



## Clinical trial results:

### A Phase III Randomized, Placebo-Controlled Clinical Trial to Assess the Safety and Efficacy of Odanacatib (MK-0822) to reduce the Risk of Fracture in Osteoporotic Men Treated with Vitamin D and Calcium Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2010-019454-41       |
| Trial protocol           | LV DK GB NL EE IT BG |
| Global end of trial date | 22 July 2013         |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2 (current) |
| This version publication date  | 02 July 2016 |
| First version publication date | 15 July 2015 |
| Version creation reason        |              |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 0822-053 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01120600 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                              |
|------------------------------|----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.                                                                    |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033                               |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.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:

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**Results analysis stage**

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|                                                      |              |
|------------------------------------------------------|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 22 July 2013 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 22 July 2013 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 22 July 2013 |
| Was the trial ended prematurely?                     | No           |

Notes:

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**General information about the trial**

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Main objective of the trial:

1. To assess the effect in men with osteoporosis of odanacatib 50 mg once weekly versus placebo on lumbar spine bone mineral density (BMD) over 24 months; 2. To assess the safety and tolerability of odanacatib 50 mg once weekly compared to placebo.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Calcium and Vitamin D3

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 09 June 2010 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Colombia: 20           |
| Country: Number of subjects enrolled | Chile: 2               |
| Country: Number of subjects enrolled | United States: 61      |
| Country: Number of subjects enrolled | Russian Federation: 20 |
| Country: Number of subjects enrolled | Netherlands: 6         |
| Country: Number of subjects enrolled | United Kingdom: 59     |
| Country: Number of subjects enrolled | Denmark: 43            |
| Country: Number of subjects enrolled | Estonia: 9             |
| Country: Number of subjects enrolled | France: 16             |
| Country: Number of subjects enrolled | Italy: 17              |
| Country: Number of subjects enrolled | Latvia: 11             |
| Country: Number of subjects enrolled | Japan: 24              |
| Country: Number of subjects enrolled | Mexico: 6              |
| Worldwide total number of subjects   | 294                    |
| EEA total number of subjects         | 161                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 77  |
| From 65 to 84 years                       | 210 |
| 85 years and over                         | 7   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants were men between 40 and 95 years of age, with idiopathic osteoporosis or osteoporosis due to hypogonadism. Additional inclusion and exclusion criteria applied.

### Period 1

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

### Arms

|                              |                              |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes                          |
| <b>Arm title</b>             | Odanacatib 50 mg once weekly |

Arm description:

Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Odanacatib   |
| Investigational medicinal product code |              |
| Other name                             | MK-0822      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Odanacatib, 50 mg tablet, once weekly

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

Arm description:

Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.

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

Dosage and administration details:

Participants received one placebo to Odanacatib tablet once weekly.

| <b>Number of subjects in period 1</b> | Odanacatib 50 mg<br>once weekly | Placebo once weekly |
|---------------------------------------|---------------------------------|---------------------|
| Started                               | 147                             | 147                 |
| Treated                               | 146                             | 146                 |
| Completed                             | 128                             | 115                 |
| Not completed                         | 19                              | 32                  |
| Adverse event, serious fatal          | 2                               | 1                   |
| Consent withdrawn by subject          | 10                              | 11                  |
| Physician decision                    | 1                               | 3                   |
| Adverse event, non-fatal              | 5                               | 6                   |
| Excessive bone loss                   | -                               | 4                   |
| Lost to follow-up                     | 1                               | 3                   |
| Protocol deviation                    | -                               | 4                   |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                        |                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                  | Odanacatib 50 mg once weekly |
| Reporting group description:                                                                                                                                                                                                                                                                                           |                              |
| Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg. |                              |
| Reporting group title                                                                                                                                                                                                                                                                                                  | Placebo once weekly          |
| Reporting group description:                                                                                                                                                                                                                                                                                           |                              |
| Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.          |                              |

| Reporting group values                             | Odanacatib 50 mg once weekly | Placebo once weekly | Total |
|----------------------------------------------------|------------------------------|---------------------|-------|
| Number of subjects                                 | 147                          | 147                 | 294   |
| Age categorical                                    |                              |                     |       |
| Units: Subjects                                    |                              |                     |       |
| In utero                                           | 0                            | 0                   | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                            | 0                   | 0     |
| Newborns (0-27 days)                               | 0                            | 0                   | 0     |
| Infants and toddlers (28 days-23 months)           | 0                            | 0                   | 0     |
| Children (2-11 years)                              | 0                            | 0                   | 0     |
| Adolescents (12-17 years)                          | 0                            | 0                   | 0     |
| Adults (18-64 years)                               | 40                           | 37                  | 77    |
| From 65-84 years                                   | 103                          | 107                 | 210   |
| 85 years and over                                  | 4                            | 3                   | 7     |
| Age continuous                                     |                              |                     |       |
| Units: years                                       |                              |                     |       |
| arithmetic mean                                    | 68.9                         | 68.7                | -     |
| standard deviation                                 | ± 8.2                        | ± 7.7               | -     |
| Gender categorical                                 |                              |                     |       |
| Units: Subjects                                    |                              |                     |       |
| Female                                             | 0                            | 0                   | 0     |
| Male                                               | 147                          | 147                 | 294   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                        |                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                  | Odanacatib 50 mg once weekly |
| Reporting group description:<br>Participants received one Odanacatib 50 mg tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg. |                              |
| Reporting group title                                                                                                                                                                                                                                                                                                                                  | Placebo once weekly          |
| Reporting group description:<br>Participants received one Placebo tablet once weekly. In addition, they received a weekly dose 5600 IU of open-label Vitamin D3 as well as a sufficient supply of open-label calcium carbonate so that their total daily calcium intake from both dietary and supplemental sources was approximately 1200 mg.          |                              |

### Primary: Percentage Change from Baseline in Lumbar Spine Bone Mineral Density at Month 24

|                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                    | Percentage Change from Baseline in Lumbar Spine Bone Mineral Density at Month 24 |
| End point description:<br>Lumbar spine BMD was assessed by dual energy X-ray absorptiometry (DXA) at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the full analysis set (FAS) population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded. |                                                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                                          |
| End point timeframe:<br>Baseline and Months 3, 6, 12, and 24                                                                                                                                                                                                                                                                                                                                       |                                                                                  |

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly |  |  |
|----------------------------------------------|------------------------------|---------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group     |  |  |
| Number of subjects analysed                  | 112                          | 107                 |  |  |
| Units: percent change                        |                              |                     |  |  |
| least squares mean (confidence interval 95%) | 6.86 (6.08 to 7.64)          | 1.27 (0.48 to 2.06) |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                                                                                                               | Pct Change in Lumbar Spine BMD at Month 24         |
| Statistical analysis description:<br>A constrained full likelihood longitudinal data analysis (cLDA) method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction. |                                                    |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Odanacatib 50 mg once weekly v Placebo once weekly |

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 219                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | < 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS means |
| Point estimate                          | 5.59                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 4.48                   |
| upper limit                             | 6.7                    |

## Secondary: Percentage Change from Baseline in Total Hip BMD at Month 24

|                                                                                                                                                                                                                                                                                                            |                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                            | Percentage Change from Baseline in Total Hip BMD at Month 24 |
| End point description:                                                                                                                                                                                                                                                                                     |                                                              |
| Total hip BMD was assessed by DXA at Baseline at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded. |                                                              |
| End point type                                                                                                                                                                                                                                                                                             | Secondary                                                    |
| End point timeframe:                                                                                                                                                                                                                                                                                       |                                                              |
| Baseline and Months 3, 6, 12, and 24                                                                                                                                                                                                                                                                       |                                                              |

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly   |  |  |
|----------------------------------------------|------------------------------|-----------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group       |  |  |
| Number of subjects analysed                  | 111                          | 105                   |  |  |
| Units: percent change                        |                              |                       |  |  |
| least squares mean (confidence interval 95%) | 1.91 (1.38 to 2.43)          | -0.11 (-0.65 to 0.42) |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                            |                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                 | Pct Chg from Baseline in Total Hip BMD at Month 24 |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                          |                                                    |
| A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction. |                                                    |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                          | Odanacatib 50 mg once weekly v Placebo once weekly |



|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 216                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | < 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | 2.02                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 1.27                   |
| upper limit                             | 2.77                   |

## Secondary: Percentage Change from Baseline in Femoral Neck BMD at Month 24

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Percentage Change from Baseline in Femoral Neck BMD at Month 24 |
|-----------------|-----------------------------------------------------------------|

End point description:

Femoral neck BMD was assessed by DXA at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

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

End point timeframe:

Baseline and Months 3, 6, 12, and 24

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly |  |  |
|----------------------------------------------|------------------------------|---------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group     |  |  |
| Number of subjects analysed                  | 111                          | 105                 |  |  |
| Units: percent change                        |                              |                     |  |  |
| least squares mean (confidence interval 95%) | 1.69 (0.82 to 2.55)          | 0 (-0.89 to 0.88)   |  |  |

## Statistical analyses

|                            |                                                   |
|----------------------------|---------------------------------------------------|
| Statistical analysis title | Pct Chg from Baseline in Fem Neck BMD at Month 24 |
|----------------------------|---------------------------------------------------|

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction.

|                   |                                                    |
|-------------------|----------------------------------------------------|
| Comparison groups | Odanacatib 50 mg once weekly v Placebo once weekly |
|-------------------|----------------------------------------------------|

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 216                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.008                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | 1.69                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 0.45                   |
| upper limit                             | 2.93                   |

## Secondary: Percentage Change from Baseline in Trochanter BMD at Month 24

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Percentage Change from Baseline in Trochanter BMD at Month 24 |
|-----------------|---------------------------------------------------------------|

End point description:

Trochanter BMD was assessed by DXA at Baseline and at Months 3, 6, 12, and 24. This endpoint was based on the FAS population, which consisted of all randomized participants who took at least one dose of blinded study treatment. Participants without a baseline measurement for the endpoint were excluded.

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

End point timeframe:

Baseline and Months 3, 6, 12, and 24

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly |  |  |
|----------------------------------------------|------------------------------|---------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group     |  |  |
| Number of subjects analysed                  | 111                          | 105                 |  |  |
| Units: percent change                        |                              |                     |  |  |
| least squares mean (confidence interval 95%) | 2.77 (1.94 to 3.6)           | 0.66 (-0.18 to 1.5) |  |  |

## Statistical analyses

|                            |                                                  |
|----------------------------|--------------------------------------------------|
| Statistical analysis title | Pct Chg from Baseline in Trochanter BMD at Mo 24 |
|----------------------------|--------------------------------------------------|

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model included the baseline measurement and all post-baseline percent changes from baseline in the response vector, with fixed effects for treatment, time, geographic region, machine type and treatment-by-time interaction, geographic region-by-time interaction, and machine type-by-time interaction.

|                   |                                                    |
|-------------------|----------------------------------------------------|
| Comparison groups | Odanacatib 50 mg once weekly v Placebo once weekly |
|-------------------|----------------------------------------------------|

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 216                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | < 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | 2.12                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 0.93                   |
| upper limit                             | 3.3                    |

### Secondary: Percentage Change from Baseline in Serum C-Telopeptides of Type 1 Collagen (s-CTx) at Month 24

|                        |                                                                                                                                                                                                                                                                                                                                      |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Percentage Change from Baseline in Serum C-Telopeptides of Type 1 Collagen (s-CTx) at Month 24                                                                                                                                                                                                                                       |
| End point description: | Serum samples were collected to evaluate biochemical markers for s-CTx, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results. |
| End point type         | Secondary                                                                                                                                                                                                                                                                                                                            |
| End point timeframe:   | Baseline and Months 3, 6, 12, 18, and 24                                                                                                                                                                                                                                                                                             |

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly    |  |  |
|----------------------------------------------|------------------------------|------------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group        |  |  |
| Number of subjects analysed                  | 112                          | 102                    |  |  |
| Units: percent change                        |                              |                        |  |  |
| least squares mean (confidence interval 95%) | -20.07 (-28.36 to -10.82)    | 56.51 (40.01 to 74.96) |  |  |

### Statistical analyses

|                                   |                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title        | Pct Change from Baseline in s-CTx at Month 24                                                                                                                                                                                                                                                                                        |
| Statistical analysis description: | A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction. |
| Comparison groups                 | Odanacatib 50 mg once weekly v Placebo once weekly                                                                                                                                                                                                                                                                                   |

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 214                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | < 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | -76.58                 |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -92.56                 |
| upper limit                             | -60.61                 |

### Secondary: Percentage Change from Baseline in Urine Collagen N-Telopeptide/Creatinine Ratio (U-NTx/Cr) at Month 24

|                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                   | Percentage Change from Baseline in Urine Collagen N-Telopeptide/Creatinine Ratio (U-NTx/Cr) at Month 24 |
| End point description:<br>Urine samples were collected to evaluate biochemical markers for u-NTx/Cr, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results. |                                                                                                         |
| End point type                                                                                                                                                                                                                                                                                                                                                    | Secondary                                                                                               |
| End point timeframe:<br>Baseline and Months 3, 6, 12, 18, and 24                                                                                                                                                                                                                                                                                                  |                                                                                                         |

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly   |  |  |
|----------------------------------------------|------------------------------|-----------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group       |  |  |
| Number of subjects analysed                  | 111                          | 102                   |  |  |
| Units: percent change                        |                              |                       |  |  |
| least squares mean (confidence interval 95%) | -61.43 (-64.71 to -57.85)    | 6.65 (-2.68 to 16.87) |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                           |                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                | Pct Change from Baseline in u-NTx/Cr at Month 24   |
| Statistical analysis description:<br>A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction. |                                                    |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                         | Odanacatib 50 mg once weekly v Placebo once weekly |

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 213                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | < 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | -68.08                 |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -78.1                  |
| upper limit                             | -58.06                 |

### Secondary: Percentage Change from Baseline in Serum Bone-Specific Alkaline Phosphatase (s-BSAP) at Month 24

|                        |                                                                                                                                                                                                                                                                                       |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Percentage Change from Baseline in Serum Bone-Specific Alkaline Phosphatase (s-BSAP) at Month 24                                                                                                                                                                                      |
| End point description: | Biochemical markers for s-BSAP were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results. |
| End point type         | Secondary                                                                                                                                                                                                                                                                             |
| End point timeframe:   | Months 3, 6, 12, 18, and 24                                                                                                                                                                                                                                                           |

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly  |  |  |
|----------------------------------------------|------------------------------|----------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group      |  |  |
| Number of subjects analysed                  | 114                          | 110                  |  |  |
| Units: percent change                        |                              |                      |  |  |
| least squares mean (confidence interval 95%) | -5.28 (-9.76 to -0.57)       | 2.66 (-2.25 to 7.82) |  |  |

### Statistical analyses

|                                   |                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Statistical analysis title        | Pct Change From Baseline in s-BSAP at Month 24                                                                                                                                                                                                                                                                                       |
| Statistical analysis description: | A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction. |
| Comparison groups                 | Odanacatib 50 mg once weekly v Placebo once weekly                                                                                                                                                                                                                                                                                   |

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 224                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | other                  |
| P-value                                 | = 0.019                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | -7.94                  |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -14.58                 |
| upper limit                             | -1.31                  |

### Secondary: Percentage Change from Baseline in Serum N-Terminal Propeptides of Type I Collagen (s-P1NP) at Month 24

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| End point title | Percentage Change from Baseline in Serum N-Terminal Propeptides of Type I Collagen (s-P1NP) at Month 24 |
|-----------------|---------------------------------------------------------------------------------------------------------|

End point description:

Serum samples were collected to evaluate biochemical markers for s-P1NP, which were measured at Baseline and at Months 3, 6, 12, 18, and 24. This endpoint was based on the Per-Protocol (PP) population, which excluded participants due to important deviations from the protocol that may have substantially affected the results.

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

End point timeframe:

Baseline and Months 3, 6, 12, 18, and 24

| End point values                             | Odanacatib 50 mg once weekly | Placebo once weekly   |  |  |
|----------------------------------------------|------------------------------|-----------------------|--|--|
| Subject group type                           | Reporting group              | Reporting group       |  |  |
| Number of subjects analysed                  | 114                          | 110                   |  |  |
| Units: percent change                        |                              |                       |  |  |
| least squares mean (confidence interval 95%) | -10.94 (-17.27 to -4.14)     | 5.06 (-2.47 to 13.17) |  |  |

### Statistical analyses

|                            |                                                |
|----------------------------|------------------------------------------------|
| Statistical analysis title | Pct Change from Baseline in s-P1NP at Month 24 |
|----------------------------|------------------------------------------------|

Statistical analysis description:

A cLDA method was used for this statistical analysis. The cLDA model includes the log-transformed baseline and log-transformed post-baseline measurements up to Month 24 in the response vector, with fixed effects for treatment, time, geographic region, treatment-by-time interaction and geographic region-by-time interaction.

|                   |                                                    |
|-------------------|----------------------------------------------------|
| Comparison groups | Odanacatib 50 mg once weekly v Placebo once weekly |
|-------------------|----------------------------------------------------|

|                                         |                        |
|-----------------------------------------|------------------------|
| Number of subjects included in analysis | 224                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | other                  |
| P-value                                 | = 0.001                |
| Method                                  | cLDA                   |
| Parameter estimate                      | Difference in LS Means |
| Point estimate                          | -16                    |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | -25.74                 |
| upper limit                             | -6.27                  |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 24 Months after first dose of study drug

Adverse event reporting additional description:

Safety analyses were performed using the All-Patients-as-Treated (APaT) population, which included all participants who took at least one dose of study medication.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Placebo once weekly |
|-----------------------|---------------------|

Reporting group description: -

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Odanacatib 50 mg once weekly |
|-----------------------|------------------------------|

Reporting group description: -

| Serious adverse events                                              | Placebo once weekly | Odanacatib 50 mg once weekly |  |
|---------------------------------------------------------------------|---------------------|------------------------------|--|
| Total subjects affected by serious adverse events                   |                     |                              |  |
| subjects affected / exposed                                         | 26 / 146 (17.81%)   | 26 / 146 (17.81%)            |  |
| number of deaths (all causes)                                       | 2                   | 2                            |  |
| number of deaths resulting from adverse events                      | 0                   | 0                            |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                              |  |
| Basal cell carcinoma                                                |                     |                              |  |
| subjects affected / exposed                                         | 1 / 146 (0.68%)     | 0 / 146 (0.00%)              |  |
| occurrences causally related to treatment / all                     | 0 / 1               | 0 / 0                        |  |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                        |  |
| Benign gastric neoplasm                                             |                     |                              |  |
| subjects affected / exposed                                         | 0 / 146 (0.00%)     | 1 / 146 (0.68%)              |  |
| occurrences causally related to treatment / all                     | 0 / 0               | 0 / 1                        |  |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                        |  |
| Bladder transitional cell carcinoma                                 |                     |                              |  |
| subjects affected / exposed                                         | 1 / 146 (0.68%)     | 0 / 146 (0.00%)              |  |
| occurrences causally related to treatment / all                     | 0 / 1               | 0 / 0                        |  |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                        |  |
| Bronchial carcinoma                                                 |                     |                              |  |



|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Chronic lymphocytic leukaemia                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haemangioma of bone                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung neoplasm malignant                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malignant melanoma                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Non-Hodgkin's lymphoma                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatic carcinoma                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Prostate cancer                                 |                 |                 |  |
| subjects affected / exposed                     | 2 / 146 (1.37%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal cell carcinoma                            |                 |                 |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Small cell lung cancer                               |                 |                 |  |
| subjects affected / exposed                          | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Squamous cell carcinoma                              |                 |                 |  |
| subjects affected / exposed                          | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 4           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                   |                 |                 |  |
| Hypertension                                         |                 |                 |  |
| subjects affected / exposed                          | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Hypotension                                          |                 |                 |  |
| subjects affected / exposed                          | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Death                                                |                 |                 |  |
| subjects affected / exposed                          | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Multi-organ failure                                  |                 |                 |  |
| subjects affected / exposed                          | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Benign prostatic hyperplasia                         |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 146 (0.00%) | 2 / 146 (1.37%) |  |
| 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 |                 |                 |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (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                     | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Investigations                                  |                 |                 |  |
| Weight decreased                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Clavicle fracture                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 2 / 146 (1.37%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Fractured sacrum                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Fibula fracture                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Heat exhaustion                                 |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hip fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ilium fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pelvic fracture                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Postoperative hernia                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Rib fracture                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tendon rupture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tibia fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Congenital, familial and genetic disorders      |                 |                 |  |
| Hydrocele                                       |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Angina pectoris                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Angina unstable                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrioventricular block second degree            |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure congestive                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coronary artery stenosis                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 2 / 146 (1.37%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial ischaemia                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pericarditis                                    |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sick sinus syndrome                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Cerebral ischaemia                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cerebrovascular accident                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Syncope                                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Lymphadenopathy                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Splenic infarction                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Inguinal hernia                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| Mallory-Weiss syndrome                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Melaena                                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Alcoholic liver disease                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Cholecystitis acute                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholelithiasis obstructive                      |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Calculus ureteric                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haematuria                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Haemarthrosis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Intervertebral disc protrusion                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 2 / 146 (1.37%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myopathy                                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tendonitis                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Appendicitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Arthritis infective                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bacteraemia                                     |                 |                 |  |



|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Erysipelas                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 146 (0.00%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Peritonitis                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (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                     | 1 / 146 (0.68%) | 1 / 146 (0.68%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retroperitoneal infection                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 146 (0.68%) | 0 / 146 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Placebo once weekly | Odanacatib 50 mg once weekly |  |
|-------------------------------------------------------|---------------------|------------------------------|--|
| Total subjects affected by non-serious adverse events |                     |                              |  |
| subjects affected / exposed                           | 44 / 146 (30.14%)   | 30 / 146 (20.55%)            |  |
| General disorders and administration site conditions  |                     |                              |  |
| Influenza like illness                                |                     |                              |  |
| subjects affected / exposed                           | 9 / 146 (6.16%)     | 4 / 146 (2.74%)              |  |
| occurrences (all)                                     | 11                  | 4                            |  |
| Musculoskeletal and connective tissue                 |                     |                              |  |

|                             |                   |                  |  |
|-----------------------------|-------------------|------------------|--|
| disorders                   |                   |                  |  |
| Arthralgia                  |                   |                  |  |
| subjects affected / exposed | 10 / 146 (6.85%)  | 4 / 146 (2.74%)  |  |
| occurrences (all)           | 11                | 4                |  |
| Back pain                   |                   |                  |  |
| subjects affected / exposed | 12 / 146 (8.22%)  | 9 / 146 (6.16%)  |  |
| occurrences (all)           | 15                | 11               |  |
| Pain in extremity           |                   |                  |  |
| subjects affected / exposed | 10 / 146 (6.85%)  | 3 / 146 (2.05%)  |  |
| occurrences (all)           | 12                | 3                |  |
| Infections and infestations |                   |                  |  |
| Nasopharyngitis             |                   |                  |  |
| subjects affected / exposed | 15 / 146 (10.27%) | 14 / 146 (9.59%) |  |
| occurrences (all)           | 18                | 18               |  |

## **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