

**Clinical trial results:****Open-label, Single-arm, Multicenter Study to Evaluate the Safety, Tolerability and Efficacy of Evolocumab for LDL-C Reduction, as Add-on to Diet and Lipid-lowering Therapy, in Pediatric Subjects From 10 to 17 Years of Age With Heterozygous Familial Hypercholesterolemia (HeFH) or Homozygous (HAUSER-OLE)****Summary**

|                          |  |
|--------------------------|--|
| EudraCT number           | 2015-002276-25                               |
| Trial protocol           | DE GB NO HU AT BE CZ GR ES NL PT SI PL IT RO |
| Global end of trial date | 01 June 2021                                 |

**Results information**

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 18 November 2021 |
| First version publication date | 18 November 2021 |

**Trial information****Trial identification**

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 20120124 |
|-----------------------|----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02624869 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Amgen Inc.   |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, 91320                        |
| Public contact               | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH., MedInfoInternational@amgen.com |
| Scientific contact           | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH., MedInfoInternational@amgen.com |

Notes:

**Paediatric regulatory details**

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001268-PIP01-12 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 01 June 2021 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 01 June 2021 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study is to describe the safety and tolerability of 80 weeks of subcutaneous (SC) evolocumab when added to standard of care in children 10 to 17 years of age with familial hypercholesterolemia.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

The study protocol and all amendments, the informed consent form, and any accompanying materials provided to the subjects were reviewed and approved by an Institutional Review Board (IRB) or Independent Ethics Committee (IEC) at each study center.

The investigator or his/her designee informed the subject or legally acceptable representative of all aspects pertaining to the subject's participation in the study and obtained written informed consent from the subject or legally acceptable representative before any screening procedures were performed or any investigational product(s) were administered.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 10 September 2016 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Canada: 17            |
| Country: Number of subjects enrolled | United States: 3      |
| Country: Number of subjects enrolled | Austria: 10           |
| Country: Number of subjects enrolled | Belgium: 5            |
| Country: Number of subjects enrolled | Czechia: 5            |
| Country: Number of subjects enrolled | Greece: 1             |
| Country: Number of subjects enrolled | Hungary: 10           |
| Country: Number of subjects enrolled | Italy: 25             |
| Country: Number of subjects enrolled | Netherlands: 22       |
| Country: Number of subjects enrolled | Norway: 6             |
| Country: Number of subjects enrolled | Poland: 4             |
| Country: Number of subjects enrolled | Portugal: 1           |
| Country: Number of subjects enrolled | Russian Federation: 1 |
| Country: Number of subjects enrolled | Slovenia: 1           |
| Country: Number of subjects enrolled | Spain: 4              |

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Switzerland: 3    |
| Country: Number of subjects enrolled | Turkey: 4         |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Brazil: 20        |
| Country: Number of subjects enrolled | Colombia: 6       |
| Country: Number of subjects enrolled | Australia: 3      |
| Country: Number of subjects enrolled | Malaysia: 1       |
| Country: Number of subjects enrolled | South Africa: 8   |
| Worldwide total number of subjects   | 163               |
| EEA total number of subjects         | 94                |

Notes:

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### Subjects enrolled per age group

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 35  |
| Adolescents (12-17 years)                 | 120 |
| Adults (18-64 years)                      | 8   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 46 centers in 23 countries (Australia, Austria, Belgium, Brazil, Canada, Colombia, Czech Republic, Greece, Hungary, Italy, Malaysia, Netherlands, Norway, Poland, Portugal, Russia, Slovenia, South Africa, Spain, Switzerland, Turkey, United Kingdom, and United States of America).

### Pre-assignment

Screening details:

This study enrolled participants with heterozygous familial hypercholesterolemia (HeFH) who had completed the parent study 20120123 (EudraCT #: 2014-002277-11) without experiencing a treatment-related serious adverse event or children 10 to 17 years of age with a diagnosis of homozygous familial hypercholesterolemia (HoFH).

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM |

Arm description:

Participants with heterozygous familial hypercholesterolemia (HeFH) who had received placebo in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks (QM) for up to 80 weeks.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Evolocumab   |
| Investigational medicinal product code | AMG 145  |
| Other name                             | Repatha®   |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen, Solution for injection in needle-free injector |
| Routes of administration               | Subcutaneous use   |

Dosage and administration details:

Administered once a month by subcutaneous injection

|                  |   |
|------------------|---|
| <b>Arm title</b> | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |
|------------------|---|

Arm description:

Participants with heterozygous familial hypercholesterolemia who had received evolocumab in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Evolocumab   |
| Investigational medicinal product code | AMG 145  |
| Other name                             | Repatha®   |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen, Solution for injection in needle-free injector |
| Routes of administration               | Subcutaneous use   |

Dosage and administration details:

Administered once a month by subcutaneous injection

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | HoFH: Evolocumab 420 mg QM |
|------------------|----------------------------|

Arm description:

Participants with homozygous familial hypercholesterolemia (HoFH) received 420 mg evolocumab

administered by subcutaneous injection every 4 weeks for up to 80 weeks.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Evolocumab   |
| Investigational medicinal product code | AMG 145  |
| Other name                             | Repatha®   |
| Pharmaceutical forms                   | Solution for injection in pre-filled pen, Solution for injection in needle-free injector |
| Routes of administration               | Subcutaneous use   |

Dosage and administration details:

Administered once a month by subcutaneous injection

| <b>Number of subjects in period 1</b> | HeFH (Placebo in Parent Study):<br>Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study):<br>Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |
|---------------------------------------|---|--|----------------------------|
| Started                               | 49  | 101  | 13                         |
| Received Study Drug                   | 49  | 101  | 12                         |
| Completed                             | 48  | 98   | 11                         |
| Not completed                         | 1   | 3  | 2                          |
| Consent withdrawn by subject          | 1   | 3  | 1                          |
| Lost to follow-up                     | -   | -  | 1                          |

## Baseline characteristics

### Reporting groups

|   |   |
|---|---|
| Reporting group title   | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM    |
| Reporting group description:<br>Participants with heterozygous familial hypercholesterolemia (HeFH) who had received placebo in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks (QM) for up to 80 weeks. |   |
| Reporting group title   | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |
| Reporting group description:<br>Participants with heterozygous familial hypercholesterolemia who had received evolocumab in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.          |   |
| Reporting group title   | HoFH: Evolocumab 420 mg QM                              |
| Reporting group description:<br>Participants with homozygous familial hypercholesterolemia (HoFH) received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.   |   |

| Reporting group values   | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |
|--|--|---|----------------------------|
| Number of subjects   | 49   | 101   | 13                         |
| Age Categorical  |  |   |                            |
| Eight HeFH participants were 18 years old at the time of rollover into Study 20120124, however all were ≤ 17 years old at the time of enrollment into the parent study 20120123. |  |   |                            |
| Units: participants  |  |   |                            |
| 2 - 11 years   | 11   | 18  | 6                          |
| 12 - 17 years  | 37   | 76  | 7                          |
| 18 - 64 years  | 1  | 7   | 0                          |
| Age Continuous   |  |   |                            |
| Units: years   |  |   |                            |
| arithmetic mean  | 13.8   | 14.2  | 12.4                       |
| standard deviation   | ± 2.5  | ± 2.4   | ± 2.0                      |
| Sex: Female, Male  |  |   |                            |
| Units: participants  |  |   |                            |
| Female   | 24   | 59  | 2                          |
| Male   | 25   | 42  | 11                         |
| Ethnicity (NIH/OMB)  |  |   |                            |
| Units: Subjects  |  |   |                            |
| Hispanic or Latino   | 7  | 6   | 0                          |
| Not Hispanic or Latino   | 42   | 95  | 13                         |
| Unknown or Not Reported  | 0  | 0   | 0                          |
| Race/Ethnicity, Customized   |  |   |                            |
| Units: Subjects  |  |   |                            |
| American Indian or Alaska Native   | 0  | 0   | 0                          |
| Asian  | 0  | 2   | 2                          |
| Black or African American  | 0  | 2   | 0                          |
| Native Hawaiian or Other Pacific Islander  | 0  | 0   | 0                          |
| White  | 40   | 86  | 9                          |
| Other  | 9  | 11  | 2                          |

|   |         |         |         |
|---|---------|---------|---------|
| Region  |         |         |         |
| Units: Subjects   |         |         |         |
| North America   | 8       | 12      | 0       |
| Europe  | 33      | 65      | 7       |
| Latin America   | 8       | 18      | 0       |
| Asia Pacific  | 0       | 6       | 6       |
| Low-density Lipoprotein Cholesterol (LDL-C) Concentration   |         |         |         |
| <p>For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.</p> <p>Data are provided for the full analysis set which includes all participants with HeFH from parent Study 20120123 who were enrolled and dosed as well as all participants with HoFH who were enrolled and dosed in this study (49, 101, and 12 subjects in each arm respectively).</p> |         |         |         |
| Units: mg/dL  |         |         |         |
| arithmetic mean   | 184.0   | 184.4   | 426.0   |
| standard deviation  | ± 48.3  | ± 45.2  | ± 166.4 |
| Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) Concentration  |         |         |         |
| <p>For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.</p> <p>Data are provided for the full analysis set (49, 101, and 12 subjects in each arm respectively).</p>  |         |         |         |
| Units: mg/dL  |         |         |         |
| arithmetic mean   | 201.0   | 203.4   | 443.7   |
| standard deviation  | ± 49.3  | ± 47.5  | ± 170.8 |
| Apolipoprotein B (ApoB) Concentration   |         |         |         |
| <p>For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.</p> <p>Data are provided for the full analysis set with available baseline data (47, 100, and 12 subjects in each arm respectively).</p>   |         |         |         |
| Units: mg/dL  |         |         |         |
| arithmetic mean   | 119.1   | 123.1   | 250.1   |
| standard deviation  | ± 28.1  | ± 27.4  | ± 84.9  |
| Total Cholesterol/High-density Lipoprotein Cholesterol (HDL-C) Ratio  |         |         |         |
| <p>For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.</p> <p>Data are provided for the full analysis set (49, 101, and 12 subjects in each arm respectively).</p>  |         |         |         |
| Units: ratio  |         |         |         |
| arithmetic mean   | 5.546   | 5.716   | 14.707  |
| standard deviation  | ± 1.541 | ± 1.809 | ± 7.891 |
| Apolipoprotein B/Apolipoprotein A1 Ratio  |         |         |         |
| <p>For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.</p> <p>Data are provided for the full analysis set with available baseline data (47, 100, and 12 subjects in each arm respectively).</p>   |         |         |         |
| Units: ratio  |         |         |         |
| arithmetic mean   | 0.943   | 0.972   | 2.388   |
| standard deviation  | ± 0.265 | ± 0.306 | ± 1.036 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>  | Total |  |  |
| Number of subjects   | 163   |  |  |
| Age Categorical  |       |  |  |
| Eight HeFH participants were 18 years old at the time of rollover into Study 20120124, however all were ≤ 17 years old at the time of enrollment into the parent study 20120123.   |       |  |  |
| Units: participants  |       |  |  |
| 2 - 11 years   | 35    |  |  |
| 12 - 17 years  | 120   |  |  |
| 18 - 64 years  | 8     |  |  |
| Age Continuous   |       |  |  |
| Units: years   |       |  |  |
| arithmetic mean  |       |  |  |
| standard deviation   | -     |  |  |
| Sex: Female, Male  |       |  |  |
| Units: participants  |       |  |  |
| Female   | 85    |  |  |
| Male   | 78    |  |  |
| Ethnicity (NIH/OMB)  |       |  |  |
| Units: Subjects  |       |  |  |
| Hispanic or Latino   | 13    |  |  |
| Not Hispanic or Latino   | 150   |  |  |
| Unknown or Not Reported  | 0     |  |  |
| Race/Ethnicity, Customized   |       |  |  |
| Units: Subjects  |       |  |  |
| American Indian or Alaska Native   | 0     |  |  |
| Asian  | 4     |  |  |
| Black or African American  | 2     |  |  |
| Native Hawaiian or Other Pacific Islander  | 0     |  |  |
| White  | 135   |  |  |
| Other  | 22    |  |  |
| Region   |       |  |  |
| Units: Subjects  |       |  |  |
| North America  | 20    |  |  |
| Europe   | 105   |  |  |
| Latin America  | 26    |  |  |
| Asia Pacific   | 12    |  |  |
| Low-density Lipoprotein Cholesterol (LDL-C) Concentration  |       |  |  |
| For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.<br>Data are provided for the full analysis set which includes all participants with HeFH from parent Study 20120123 who were enrolled and dosed as well as all participants with HoFH who were enrolled and dosed in this study (49, 101, and 12 subjects in each arm respectively). |       |  |  |
| Units: mg/dL   |       |  |  |
| arithmetic mean  |       |  |  |
| standard deviation   | -     |  |  |
| Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) Concentration   |       |  |  |
| For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.  |       |  |  |



|  |   |  |  |
|--|---|--|--|
| Data are provided for the full analysis set (49, 101, and 12 subjects in each arm respectively).   |   |  |  |
| Units: mg/dL<br>arithmetic mean<br>standard deviation  | - |  |  |
| Apolipoprotein B (ApoB) Concentration  |   |  |  |
| For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.<br>Data are provided for the full analysis set with available baseline data (47, 100, and 12 subjects in each arm respectively). |   |  |  |
| Units: mg/dL<br>arithmetic mean<br>standard deviation  | - |  |  |
| Total Cholesterol/High-density Lipoprotein Cholesterol (HDL-C) Ratio   |   |  |  |
| For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.<br>Data are provided for the full analysis set (49, 101, and 12 subjects in each arm respectively).                              |   |  |  |
| Units: ratio<br>arithmetic mean<br>standard deviation  | - |  |  |
| Apolipoprotein B/Apolipoprotein A1 Ratio   |   |  |  |
| For participants with HeFH who rolled over from parent study 20120123, baseline values are defined as parent study baseline concentrations; for de novo participants with HoFH, baseline values are defined as the mean of the two most recent non-missing concentrations measured through the central laboratory prior to or on Study Day 1.<br>Data are provided for the full analysis set with available baseline data (47, 100, and 12 subjects in each arm respectively). |   |  |  |
| Units: ratio<br>arithmetic mean<br>standard deviation  | - |  |  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM    |
| Reporting group description:<br>Participants with heterozygous familial hypercholesterolemia (HeFH) who had received placebo in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks (QM) for up to 80 weeks. |   |
| Reporting group title   | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |
| Reporting group description:<br>Participants with heterozygous familial hypercholesterolemia who had received evolocumab in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.          |   |
| Reporting group title   | HoFH: Evolocumab 420 mg QM                              |
| Reporting group description:<br>Participants with homozygous familial hypercholesterolemia (HoFH) received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.   |   |

### Primary: Number of Participants with Treatment-emergent Adverse Events (TEAEs)

|   |  |
|---|--|
| End point title   | Number of Participants with Treatment-emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>An adverse event is defined as any untoward medical occurrence in a clinical trial participant, not necessarily having a causal relationship with study treatment.<br>A serious AE is as an AE that met at least 1 of the following criteria: <ul style="list-style-type: none"><li>• fatal;</li><li>• life threatening;</li><li>• required in-patient hospitalization or prolongation of existing hospitalization;</li><li>• resulted in persistent or significant disability/incapacity;</li><li>• congenital anomaly/birth defect;</li><li>• other medically important serious event.</li></ul> AEs were graded for severity using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0:<br>Grade 1: Mild; asymptomatic or mild symptoms;<br>Grade 2: Moderate; minimal, local or noninvasive intervention indicated;<br>Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated;<br>Grade 4: Life-threatening consequences; urgent intervention indicated;<br>Grade 5: Death related to AE. |  |
| End point type  | Primary  |
| End point timeframe:<br>From first dose of evolocumab in this study up to and including 30 days after the last dose or up to the end of study date, whichever was earlier; up to 80 weeks.  |  |

Notes:

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

Justification: Statistical analyses in this open-label study were descriptive in nature. No statistical inference or missing value imputation was planned.

| End point values            | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|-----------------------------|--|---|----------------------------|--|
| Subject group type          | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 49   | 101   | 12                         |  |
| Units: participants         |  |   |                            |  |

|   |    |    |   |  |
|---|----|----|---|--|
| Any treatment-emergent adverse event (TEAE)   | 36 | 69 | 7 |  |
| TEAE ≥ Grade 2                                | 25 | 56 | 5 |  |
| TEAE ≥ Grade 3                                | 4  | 2  | 2 |  |
| TEAE ≥ Grade 4                                | 0  | 1  | 0 |  |
| Serious adverse events                        | 2  | 2  | 2 |  |
| TEAE leading to discontinuation of evolocumab | 0  | 0  | 0 |  |
| Fatal adverse events                          | 0  | 0  | 0 |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change from Baseline to Week 80 in Low-density Lipoprotein Cholesterol (LDL-C) in HeFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Low-density Lipoprotein Cholesterol (LDL-C) in HeFH Participants <sup>[2]</sup> |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value of the parent study 20120123. Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                 | HeFH (Placebo in Parent Study):<br>Evolocumab<br>420 mg QM | HeFH (Evolocumab in Parent Study):<br>Evolocumab<br>420 mg QM |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed      | 40   | 88  |  |  |
| Units: percent change            |  |   |  |  |
| arithmetic mean (standard error) | -36.01 (± 4.28)  | -34.96 (± 3.05)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change from Baseline to Week 80 in LDL-C in HoFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in LDL-C in HoFH Participants <sup>[3]</sup> |
|-----------------|--|

End point description:

For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Results are reported separately for subjects with HeFH and HoFH.

|                                       |                                  |  |  |  |
|---------------------------------------|----------------------------------|--|--|--|
| <b>End point values</b>               | HoFH:<br>Evolocumab<br>420 mg QM |  |  |  |
| Subject group type                    | Reporting group                  |  |  |  |
| Number of subjects analysed           | 11                               |  |  |  |
| Units: percent change                 |                                  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | -14.29 (-40.61<br>to 3.54)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Non-HDL-C in HeFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Non-HDL-C in HeFH Participants <sup>[4]</sup> |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value of the parent study 20120123.  
Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Results are reported separately for subjects with HeFH and HoFH.

|                                  |  |   |  |  |
|----------------------------------|--|---|--|--|
| <b>End point values</b>          | HeFH (Placebo<br>in Parent<br>Study):<br>Evolocumab<br>420 mg QM | HeFH<br>(Evolocumab in<br>Parent Study):<br>Evolocumab<br>420 mg QM |  |  |
| Subject group type               | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed      | 40   | 88  |  |  |
| Units: percent change            |  |   |  |  |
| arithmetic mean (standard error) | -32.37 (±<br>3.96)   | -31.95 (±<br>2.89)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Non-HDL-C in HoFH

## Participants

|   |  |
|---|--|
| End point title   | Percent Change from Baseline to Week 80 in Non-HDL-C in HoFH Participants <sup>[5]</sup> |
| End point description:<br>For HoFH participants baseline was defined as the baseline value in this study (20120124).<br>Results are reported for the full analysis set with available data. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline and week 80  |  |

### Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Results are reported separately for subjects with HeFH and HoFH.

|                                       |                                  |  |  |  |
|---------------------------------------|----------------------------------|--|--|--|
| <b>End point values</b>               | HoFH:<br>Evolocumab<br>420 mg QM |  |  |  |
| Subject group type                    | Reporting group                  |  |  |  |
| Number of subjects analysed           | 11                               |  |  |  |
| Units: percent change                 |                                  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | -13.03 (-40.68 to 2.69)          |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change from Baseline to Week 80 in Apolipoprotein B in HeFH Participants

|   |   |
|---|---|
| End point title   | Percent Change from Baseline to Week 80 in Apolipoprotein B in HeFH Participants <sup>[6]</sup> |
| End point description:<br>For HeFH participants baseline was defined as the baseline value in the parent study 20120123.<br>Results are reported for the full analysis set with available data. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline and week 80  |   |

### Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Results are reported separately for subjects with HeFH and HoFH.

|                                  |  |   |  |  |
|----------------------------------|--|---|--|--|
| <b>End point values</b>          | HeFH (Placebo in Parent Study):<br>Evolocumab<br>420 mg QM | HeFH (Evolocumab in Parent Study):<br>Evolocumab<br>420 mg QM |  |  |
| Subject group type               | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed      | 44   | 87  |  |  |
| Units: percent change            |  |   |  |  |
| arithmetic mean (standard error) | -27.10 ( $\pm$ 3.32)                                       | -24.15 ( $\pm$ 2.99)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Apolipoprotein B in HoFH Participants

|                 |   |
|-----------------|---|
| End point title | Percent Change from Baseline to Week 80 in Apolipoprotein B in HoFH Participants <sup>[7]</sup> |
|-----------------|---|

End point description:

For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

|                                       |                                  |  |  |  |
|---------------------------------------|----------------------------------|--|--|--|
| End point values                      | HoFH:<br>Evolocumab<br>420 mg QM |  |  |  |
| Subject group type                    | Reporting group                  |  |  |  |
| Number of subjects analysed           | 11                               |  |  |  |
| Units: percent change                 |                                  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | -19.17 (-33.33 to 11.59)         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Total Cholesterol/HDL-C Ratio in HeFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Total Cholesterol/HDL-C Ratio in HeFH Participants <sup>[8]</sup> |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group   |  |  |
| Number of subjects analysed      | 40   | 88  |  |  |
| Units: percent change            |  |   |  |  |
| arithmetic mean (standard error) | -28.78 (± 3.48)                                      | -28.32 (± 2.47)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Total Cholesterol/HDL-C Ratio in HoFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Total Cholesterol/HDL-C Ratio in HoFH Participants <sup>[9]</sup> |
|-----------------|--|

End point description:

For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                      | HoFH: Evolocumab 420 mg QM |  |  |  |
|---------------------------------------|----------------------------|--|--|--|
| Subject group type                    | Reporting group            |  |  |  |
| Number of subjects analysed           | 11                         |  |  |  |
| Units: percent change                 |                            |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 3.71 (-41.17 to 7.57)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change from Baseline to Week 80 in Apolipoprotein B / Apolipoprotein A1 Ratio in HeFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Apolipoprotein B / Apolipoprotein A1 Ratio in HeFH Participants <sup>[10]</sup> |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group   |  |  |
| Number of subjects analysed      | 44   | 87  |  |  |
| Units: percent change            |  |   |  |  |
| arithmetic mean (standard error) | -31.00 ( $\pm$ 3.66)                                 | -29.89 ( $\pm$ 2.80)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change from Baseline to Week 80 in Apolipoprotein B/Apolipoprotein A1 Ratio in HoFH Participants

|                 |  |
|-----------------|--|
| End point title | Percent Change from Baseline to Week 80 in Apolipoprotein B/Apolipoprotein A1 Ratio in HoFH Participants <sup>[11]</sup> |
|-----------------|--|

End point description:

For HoFH participants baseline was defined as the baseline value in this study (20120124).

Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                      | HoFH: Evolocumab 420 mg QM |  |  |  |
|---------------------------------------|----------------------------|--|--|--|
| Subject group type                    | Reporting group            |  |  |  |
| Number of subjects analysed           | 11                         |  |  |  |
| Units: percent change                 |                            |  |  |  |
| median (inter-quartile range (Q1-Q3)) | -2.96 (-35.71 to 9.30)     |  |  |  |

## Statistical analyses



No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in LDL-C in HeFH Participants

|                 |   |
|-----------------|---|
| End point title | Change from Baseline to Week 80 in LDL-C in HeFH Participants <sup>[12]</sup> |
|-----------------|---|

End point description:

For HeFH participants baseline was defined as the baseline value of the parent study 20120123. Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |  |  |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group   |  |  |
| Number of subjects analysed      | 40   | 88  |  |  |
| Units: mg/dL                     |  |   |  |  |
| arithmetic mean (standard error) | -67.2 (± 8.2)  | -63.1 (± 5.6)   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in LDL-C in HoFH Participants

|                 |   |
|-----------------|---|
| End point title | Change from Baseline to Week 80 in LDL-C in HoFH Participants <sup>[13]</sup> |
|-----------------|---|

End point description:

For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

Notes:

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

Justification: Results are reported separately for subjects with HeFH and HoFH.

| End point values                      | HoFH: Evolocumab 420 mg QM |  |  |  |
|---------------------------------------|----------------------------|--|--|--|
| Subject group type                    | Reporting group            |  |  |  |
| Number of subjects analysed           | 11                         |  |  |  |
| Units: mg/dL                          |                            |  |  |  |
| median (inter-quartile range (Q1-Q3)) | -36.5 (-180.5)             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in Estradiol Levels

|                 |   |
|-----------------|---|
| End point title | Change from Baseline to Week 80 in Estradiol Levels |
|-----------------|---|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124).

Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 23   | 54  | 2                          |  |
| Units: pmol/L                    |  |   |                            |  |
| arithmetic mean (standard error) | 131.3 (± 45.3)                                       | 48.2 (± 58.1)   | 283.0 (± 130.0)            |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in Testosterone Levels

|                 |  |
|-----------------|--|
| End point title | Change from Baseline to Week 80 in Testosterone Levels |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124).

Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 18   | 34  | 7                          |  |
| Units: nmol/L                    |  |   |                            |  |
| arithmetic mean (standard error) | 5.282 ( $\pm$ 1.567)                                 | 3.230 ( $\pm$ 1.167)                                    | 2.916 ( $\pm$ 0.984)       |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline to Week 80 in Follicle Stimulating Hormone (FSH) Levels

|   |  |
|---|--|
| End point title   | Change from Baseline to Week 80 in Follicle Stimulating Hormone (FSH) Levels |
| End point description:<br>For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline and week 80  |  |

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 44   | 91  | 10                         |  |
| Units: IU/L                      |  |   |                            |  |
| arithmetic mean (standard error) | 1.88 ( $\pm$ 0.90)                                   | 0.60 ( $\pm$ 0.37)                                      | 1.18 ( $\pm$ 0.35)         |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline to Week 80 in Luteinizing Hormone (LH) Levels

|   |  |
|---|--|
| End point title   | Change from Baseline to Week 80 in Luteinizing Hormone (LH) Levels |
| End point description:<br>For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data. |  |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and week 80 |           |

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 44   | 92  | 10                         |  |
| Units: IU/L                      |  |   |                            |  |
| arithmetic mean (standard error) | 2.88 (± 1.51)  | 1.04 (± 0.95)   | 1.76 (± 0.84)              |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in Adenocorticotrophic Hormone (ACTH) Levels

|   |  |
|---|--|
| End point title   | Change from Baseline to Week 80 in Adenocorticotrophic Hormone (ACTH) Levels |
| End point description:  |  |
| For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline and week 80  |  |

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 43   | 84  | 11                         |  |
| Units: pmol/L                    |  |   |                            |  |
| arithmetic mean (standard error) | 0.78 (± 0.55)  | 0.55 (± 0.61)   | -0.75 (± 1.79)             |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: Change from Baseline to Week 80 in Dehydroepiandrosterone Sulfate (DHEA-S) Levels**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline to Week 80 in Dehydroepiandrosterone Sulfate (DHEA-S) Levels |
|-----------------|---|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 43   | 89  | 11                         |  |
| Units: $\mu\text{mol/L}$         |  |   |                            |  |
| arithmetic mean (standard error) | 1.051 ( $\pm$ 0.222)                                 | 0.956 ( $\pm$ 0.126)                                    | 0.944 ( $\pm$ 0.247)       |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline to Week 80 in Cortisol Levels**

|                 |  |
|-----------------|--|
| End point title | Change from Baseline to Week 80 in Cortisol Levels |
|-----------------|--|

End point description:

For HeFH participants baseline was defined as the baseline value in the parent study 20120123. For HoFH participants baseline was defined as the baseline value in this study (20120124). Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

| End point values                 | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 43   | 90  | 11                         |  |
| Units: nmol/L                    |  |   |                            |  |
| arithmetic mean (standard error) | 29.81 ( $\pm$ 28.34)                                 | 51.18 ( $\pm$ 25.19)                                    | 57.26 ( $\pm$ 56.11)       |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Liver Function Test Abnormalities at Week 80

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Liver Function Test Abnormalities at Week 80 |
|-----------------|--|

End point description:

Liver function tests included alanine aminotransferase (ALT) levels, aspartate aminotransferase (AST) levels and total bilirubin levels.

Results are reported for the full analysis set with available data.

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

End point timeframe:

Week 80

| End point values            | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|-----------------------------|--|---|----------------------------|--|
| Subject group type          | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 45   | 91  | 10                         |  |
| Units: participants         |  |   |                            |  |
| ALT or AST > 3 x ULN        | 0  | 0   | 0                          |  |
| ALT or AST > 5 x ULN        | 0  | 0   | 0                          |  |
| Total bilirubin > 2 x ULN   | 0  | 2   | 1                          |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Abnormalities in Levels of Creatine Kinase (CK) at Week 80

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Abnormalities in Levels of Creatine Kinase (CK) at Week 80 |
|-----------------|--|

End point description:

The number of participants with levels of creatine kinase greater than 5 times the upper limit of normal (ULN) and greater than 10 times the ULN, measured by the central laboratory.

Results are reported for the full analysis set with available data.

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

End point timeframe:

Week 80

| <b>End point values</b>     | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|-----------------------------|--|---|----------------------------|--|
| Subject group type          | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed | 45   | 90  | 10                         |  |
| Units: participants         |  |   |                            |  |
| CK > 5 x ULN                | 0  | 0   | 1                          |  |
| CK > 10 x ULN               | 0  | 0   | 0                          |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline to Week 80 in Carotid Intima-media Thickness (cIMT)

|                 |  |
|-----------------|--|
| End point title | Change from Baseline to Week 80 in Carotid Intima-media Thickness (cIMT) |
|-----------------|--|

End point description:

Carotid intima-media thickness measures the thickness of the intima and media, the inner two layers of the carotid artery, and is used to determine the extent of plaque buildup in the walls of the arteries (atherosclerosis) supplying blood to the head.

CIMT was measured by ultrasonography and analyzed at a core laboratory.

The largest values measured in the left common carotid artery (LCCA) and the right common carotid artery (RCCA) are averaged in this analysis.

Results are reported for the full analysis set with available data.

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

End point timeframe:

Baseline and week 80

| <b>End point values</b>          | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|----------------------------------|--|---|----------------------------|--|
| Subject group type               | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed      | 34   | 59  | 7                          |  |
| Units: mm                        |  |   |                            |  |
| arithmetic mean (standard error) | -0.019 (± 0.007)                                     | -0.012 (± 0.006)  | 0.006 (± 0.032)            |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Height at Weeks 24, 48, and 80

End point title Change from Baseline in Height at Weeks 24, 48, and 80

End point description:

Results are reported for the full analysis set with available data at each time point.

End point type Secondary

End point timeframe:

Baseline and weeks 24, 48, and 80

| End point values                           | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|--|--|---|----------------------------|--|
| Subject group type                         | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed                | 49   | 101   | 12                         |  |
| Units: cm                                  |  |   |                            |  |
| arithmetic mean (standard error)           |  |   |                            |  |
| Females: Baseline (n = 24, 59, 2)          | 158.1 (± 2.3)  | 157.9 (± 1.3)   | 149.4 (± 7.1)              |  |
| Females: Change at week 24 (n = 21, 55, 2) | 2.8 (± 0.7)  | 2.0 (± 0.4)   | 1.6 (± 1.1)                |  |
| Females: Change at week 48 (n = 22, 55, 2) | 4.2 (± 1.0)  | 2.8 (± 0.5)   | 1.4 (± 2.4)                |  |
| Females: Change at week 80 (n = 24, 56, 2) | 4.0 (± 1.7)  | 3.4 (± 0.7)   | 2.4 (± 3.9)                |  |
| Males: Baseline (n = 25, 42, 10)           | 158.2 (± 3.0)  | 163.7 (± 1.9)   | 158.9 (± 4.8)              |  |
| Males: Change at week 24 (n = 23, 40, 10)  | 3.4 (± 0.5)  | 3.8 (± 0.5)   | 3.8 (± 0.8)                |  |
| Males: Change at week 48 (n = 23, 39, 9)   | 6.2 (± 0.8)  | 6.2 (± 0.7)   | 5.3 (± 1.2)                |  |
| Males: Change at week 80 (n = 21, 36, 9)   | 9.3 (± 1.5)  | 9.0 (± 1.1)   | 9.2 (± 1.6)                |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Weight at Weeks 24, 48, and 80

End point title Change from Baseline in Weight at Weeks 24, 48, and 80

End point description:

Results are reported for the full analysis set with available data at each time point.

End point type Secondary

End point timeframe:

Baseline and weeks 24, 48, and 80



| End point values                           | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|--|--|---|----------------------------|--|
| Subject group type                         | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed                | 49   | 101   | 12                         |  |
| Units: kg                                  |  |   |                            |  |
| arithmetic mean (standard error)           |  |   |                            |  |
| Females: Baseline (n = 24, 59, 2)          | 52.8 (± 2.9)   | 57.0 (± 2.0)  | 42.7 (± 1.3)               |  |
| Females: Change at week 24 (n = 21, 55, 2) | 3.3 (± 0.8)  | 2.3 (± 0.6)   | 3.4 (± 2.1)                |  |
| Females: Change at week 48(n= 22, 54, 2)   | 4.3 (± 1.1)  | 3.5 (± 0.7)   | 4.7 (± 5.3)                |  |
| Females: Change at week 80 (n = 24, 56, 2) | 5.6 (± 1.3)  | 5.2 (± 0.8)   | 5.5 (± 4.2)                |  |
| Males: Baseline (n = 25, 42, 10)           | 54.1 (± 3.6)   | 61.0 (± 3.2)  | 51.7 (± 4.9)               |  |
| Males: Change at week 24 (n = 23, 40, 10)  | 4.4 (± 0.9)  | 4.6 (± 0.7)   | 4.6 (± 0.9)                |  |
| Males: Change at week 48 (n = 23, 39, 9)   | 6.8 (± 1.3)  | 7.4 (± 1.0)   | 7.6 (± 1.2)                |  |
| Males: Change at week 80 (n = 21, 36, 9)   | 10.9 (± 1.6)   | 11.2 (± 1.4)  | 10.6 (± 2.3)               |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Change in Tanner Staging from Baseline to Week 80

|   |   |
|---|---|
| End point title   | Number of Participants with Change in Tanner Staging from Baseline to Week 80 |
| End point description:  |   |
| Pubertal growth and sexual maturity was assessed separately for males and females using the 5 Tanner stages where stage 1 = prepubertal and stage 5 = mature. Results are reported for the full analysis set. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Baseline and week 80  |   |

| End point values                       | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |  |
|--|--|---|----------------------------|--|
| Subject group type                     | Reporting group                                      | Reporting group   | Reporting group            |  |
| Number of subjects analysed            | 49   | 101   | 12                         |  |
| Units: participants                    |  |   |                            |  |
| Males: Staging by genital size         | 13   | 20  | 6                          |  |
| Males: Staging by pubic hair           | 14   | 21  | 6                          |  |
| Females: Staging by breast development | 11   | 27  | 1                          |  |

|                                |    |    |   |  |
|--------------------------------|----|----|---|--|
| Females: Staging by pubic hair | 11 | 26 | 1 |  |
|--------------------------------|----|----|---|--|

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of evolocumab in this study up to and including 30 days after the last dose or up to the end of study date, whichever was earlier; up to 80 weeks.

Adverse event reporting additional description:

Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM |
|-----------------------|--|

Reporting group description:

Participants with heterozygous familial hypercholesterolemia (HeFH) who had received placebo in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks (QM) for up to 80 weeks.

|                       |   |
|-----------------------|---|
| Reporting group title | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM |
|-----------------------|---|

Reporting group description:

Participants with heterozygous familial hypercholesterolemia who had received evolocumab in the parent study received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | HoFH: Evolocumab 420 mg QM |
|-----------------------|----------------------------|

Reporting group description:

Participants with homozygous familial hypercholesterolemia (HoFH) received 420 mg evolocumab administered by subcutaneous injection every 4 weeks for up to 80 weeks.

| Serious adverse events                            | HeFH (Placebo in Parent Study): Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study): Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |
|---|--|---|----------------------------|
| Total subjects affected by serious adverse events |  |   |                            |
| subjects affected / exposed                       | 2 / 49 (4.08%)                                       | 2 / 101 (1.98%)   | 2 / 12 (16.67%)            |
| number of deaths (all causes)                     | 0  | 0   | 0                          |
| number of deaths resulting from adverse events    |  |   |                            |
| Injury, poisoning and procedural complications    |  |   |                            |
| Arteriovenous fistula aneurysm                    |  |   |                            |
| subjects affected / exposed                       | 0 / 49 (0.00%)                                       | 0 / 101 (0.00%)   | 1 / 12 (8.33%)             |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0   | 0 / 1                      |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0   | 0 / 0                      |
| Wrist fracture                                    |  |   |                            |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 101 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Nervous system disorders</b>                 |                |                 |                |
| Headache  |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 101 (0.99%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Psychiatric disorders</b>                    |                |                 |                |
| Anorexia nervosa                                |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 101 (0.99%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Infections and infestations</b>              |                |                 |                |
| Appendicitis                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 101 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Appendicitis perforated                         |                |                 |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 101 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Peritonitis                                     |                |                 |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 101 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |

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

| <b>Non-serious adverse events</b>                                   | HeFH (Placebo in Parent Study):<br>Evolocumab 420 mg QM | HeFH (Evolocumab in Parent Study):<br>Evolocumab 420 mg QM | HoFH: Evolocumab 420 mg QM |
|---|---|--|----------------------------|
| Total subjects affected by non-serious adverse events               |   |  |                            |
| subjects affected / exposed   | 27 / 49 (55.10%)  | 45 / 101 (44.55%)  | 7 / 12 (58.33%)            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |                            |

|   |                      |                       |                     |
|---|----------------------|-----------------------|---------------------|
| Lipoma<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0  | 0 / 101 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Injury, poisoning and procedural complications<br>Vascular pseudoaneurysm<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0  | 0 / 101 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                                      | 4 / 49 (8.16%)<br>7  | 9 / 101 (8.91%)<br>16 | 1 / 12 (8.33%)<br>1 |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)           | 4 / 49 (8.16%)<br>4  | 3 / 101 (2.97%)<br>3  | 0 / 12 (0.00%)<br>0 |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)  | 5 / 49 (10.20%)<br>8 | 8 / 101 (7.92%)<br>10 | 0 / 12 (0.00%)<br>0 |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)   | 4 / 49 (8.16%)<br>11 | 1 / 101 (0.99%)<br>2  | 0 / 12 (0.00%)<br>0 |
| Injection site haemorrhage<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0  | 1 / 101 (0.99%)<br>2  | 1 / 12 (8.33%)<br>1 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 5 / 49 (10.20%)<br>7 | 1 / 101 (0.99%)<br>1  | 0 / 12 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 49 (2.04%)<br>1  | 5 / 101 (4.95%)<br>6  | 1 / 12 (8.33%)<br>1 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0  | 1 / 101 (0.99%)<br>1  | 1 / 12 (8.33%)<br>1 |
| Respiratory, thoracic and mediastinal disorders   |                      |                       |                     |

|   |                       |                         |                      |
|---|-----------------------|-------------------------|----------------------|
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0   | 1 / 101 (0.99%)<br>1    | 2 / 12 (16.67%)<br>6 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 4 / 49 (8.16%)<br>5   | 5 / 101 (4.95%)<br>5    | 0 / 12 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 49 (0.00%)<br>0   | 3 / 101 (2.97%)<br>3    | 1 / 12 (8.33%)<br>1  |
| Psychiatric disorders<br>Attention deficit hyperactivity disorder<br>subjects affected / exposed<br>occurrences (all) | 2 / 49 (4.08%)<br>2   | 2 / 101 (1.98%)<br>2    | 1 / 12 (8.33%)<br>1  |
| Musculoskeletal and connective tissue disorders<br>Myositis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 49 (0.00%)<br>0   | 0 / 101 (0.00%)<br>0    | 1 / 12 (8.33%)<br>1  |
| Infections and infestations<br>Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 49 (6.12%)<br>3   | 7 / 101 (6.93%)<br>9    | 0 / 12 (0.00%)<br>0  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0   | 3 / 101 (2.97%)<br>3    | 1 / 12 (8.33%)<br>1  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)   | 8 / 49 (16.33%)<br>10 | 14 / 101 (13.86%)<br>20 | 0 / 12 (0.00%)<br>0  |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0   | 1 / 101 (0.99%)<br>2    | 1 / 12 (8.33%)<br>1  |
| Tonsillitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0   | 4 / 101 (3.96%)<br>4    | 1 / 12 (8.33%)<br>1  |
| Upper respiratory tract infection   |                       |                         |                      |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 3 / 49 (6.12%)<br>3 | 6 / 101 (5.94%)<br>6 | 1 / 12 (8.33%)<br>2 |
| Metabolism and nutrition disorders<br>Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 3 / 101 (2.97%)<br>3 | 1 / 12 (8.33%)<br>2 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 10 September 2015 | <ul style="list-style-type: none"><li>• Added safety endpoint of incidence of abnormal neurological examination at week 80.</li><li>• Changed endpoint of change from baseline in cognitive function at week 80 as assessed by Cogstate battery from an exploratory endpoint to a safety endpoint.</li><li>• Added that adverse device effects and disease related events would be collected at every study visit.</li><li>• Added collection of sample for assessment of fasting vitamins A, D, E, and K levels.</li><li>• Deleted papilla elevation from tanner stages (sexual maturity ratings) for stage 1 male genital size.</li></ul>   |
| 22 June 2016      | <ul style="list-style-type: none"><li>• Clarified primary endpoint timepoint at week 80.</li><li>• Added language that defines baseline lab values for rollover and de novo subjects.</li><li>• Clarified eligibility criteria; rollover subjects should not have experienced treatment related serious adverse events in Study 20120123.</li><li>• Updated schedule of assessments and study procedures:<ul style="list-style-type: none"><li>- allowed for a 4 week screening window for rollover subjects and for those subjects who exceed the 4-week window noted which procedures must be redone;</li><li>- updated collection points for creatinine kinase;</li><li>- added additional analytes for urinalysis;</li><li>- removed thyroid stimulating hormone (TSH) as an analyte.</li></ul></li></ul> |
| 26 April 2017     | <ul style="list-style-type: none"><li>• Updated the number of sites expected.</li><li>• Added AMD product information and option for device use.</li><li>• Clarified enrollment should be on day 1 or as close as possible to day 1 and no earlier than 5 days prior to day 1.</li><li>• Aligned safety definitions and reporting procedures with current protocol template.</li></ul>  |
| 27 May 2020       | <ul style="list-style-type: none"><li>• Added interim analysis for all enrolled subjects.</li><li>• Updated number of subjects expected to roll over from Study 20120123 into Study 20120124.</li><li>• Aligned with current protocol template:<ul style="list-style-type: none"><li>- removed language regarding the collection of disease related events;</li><li>- removed details from study monitoring and data collection to restrict Amgen (or designee) correcting obvious data errors in the clinical trial database.</li></ul></li></ul>  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported