
| Reporting group title | Olesoxime |
|-----------------------|-----------|

Reporting group description:

Olesoxime, 10 mg/kg body weight once a day for 104 weeks.

| Serious adverse events                            | Placebo          | Olesoxime         |  |
|---------------------------------------------------|------------------|-------------------|--|
| Total subjects affected by serious adverse events |                  |                   |  |
| subjects affected / exposed                       | 29 / 57 (50.88%) | 34 / 108 (31.48%) |  |
| number of deaths (all causes)                     | 1                | 1                 |  |
| number of deaths resulting from adverse events    |                  |                   |  |
| Surgical and medical procedures                   |                  |                   |  |
| Appendicectomy                                    |                  |                   |  |
| subjects affected / exposed                       | 1 / 57 (1.75%)   | 0 / 108 (0.00%)   |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0             |  |
| Arthrodesis                                       |                  |                   |  |
| subjects affected / exposed                       | 1 / 57 (1.75%)   | 0 / 108 (0.00%)   |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0             |  |
| Device therapy                                    |                  |                   |  |
| subjects affected / exposed                       | 1 / 57 (1.75%)   | 0 / 108 (0.00%)   |  |
| occurrences causally related to treatment / all   | 0 / 4            | 0 / 0             |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0             |  |
| Fracture treatment                                |                  |                   |  |



|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Gastrostomy                                     |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hospitalisation                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Mechanical ventilation                          |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Scoliosis surgery                               |                |                 |  |
| subjects affected / exposed                     | 2 / 57 (3.51%) | 5 / 108 (4.63%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 5           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Spinal fusion surgery                           |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Spinal operation                                |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Spinal rod insertion                            |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Tenotomy                                        |                |                 |  |

|                                                      |                |                 |  |
|------------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Tooth extraction                                     |                |                 |  |
| subjects affected / exposed                          | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| 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 |                |                 |  |
| Asthenia                                             |                |                 |  |
| subjects affected / exposed                          | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Chest pain                                           |                |                 |  |
| subjects affected / exposed                          | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Pyrexia                                              |                |                 |  |
| subjects affected / exposed                          | 2 / 57 (3.51%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all      | 0 / 3          | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Unevaluable event                                    |                |                 |  |
| subjects affected / exposed                          | 0 / 57 (0.00%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders      |                |                 |  |
| Acute respiratory failure                            |                |                 |  |
| subjects affected / exposed                          | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |
| Atelectasis                                          |                |                 |  |
| subjects affected / exposed                          | 1 / 57 (1.75%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 1 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| Cough                                           |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Dyspnoea                                        |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hypoventilation                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Lung disorder                                   |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Obstructive airways disorder                    |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1           |  |
| Pleurisy                                        |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Respiratory failure                             |                |                 |  |
| subjects affected / exposed                     | 2 / 57 (3.51%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Restrictive pulmonary disease                   |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Tonsillar hypertrophy                           |                |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Tracheal disorder                               |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Investigations                                  |                |                 |  |
| Activated partial thromboplastin time prolonged |                |                 |  |
| subjects affected / exposed                     | 2 / 57 (3.51%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Alanine aminotransferase increased              |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Aspartate aminotransferase increased            |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Bronchoscopy                                    |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Coagulation factor VIII level decreased         |                |                 |  |
| subjects affected / exposed                     | 2 / 57 (3.51%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hepatic enzyme increased                        |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |

|                                                            |                |                 |  |
|------------------------------------------------------------|----------------|-----------------|--|
| Oxygen saturation decreased<br>subjects affected / exposed | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 2           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Pulmonary function test<br>subjects affected / exposed     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Sleep study<br>subjects affected / exposed                 | 0 / 57 (0.00%) | 2 / 108 (1.85%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 2           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Transaminases increased<br>subjects affected / exposed     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to<br>treatment / all         | 1 / 1          | 0 / 0           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Injury, poisoning and procedural<br>complications          |                |                 |  |
| Concussion<br>subjects affected / exposed                  | 0 / 57 (0.00%) | 2 / 108 (1.85%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 2           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Fall<br>subjects affected / exposed                        | 2 / 57 (3.51%) | 2 / 108 (1.85%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 2          | 0 / 2           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Femur fracture<br>subjects affected / exposed              | 0 / 57 (0.00%) | 2 / 108 (1.85%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 2           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |
| Fibula fracture<br>subjects affected / exposed             | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all         | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all              | 0 / 0          | 0 / 0           |  |

|                                                      |                |                 |  |
|------------------------------------------------------|----------------|-----------------|--|
| Fracture displacement<br>subjects affected / exposed | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 1          | 0 / 0           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Greenstick fracture<br>subjects affected / exposed   | 1 / 57 (1.75%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 1          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Head injury<br>subjects affected / exposed           | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Humerus fracture<br>subjects affected / exposed      | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Road traffic accident<br>subjects affected / exposed | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Tibia fracture<br>subjects affected / exposed        | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Congenital, familial and genetic<br>disorders        |                |                 |  |
| Cryptorchism<br>subjects affected / exposed          | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |
| Frenulum breve<br>subjects affected / exposed        | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all        | 0 / 0          | 0 / 0           |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| Cardiac disorders                               |                |                 |  |
| Cardiac arrest                                  |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0           |  |
| Nervous system disorders                        |                |                 |  |
| Neuralgia                                       |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Subarachnoid haemorrhage                        |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Tremor                                          |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Blood and lymphatic system disorders            |                |                 |  |
| Coagulopathy                                    |                |                 |  |
| subjects affected / exposed                     | 2 / 57 (3.51%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 2 / 2          | 2 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Gastrointestinal disorders                      |                |                 |  |
| Abdominal pain                                  |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Abdominal pain upper                            |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Nausea                                          |                |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Vomiting                                        |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 3 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Renal and urinary disorders                     |                |                 |  |
| Haematuria                                      |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Ketonuria                                       |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Nephrolithiasis                                 |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                |                 |  |
| Back pain                                       |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Kyphoscoliosis                                  |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Scoliosis                                       |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |



|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Infections and infestations                     |                 |                 |  |
| Appendicitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%)  | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%)  | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 4 / 57 (7.02%)  | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 1 / 5           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Influenza                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%)  | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 3 / 57 (5.26%)  | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 4           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningitis                                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%)  | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pharyngotonsillitis                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%)  | 0 / 108 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 6 / 57 (10.53%) | 7 / 108 (6.48%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 5 / 9           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory tract infection                     |                 |                 |  |

|                                                 |                |                 |  |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 57 (0.00%) | 4 / 108 (3.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 5           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Respiratory tract infection viral               |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Tooth abscess                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Upper respiratory tract infection               |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Metabolism and nutrition disorders              |                |                 |  |
| Dehydration                                     |                |                 |  |
| subjects affected / exposed                     | 1 / 57 (1.75%) | 2 / 108 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hypoglycaemia                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Metabolic acidosis                              |                |                 |  |
| subjects affected / exposed                     | 0 / 57 (0.00%) | 1 / 108 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           |  |
| 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          | Olesoxime         |  |
|-------------------------------------------------------|------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                  |                   |  |
| subjects affected / exposed                           | 52 / 57 (91.23%) | 96 / 108 (88.89%) |  |
| Investigations                                        |                  |                   |  |
| Weight increased                                      |                  |                   |  |
| subjects affected / exposed                           | 3 / 57 (5.26%)   | 4 / 108 (3.70%)   |  |
| occurrences (all)                                     | 3                | 4                 |  |
| Injury, poisoning and procedural complications        |                  |                   |  |
| Fall                                                  |                  |                   |  |
| subjects affected / exposed                           | 5 / 57 (8.77%)   | 8 / 108 (7.41%)   |  |
| occurrences (all)                                     | 6                | 11                |  |
| Nervous system disorders                              |                  |                   |  |
| Headache                                              |                  |                   |  |
| subjects affected / exposed                           | 13 / 57 (22.81%) | 22 / 108 (20.37%) |  |
| occurrences (all)                                     | 19               | 57                |  |
| General disorders and administration site conditions  |                  |                   |  |
| Pain                                                  |                  |                   |  |
| subjects affected / exposed                           | 0 / 57 (0.00%)   | 6 / 108 (5.56%)   |  |
| occurrences (all)                                     | 0                | 6                 |  |
| Pyrexia                                               |                  |                   |  |
| subjects affected / exposed                           | 15 / 57 (26.32%) | 33 / 108 (30.56%) |  |
| occurrences (all)                                     | 22               | 57                |  |
| Unevaluable event                                     |                  |                   |  |
| subjects affected / exposed                           | 5 / 57 (8.77%)   | 3 / 108 (2.78%)   |  |
| occurrences (all)                                     | 5                | 3                 |  |
| Ear and labyrinth disorders                           |                  |                   |  |
| Ear pain                                              |                  |                   |  |
| subjects affected / exposed                           | 3 / 57 (5.26%)   | 3 / 108 (2.78%)   |  |
| occurrences (all)                                     | 1                | 1                 |  |
| Gastrointestinal disorders                            |                  |                   |  |
| Abdominal pain                                        |                  |                   |  |
| subjects affected / exposed                           | 10 / 57 (17.54%) | 20 / 108 (18.52%) |  |
| occurrences (all)                                     | 18               | 39                |  |
| Abdominal pain upper                                  |                  |                   |  |
| subjects affected / exposed                           | 4 / 57 (7.02%)   | 8 / 108 (7.41%)   |  |
| occurrences (all)                                     | 4                | 11                |  |
| Constipation                                          |                  |                   |  |

|                                                                                                                   |                        |                         |  |
|-------------------------------------------------------------------------------------------------------------------|------------------------|-------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                  | 4 / 57 (7.02%)<br>6    | 5 / 108 (4.63%)<br>5    |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                                     | 12 / 57 (21.05%)<br>16 | 18 / 108 (16.67%)<br>22 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                                                        | 3 / 57 (5.26%)<br>4    | 9 / 108 (8.33%)<br>18   |  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)                                                     | 5 / 57 (8.77%)<br>5    | 1 / 108 (0.93%)<br>1    |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                                                      | 16 / 57 (28.07%)<br>25 | 25 / 108 (23.15%)<br>38 |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)      | 16 / 57 (28.07%)<br>30 | 31 / 108 (28.70%)<br>48 |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                                            | 9 / 57 (15.79%)<br>11  | 16 / 108 (14.81%)<br>30 |  |
| Respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all)                                  | 3 / 57 (5.26%)<br>4    | 3 / 108 (2.78%)<br>6    |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 7 / 57 (12.28%)<br>7   | 2 / 108 (1.85%)<br>2    |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 3 / 57 (5.26%)<br>3    | 3 / 108 (2.78%)<br>4    |  |
| Joint contracture<br>subjects affected / exposed<br>occurrences (all)                                             | 4 / 57 (7.02%)<br>4    | 5 / 108 (4.63%)<br>5    |  |
| Pain in extremity                                                                                                 |                        |                         |  |

|                                   |                  |                   |  |
|-----------------------------------|------------------|-------------------|--|
| subjects affected / exposed       | 5 / 57 (8.77%)   | 14 / 108 (12.96%) |  |
| occurrences (all)                 | 6                | 17                |  |
| Scoliosis                         |                  |                   |  |
| subjects affected / exposed       | 4 / 57 (7.02%)   | 12 / 108 (11.11%) |  |
| occurrences (all)                 | 5                | 13                |  |
| Infections and infestations       |                  |                   |  |
| Bronchitis                        |                  |                   |  |
| subjects affected / exposed       | 17 / 57 (29.82%) | 17 / 108 (15.74%) |  |
| occurrences (all)                 | 21               | 24                |  |
| Ear infection                     |                  |                   |  |
| subjects affected / exposed       | 2 / 57 (3.51%)   | 9 / 108 (8.33%)   |  |
| occurrences (all)                 | 2                | 11                |  |
| Gastroenteritis                   |                  |                   |  |
| subjects affected / exposed       | 8 / 57 (14.04%)  | 16 / 108 (14.81%) |  |
| occurrences (all)                 | 12               | 21                |  |
| Influenza                         |                  |                   |  |
| subjects affected / exposed       | 9 / 57 (15.79%)  | 10 / 108 (9.26%)  |  |
| occurrences (all)                 | 14               | 26                |  |
| Lower respiratory tract infection |                  |                   |  |
| subjects affected / exposed       | 3 / 57 (5.26%)   | 3 / 108 (2.78%)   |  |
| occurrences (all)                 | 3                | 12                |  |
| Nasopharyngitis                   |                  |                   |  |
| subjects affected / exposed       | 15 / 57 (26.32%) | 25 / 108 (23.15%) |  |
| occurrences (all)                 | 34               | 55                |  |
| Pharyngitis                       |                  |                   |  |
| subjects affected / exposed       | 6 / 57 (10.53%)  | 15 / 108 (13.89%) |  |
| occurrences (all)                 | 8                | 19                |  |
| Pneumonia                         |                  |                   |  |
| subjects affected / exposed       | 3 / 57 (5.26%)   | 3 / 108 (2.78%)   |  |
| occurrences (all)                 | 3                | 5                 |  |
| Respiratory tract infection       |                  |                   |  |
| subjects affected / exposed       | 6 / 57 (10.53%)  | 15 / 108 (13.89%) |  |
| occurrences (all)                 | 10               | 30                |  |
| Rhinitis                          |                  |                   |  |
| subjects affected / exposed       | 6 / 57 (10.53%)  | 14 / 108 (12.96%) |  |
| occurrences (all)                 | 9                | 18                |  |

|                                                                                                              |                        |                         |  |
|--------------------------------------------------------------------------------------------------------------|------------------------|-------------------------|--|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 13 / 57 (22.81%)<br>33 | 22 / 108 (20.37%)<br>36 |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                  | 4 / 57 (7.02%)<br>4    | 4 / 108 (3.70%)<br>4    |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 3 / 57 (5.26%)<br>3    | 1 / 108 (0.93%)<br>3    |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported