



## Clinical trial results:

### A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Clinical Trial to Evaluate the Safety and Efficacy of Ertugliflozin (MK8835/PF04971729) in the Treatment of Subjects with Type 2 Diabetes Mellitus Who Have Inadequate Glycemic Control on Metformin and Sitagliptin

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-003697-26 |
| Trial protocol           | CZ SK FI BG HU |
| Global end of trial date | 06 June 2016   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 04 June 2017 |
| First version publication date | 04 June 2017 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | 8835-006 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |                                  |
|------------------------------------|----------------------------------|
| ISRCTN number                      | -                                |
| ClinicalTrials.gov id (NCT number) | NCT02036515                      |
| WHO universal trial number (UTN)   | -                                |
| Other trial identifiers            | Pfizer Protocol Number: B1521015 |

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:

## Results analysis stage

|                                                      |              |
|------------------------------------------------------|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 06 June 2016 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 06 June 2016 |
| Was the trial ended prematurely? | No           |

Notes:

## General information about the trial

Main objective of the trial:

This is a safety and efficacy study of ertugliflozin (MK8835/PF04971729) in the treatment of participants with type 2 diabetes mellitus who have inadequate glycemic control on metformin and sitagliptin. The primary objective of the trial is to assess the hemoglobin A1C (A1C) lowering efficacy of the addition of ertugliflozin compared to the addition of placebo with an underlying hypothesis that addition of treatment with ertugliflozin provides greater reduction in A1C compared with the addition of placebo; the primary objective will be tested for both 5mg and 15mg doses of ertugliflozin.

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. The following additional measure(s) defined for this individual study was (were) in place for the protection of trial subjects: During the double-blind treatment period, participants who met progressively more stringent glycemic rescue criteria were to receive open-label glimepiride rescue medication. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol-specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication.

Background therapy: -

Evidence for comparator: -

|                                                           |               |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment                          | 12 March 2014 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 16          |
| Country: Number of subjects enrolled | Bulgaria: 32           |
| Country: Number of subjects enrolled | Colombia: 17           |
| Country: Number of subjects enrolled | Czech Republic: 48     |
| Country: Number of subjects enrolled | Finland: 27            |
| Country: Number of subjects enrolled | Hungary: 27            |
| Country: Number of subjects enrolled | Israel: 35             |
| Country: Number of subjects enrolled | Korea, Republic of: 63 |
| Country: Number of subjects enrolled | Malaysia: 30           |
| Country: Number of subjects enrolled | Romania: 39            |
| Country: Number of subjects enrolled | Slovakia: 36           |
| Country: Number of subjects enrolled | United States: 94      |
| Worldwide total number of subjects   | 464                    |
| EEA total number of subjects         | 209                    |

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)                      | 326 |
| From 65 to 84 years                       | 138 |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Two participants were randomized to Ertugliflozin 15 mg, but did not receive any treatment.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Randomization period    |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

### Arms

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

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Ertugliflozin 5 mg |
|------------------|--------------------|

Arm description:

Ertugliflozin, 5 mg, oral, once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Ertugliflozin 5 mg  |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Ertugliflozin, oral, 5 mg tablet once daily for 52 weeks

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

Dosage and administration details:

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the investigator according to clinical practice guidelines of the local country.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Ertugliflozin 15 mg |
|------------------|---------------------|

**Arm description:**

Ertugliflozin, 15 mg, oral, once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Ertugliflozin 5 mg  |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

**Dosage and administration details:**

Ertugliflozin, oral, 5 mg tablet once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Ertugliflozin 10 mg |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

**Dosage and administration details:**

Ertugliflozin, oral, 10 mg tablet once daily for 52 weeks

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Metformin                |
| Investigational medicinal product code |                          |
| Other name                             | Glucophage Glucophage XR |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

**Dosage and administration details:**

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

**Dosage and administration details:**

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

**Dosage and administration details:**

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the investigator according to clinical practice guidelines of the local country.

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

**Arm description:**

Matching placebo to ertugliflozin, oral, once daily for 52 weeks

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

**Dosage and administration details:**

Placebo to ertugliflozin 5 mg and 10 mg once daily for 52 weeks

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Metformin                |
| Investigational medicinal product code |                          |
| Other name                             | Glucophage Glucophage XR |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

**Dosage and administration details:**

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

**Dosage and administration details:**

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

**Dosage and administration details:**

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

**Dosage and administration details:**

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the

| <b>Number of subjects in period 1</b> | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo |
|---------------------------------------|--------------------|---------------------|---------|
| Started                               | 156                | 155                 | 153     |
| Completed                             | 156                | 153                 | 153     |
| Not completed                         | 0                  | 2                   | 0       |
| Screen failure                        | -                  | 2                   | -       |

## Period 2

|                              |                          |
|------------------------------|--------------------------|
| Period 2 title               | 52-week treatment period |
| Is this the baseline period? | Yes <sup>[1]</sup>       |
| Allocation method            | Randomised - controlled  |
| Blinding used                | Double blind             |
| Roles blinded                | Subject, Investigator    |

## Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | Ertugliflozin 5 mg |

### Arm description:

Ertugliflozin, 5 mg, oral, once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Ertugliflozin 5 mg  |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

### Dosage and administration details:

Ertugliflozin, oral, 5 mg tablet once daily for 52 weeks

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

### Dosage and administration details:

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the investigator according to clinical practice guidelines of the local country.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Ertugliflozin 15 mg |
|------------------|---------------------|

Arm description:

Ertugliflozin, 15 mg, oral, once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Ertugliflozin 5 mg  |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Ertugliflozin, oral, 5 mg tablet once daily for 52 weeks

|                                        |                     |
|----------------------------------------|---------------------|
| Investigational medicinal product name | Ertugliflozin 10 mg |
| Investigational medicinal product code |                     |
| Other name                             | MK-8835 PF-04971729 |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Ertugliflozin, oral, 10 mg tablet once daily for 52 weeks

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Metformin                |
| Investigational medicinal product code |                          |
| Other name                             | Glucophage Glucophage XR |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the investigator according to clinical practice guidelines of the local country.

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

Arm description:

Matching placebo to ertugliflozin, oral, once daily for 52 weeks

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

Dosage and administration details:

Placebo to ertugliflozin 5 mg and 10 mg once daily for 52 weeks

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Metformin                |
| Investigational medicinal product code |                          |
| Other name                             | Glucophage Glucophage XR |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Participants were to remain on their stable doses of metformin (oral,  $\geq 1500$  mg/day) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Sitagliptin |
| Investigational medicinal product code |             |
| Other name                             | Januvia     |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Participants were to remain on their stable doses of sitagliptin (oral, 100 mg once daily) while receiving blinded investigational product during the double-blind treatment period.

|                                        |             |
|----------------------------------------|-------------|
| Investigational medicinal product name | Glimepiride |
| Investigational medicinal product code |             |
| Other name                             | Amaryl      |
| Pharmaceutical forms                   | Tablet      |
| Routes of administration               | Oral use    |

Dosage and administration details:

Glimepiride rescue medication, oral, once daily, open-label glimepiride; dose determined per the investigator's discretion

|                                        |                  |
|----------------------------------------|------------------|
| Investigational medicinal product name | Insulin          |
| Investigational medicinal product code |                  |
| Other name                             | Lantus           |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Insulin glargine rescue medication, injectable, as required. In the event that an investigator considers use of glimepiride to not be appropriate for a participant meeting protocol specified glycemic rescue criteria, insulin glargine may have been initiated as the rescue medication, and managed by the investigator according to clinical practice guidelines of the local country.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The baseline period (52-week treatment period) consists of participants who received at least one dose of study medication. Period 1 includes 2 participants who were randomized but not treated.

| <b>Number of subjects in period 2<sup>[2]</sup></b> | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo |
|-----------------------------------------------------|--------------------|---------------------|---------|
| Started                                             | 156                | 153                 | 153     |
| Completed                                           | 151                | 143                 | 139     |
| Not completed                                       | 5                  | 10                  | 14      |
| Consent withdrawn by subject                        | 4                  | 7                   | 9       |
| Adverse event, non-fatal                            | 1                  | 1                   | 2       |
| Non-compliance with study drug                      | -                  | -                   | 2       |
| Lost to follow-up                                   | -                  | 2                   | -       |
| Hyperglycemia                                       | -                  | -                   | 1       |

Notes:

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

Justification: The worldwide number of subjects enrolled in the study includes 2 participants who were randomized but not treated. The baseline period (52-week treatment period) consists of participants who received at least one dose of study medication.

## Baseline characteristics

### Reporting groups

|                                                                                                  |                     |
|--------------------------------------------------------------------------------------------------|---------------------|
| Reporting group title                                                                            | Ertugliflozin 5 mg  |
| Reporting group description:<br>Ertugliflozin, 5 mg, oral, once daily for 52 weeks               |                     |
| Reporting group title                                                                            | Ertugliflozin 15 mg |
| Reporting group description:<br>Ertugliflozin, 15 mg, oral, once daily for 52 weeks              |                     |
| Reporting group title                                                                            | Placebo             |
| Reporting group description:<br>Matching placebo to ertugliflozin, oral, once daily for 52 weeks |                     |

| Reporting group values                                                                                               | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo |
|----------------------------------------------------------------------------------------------------------------------|--------------------|---------------------|---------|
| Number of subjects                                                                                                   | 156                | 153                 | 153     |
| Age categorical                                                                                                      |                    |                     |         |
| Units: Subjects                                                                                                      |                    |                     |         |
| <45 years                                                                                                            | 10                 | 9                   | 15      |
| 45 to 64 years                                                                                                       | 97                 | 102                 | 91      |
| 65 years and older                                                                                                   | 49                 | 42                  | 47      |
| Age Continuous                                                                                                       |                    |                     |         |
| Units: years                                                                                                         |                    |                     |         |
| arithmetic mean                                                                                                      | 59.2               | 59.7                | 58.3    |
| standard deviation                                                                                                   | ± 9.3              | ± 8.6               | ± 9.2   |
| Gender, Male/Female                                                                                                  |                    |                     |         |
| Units: Subjects                                                                                                      |                    |                     |         |
| Female                                                                                                               | 75                 | 71                  | 53      |
| Male                                                                                                                 | 81                 | 82                  | 100     |
| Study Specific Characteristic   Hemoglobin A1c (A1C)                                                                 |                    |                     |         |
| Participants with baseline data: ertugliflozin 5 mg, n=155; ertugliflozin 15 mg, n=152; placebo, n=152; total, n=459 |                    |                     |         |
| Units: Percent                                                                                                       |                    |                     |         |
| arithmetic mean                                                                                                      | 8.05               | 8                   | 8.03    |
| standard deviation                                                                                                   | ± 0.86             | ± 0.83              | ± 0.93  |
| Study Specific Characteristic   Fasting plasma glucose                                                               |                    |                     |         |
| Participants with baseline data: ertugliflozin 5 mg, n=156; ertugliflozin 15 mg, n=152; placebo, n=152; total, n=460 |                    |                     |         |
| Units: mg/dL                                                                                                         |                    |                     |         |
| arithmetic mean                                                                                                      | 167.7              | 171.7               | 169.6   |
| standard deviation                                                                                                   | ± 37.7             | ± 39.1              | ± 37.8  |
| Study Specific Characteristic   Body weight                                                                          |                    |                     |         |
| Units: Kilograms                                                                                                     |                    |                     |         |
| arithmetic mean                                                                                                      | 87.6               | 86.6                | 86.4    |
| standard deviation                                                                                                   | ± 18.6             | ± 19.5              | ± 20.8  |
| Study Specific Characteristic   Estimated glomerular filtration rate (eGFR)                                          |                    |                     |         |
| Units: mL/min/1.73m <sup>2</sup>                                                                                     |                    |                     |         |
| arithmetic mean                                                                                                      | 87                 | 86.9                | 89.9    |

|                    |        |        |        |
|--------------------|--------|--------|--------|
| standard deviation | ± 17.5 | ± 15.6 | ± 17.5 |
|--------------------|--------|--------|--------|

|                                                                                                                      |       |  |  |
|----------------------------------------------------------------------------------------------------------------------|-------|--|--|
| <b>Reporting group values</b>                                                                                        | Total |  |  |
| Number of subjects                                                                                                   | 462   |  |  |
| Age categorical                                                                                                      |       |  |  |
| Units: Subjects                                                                                                      |       |  |  |
| <45 years                                                                                                            | 34    |  |  |
| 45 to 64 years                                                                                                       | 290   |  |  |
| 65 years and older                                                                                                   | 138   |  |  |
| Age Continuous                                                                                                       |       |  |  |
| Units: years                                                                                                         |       |  |  |
| arithmetic mean                                                                                                      |       |  |  |
| standard deviation                                                                                                   | -     |  |  |
| Gender, Male/Female                                                                                                  |       |  |  |
| Units: Subjects                                                                                                      |       |  |  |
| Female                                                                                                               | 199   |  |  |
| Male                                                                                                                 | 263   |  |  |
| Study Specific Characteristic   Hemoglobin A1c (A1C)                                                                 |       |  |  |
| Participants with baseline data: ertugliflozin 5 mg, n=155; ertugliflozin 15 mg, n=152; placebo, n=152; total, n=459 |       |  |  |
| Units: Percent                                                                                                       |       |  |  |
| arithmetic mean                                                                                                      |       |  |  |
| standard deviation                                                                                                   | -     |  |  |
| Study Specific Characteristic   Fasting plasma glucose                                                               |       |  |  |
| Participants with baseline data: ertugliflozin 5 mg, n=156; ertugliflozin 15 mg, n=152; placebo, n=152; total, n=460 |       |  |  |
| Units: mg/dL                                                                                                         |       |  |  |
| arithmetic mean                                                                                                      |       |  |  |
| standard deviation                                                                                                   | -     |  |  |
| Study Specific Characteristic   Body weight                                                                          |       |  |  |
| Units: Kilograms                                                                                                     |       |  |  |
| arithmetic mean                                                                                                      |       |  |  |
| standard deviation                                                                                                   | -     |  |  |
| Study Specific Characteristic   Estimated glomerular filtration rate (eGFR)                                          |       |  |  |
| Units: mL/min/1.73m <sup>2</sup>                                                                                     |       |  |  |
| arithmetic mean                                                                                                      |       |  |  |
| standard deviation                                                                                                   | -     |  |  |

## End points

### End points reporting groups

|                                                                                                  |                     |
|--------------------------------------------------------------------------------------------------|---------------------|
| Reporting group title                                                                            | Ertugliflozin 5 mg  |
| Reporting group description:<br>Ertugliflozin, 5 mg, oral, once daily for 52 weeks               |                     |
| Reporting group title                                                                            | Ertugliflozin 15 mg |
| Reporting group description:<br>Ertugliflozin, 15 mg, oral, once daily for 52 weeks              |                     |
| Reporting group title                                                                            | Placebo             |
| Reporting group description:<br>Matching placebo to ertugliflozin, oral, once daily for 52 weeks |                     |
| Reporting group title                                                                            | Ertugliflozin 5 mg  |
| Reporting group description:<br>Ertugliflozin, 5 mg, oral, once daily for 52 weeks               |                     |
| Reporting group title                                                                            | Ertugliflozin 15 mg |
| Reporting group description:<br>Ertugliflozin, 15 mg, oral, once daily for 52 weeks              |                     |
| Reporting group title                                                                            | Placebo             |
| Reporting group description:<br>Matching placebo to ertugliflozin, oral, once daily for 52 weeks |                     |

### Primary: Change from baseline in hemoglobin A1C at Week 26

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Change from baseline in hemoglobin A1C at Week 26 |
| End point description:<br>A1C is measured as percent. Thus this change from baseline reflects the Week 26 A1C percent minus the Week 0 A1C percent. Laboratory measurements were performed after an overnight fast $\geq 10$ hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one A1C measurement (baseline or post-baseline). |                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Primary                                           |
| End point timeframe:<br>Baseline and Week 26                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                   |

| End point values                             | Ertugliflozin 5 mg     | Ertugliflozin 15 mg    | Placebo                |  |
|----------------------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                  | 156                    | 153                    | 153                    |  |
| Units: Percent                               |                        |                        |                        |  |
| least squares mean (confidence interval 95%) | -0.78 (-0.91 to -0.65) | -0.86 (-0.99 to -0.72) | -0.09 (-0.23 to -0.04) |  |

## Statistical analyses

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo           |
| Number of subjects included in analysis | 309                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[1]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares mean       |
| Point estimate                          | -0.69                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -0.87                                  |
| upper limit                             | -0.5                                   |

Notes:

[1] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo          |
| Number of subjects included in analysis | 306                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[2]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares mean       |
| Point estimate                          | -0.76                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -0.95                                  |
| upper limit                             | -0.58                                  |

Notes:

[2] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

### Primary: Percentage of Participants Experiencing An Adverse Event (AE)

|                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                               |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                          | Percentage of Participants Experiencing An Adverse Event (AE) |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                               |
| An adverse event is defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product, and which does not necessarily have to have a causal relationship with this treatment. Data presented include data following the initiation of rescue therapy. Analysis population consisted of all randomized participants who took at least one dose of study medication. |                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                           | Primary                                                       |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                               |
| Up to Week 54                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                               |

| <b>End point values</b>           | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 57.7               | 60.1                | 63.4            |  |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| Parameter estimate                      | Difference in percentage     |
| Point estimate                          | -5.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -16.5                        |
| upper limit                             | 5.2                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison      |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo |
| Number of subjects included in analysis | 306                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| Parameter estimate                      | Difference in percentage      |
| Point estimate                          | -3.3                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -14.1                         |
| upper limit                             | 7.6                           |

## Primary: Percentage of Participants Discontinuing Study Treatment Due to an AE

|                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                          | Percentage of Participants Discontinuing Study Treatment Due to an AE |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                       |
| An adverse event is defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product, and which does not necessarily have to have a causal relationship with this treatment. Data presented include data following the initiation of rescue therapy. Analysis population consisted of all randomized participants who took at least one dose of study medication. |                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                           | Primary                                                               |

End point timeframe:

Up to Week 52

| End point values                  | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 4.5                | 3.9                 | 3.9             |  |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| Statistical analysis title              | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| Parameter estimate                      | Difference in percentage     |
| Point estimate                          | 0.6                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -4.4                         |
| upper limit                             | 5.6                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| Statistical analysis title              | Between group comparison      |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo |
| Number of subjects included in analysis | 306                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| Parameter estimate                      | Difference in percentage      |
| Point estimate                          | 0                             |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -4.9                          |
| upper limit                             | 4.9                           |

### Secondary: Change from baseline in fasting plasma glucose (FPG) at Week 26

|                 |                                                                 |
|-----------------|-----------------------------------------------------------------|
| End point title | Change from baseline in fasting plasma glucose (FPG) at Week 26 |
|-----------------|-----------------------------------------------------------------|

End point description:

The change from baseline is the Week 26 FPG minus the Week 0 FPG. Laboratory measurements were performed after an overnight fast  $\geq 10$  hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one FPG measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 26

| End point values                             | Ertugliflozin 5 mg        | Ertugliflozin 15 mg       | Placebo              |  |
|----------------------------------------------|---------------------------|---------------------------|----------------------|--|
| Subject group type                           | Reporting group           | Reporting group           | Reporting group      |  |
| Number of subjects analysed                  | 156                       | 153                       | 153                  |  |
| Units: mg/dL                                 |                           |                           |                      |  |
| least squares mean (confidence interval 95%) | -26.91 (-32.58 to -21.24) | -33.04 (-38.71 to -27.36) | -1.76 (-7.7 to 4.18) |  |

## Statistical analyses

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo           |
| Number of subjects included in analysis | 309                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[3]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Differenc in least squares means       |
| Point estimate                          | -25.15                                 |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -32.76                                 |
| upper limit                             | -17.54                                 |

Notes:

[3] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo          |
| Number of subjects included in analysis | 306                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[4]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares means      |
| Point estimate                          | -31.28                                 |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -38.9   |
| upper limit         | -23.66  |

Notes:

[4] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

## Secondary: Change from baseline in body weight at Week 26

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Change from baseline in body weight at Week 26 |
|-----------------|------------------------------------------------|

End point description:

The change from baseline is the Week 26 body weight minus the Week 0 body weight. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one body weight measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 26

| End point values                             | Ertugliflozin 5 mg     | Ertugliflozin 15 mg   | Placebo                |  |
|----------------------------------------------|------------------------|-----------------------|------------------------|--|
| Subject group type                           | Reporting group        | Reporting group       | Reporting group        |  |
| Number of subjects analysed                  | 156                    | 153                   | 153                    |  |
| Units: kg                                    |                        |                       |                        |  |
| least squares mean (confidence interval 95%) | -3.35 (-3.78 to -2.91) | -3.04 (-3.48 to -2.6) | -1.32 (-1.77 to -0.87) |  |

## Statistical analyses

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Statistical analysis title              | Between group comparison               |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo           |
| Number of subjects included in analysis | 309                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[5]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares means      |
| Point estimate                          | -2.03                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -2.65                                  |
| upper limit                             | -1.4                                   |

Notes:

[5] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

|                            |                          |
|----------------------------|--------------------------|
| Statistical analysis title | Between group comparison |
|----------------------------|--------------------------|

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| Comparison groups                       | Ertugliflozin 15 mg v Placebo          |
| Number of subjects included in analysis | 306                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | < 0.001 <sup>[6]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares means      |
| Point estimate                          | -1.72                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -2.35                                  |
| upper limit                             | -1.09                                  |

Notes:

[6] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

### Secondary: Percentage of participants with an A1C <7% (53 mmol/mol) at Week 26

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Percentage of participants with an A1C <7% (53 mmol/mol) at Week 26 |
|-----------------|---------------------------------------------------------------------|

End point description:

A1C is measured as percent. Laboratory measurements were performed after an overnight fast  $\geq 10$  hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one A1C measurement (baseline or post-baseline).

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

End point timeframe:

Week 26

| End point values                  | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 32.1               | 39.9                | 17              |  |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| P-value                                 | < 0.001 <sup>[7]</sup>       |
| Method                                  | Regression, Logistic         |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 3.16                         |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.74    |
| upper limit         | 5.72    |

Notes:

[7] - Logistic regression model fitted with terms for treatment, baseline A1C, baseline eGFR and prior antihyperglycemic medication.

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| P-value                                 | < 0.001 <sup>[8]</sup>            |
| Method                                  | Regression, Logistic              |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 4.43                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 2.44                              |
| upper limit                             | 8.02                              |

Notes:

[8] - Logistic regression model fitted with terms for treatment, baseline A1C, baseline eGFR and prior antihyperglycemic medication.

## Secondary: Change from baseline in sitting systolic blood pressure at Week 26

|                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                    | Change from baseline in sitting systolic blood pressure at Week 26 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                    |
| The change from baseline is the Week 26 systolic blood pressure minus the Week 0 systolic blood pressure. Sitting blood pressure was measured in triplicate. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one systolic blood pressure measurement (baseline or post-baseline). |                                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                     | Secondary                                                          |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                    |
| Baseline and Week 26                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                    |

| End point values                    | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                  | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed         | 156                | 153                 | 153             |  |
| Units: mmHg                         |                    |                     |                 |  |
| least squares mean (standard error) |                    |                     |                 |  |
| Baseline                            | 130.87 (± 0.62)    | 130.87 (± 0.62)     | 130.87 (± 0.62) |  |
| Change from baseline                | -3.81 (± 0.87)     | -4.82 (± 0.88)      | -0.88 (± 0.93)  |  |

## Statistical analyses

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo           |
| Number of subjects included in analysis | 309                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | = 0.019 <sup>[9]</sup>                 |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares means      |
| Point estimate                          | -2.93                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -5.36                                  |
| upper limit                             | -0.49                                  |

Notes:

[9] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

|                                         |                                        |
|-----------------------------------------|----------------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison               |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo          |
| Number of subjects included in analysis | 306                                    |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           |                                        |
| P-value                                 | = 0.002 <sup>[10]</sup>                |
| Method                                  | Constrained longitudinal data analysis |
| Parameter estimate                      | Difference in least squares means      |
| Point estimate                          | -3.94                                  |
| Confidence interval                     |                                        |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -6.39                                  |
| upper limit                             | -1.5                                   |

Notes:

[10] - Model is fitted with effects for treatment, time, interaction of time by treatment, effects for baseline eGFR and prior antihyperglycemic medication

## Secondary: Change from baseline in hemoglobin A1C at Week 52

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Change from baseline in hemoglobin A1C at Week 52 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                   |
| A1C is measured as percent. Thus this change from baseline reflects the Week 52 A1C percent minus the Week 0 A1C percent. Laboratory measurements were performed after an overnight fast $\geq 10$ hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one A1C measurement (baseline or post-baseline). |                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Secondary                                         |

End point timeframe:  
Baseline and Week 52

| End point values                             | Ertugliflozin 5 mg    | Ertugliflozin 15 mg    | Placebo              |  |
|----------------------------------------------|-----------------------|------------------------|----------------------|--|
| Subject group type                           | Reporting group       | Reporting group        | Reporting group      |  |
| Number of subjects analysed                  | 156                   | 153                    | 153                  |  |
| Units: Percent                               |                       |                        |                      |  |
| least squares mean (confidence interval 95%) | -0.75 (-0.9 to -0.59) | -0.81 (-0.97 to -0.66) | 0.02 (-0.15 to 0.19) |  |

### Statistical analyses

| Statistical analysis title              | Between group comparison          |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.76                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -0.98                             |
| upper limit                             | -0.54                             |

| Statistical analysis title              | Between group comparison          |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.83                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -1.05                             |
| upper limit                             | -0.61                             |

### Secondary: Change from baseline in FPG at Week 52

|                 |                                        |
|-----------------|----------------------------------------|
| End point title | Change from baseline in FPG at Week 52 |
|-----------------|----------------------------------------|

End point description:

The change from baseline is the Week 52 FPG minus the Week 0 FPG. Laboratory measurements were performed after an overnight fast  $\geq 10$  hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one FPG measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 52

| End point values                             | Ertugliflozin 5 mg        | Ertugliflozin 15 mg      | Placebo              |  |
|----------------------------------------------|---------------------------|--------------------------|----------------------|--|
| Subject group type                           | Reporting group           | Reporting group          | Reporting group      |  |
| Number of subjects analysed                  | 156                       | 153                      | 153                  |  |
| Units: mg/dL                                 |                           |                          |                      |  |
| least squares mean (confidence interval 95%) | -25.57 (-30.91 to -20.23) | -26.38 (-31.8 to -20.97) | 3.19 (-3.08 to 9.47) |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -28.76                            |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -36.44                            |
| upper limit                             | -21.09                            |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -29.58                            |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -37.3                             |
| upper limit                             | -21.85                            |

---

**Secondary: Change from baseline in body weight at Week 52**

---

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Change from baseline in body weight at Week 52 |
|-----------------|------------------------------------------------|

End point description:

The change from baseline is the Week 52 body weight minus the Week 0 body weight. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one body weight measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 52

---

| End point values                             | Ertugliflozin 5 mg     | Ertugliflozin 15 mg    | Placebo                |  |
|----------------------------------------------|------------------------|------------------------|------------------------|--|
| Subject group type                           | Reporting group        | Reporting group        | Reporting group        |  |
| Number of subjects analysed                  | 156                    | 153                    | 153                    |  |
| Units: kg                                    |                        |                        |                        |  |
| least squares mean (confidence interval 95%) | -3.46 (-4.07 to -2.85) | -2.83 (-3.45 to -2.21) | -0.95 (-1.65 to -0.26) |  |

**Statistical analyses**

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Statistical analysis title              | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -2.51                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -3.43                             |
| upper limit                             | -1.59                             |

|                            |                               |
|----------------------------|-------------------------------|
| Statistical analysis title | Between group comparison      |
| Comparison groups          | Ertugliflozin 15 mg v Placebo |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -1.88                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -2.81                             |
| upper limit                             | -0.95                             |

### Secondary: Percentage of participants with an A1C <7% (53 mmol/mol) at Week 52

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Percentage of participants with an A1C <7% (53 mmol/mol) at Week 52 |
|-----------------|---------------------------------------------------------------------|

End point description:

A1C is measured as percent. Laboratory measurements were performed after an overnight fast  $\geq 10$  hours in duration. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one A1C measurement (baseline or post-baseline).

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

End point timeframe:

Week 52

| End point values                  | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 33.3               | 32.7                | 13.7            |  |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 3.63                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 1.98                         |
| upper limit                             | 6.64                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison      |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo |
| Number of subjects included in analysis | 306                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| Parameter estimate                      | Odds ratio (OR)               |
| Point estimate                          | 4.02                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 2.22                          |
| upper limit                             | 7.28                          |

### Secondary: Change from baseline in sitting systolic blood pressure at Week 52

|                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                              | Change from baseline in sitting systolic blood pressure at Week 52 |
| End point description:<br>The change from baseline is the Week 52 systolic blood pressure minus the Week 0 systolic blood pressure. Sitting blood pressure was measured in triplicate. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one systolic blood pressure measurement (baseline or post-baseline). |                                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                                                          |
| End point timeframe:<br>Baseline and Week 52                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                    |

| End point values                    | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                  | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed         | 156                | 153                 | 153             |  |
| Units: mmHg                         |                    |                     |                 |  |
| least squares mean (standard error) |                    |                     |                 |  |
| Baseline                            | 130.92 (± 0.62)    | 130.92 (± 0.62)     | 130.92 (± 0.62) |  |
| Change from baseline                | -4.16 (± 0.95)     | -4.09 (± 0.96)      | 0.83 (± 1.14)   |  |

### Statistical analyses

|                                   |                              |
|-----------------------------------|------------------------------|
| <b>Statistical analysis title</b> | Between group comparison     |
| Comparison groups                 | Ertugliflozin 5 mg v Placebo |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -4.99                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -7.82                             |
| upper limit                             | -2.15                             |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -4.92                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -7.76                             |
| upper limit                             | -2.07                             |

### Secondary: Change from baseline in sitting diastolic blood pressure at Week 26

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Change from baseline in sitting diastolic blood pressure at Week 26 |
|-----------------|---------------------------------------------------------------------|

End point description:

The change from baseline is the Week 26 diastolic blood pressure minus the Week 0 diastolic blood pressure. Sitting blood pressure was measured in triplicate. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one diastolic blood pressure measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 26

| End point values                    | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                  | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed         | 156                | 153                 | 153             |  |
| Units: mmHg                         |                    |                     |                 |  |
| least squares mean (standard error) |                    |                     |                 |  |
| Baseline                            | 78.42 (± 0.36)     | 78.42 (± 0.36)      | 78.42 (± 0.36)  |  |
| Change from baseline                | -1.68 (± 0.61)     | -1.81 (± 0.62)      | -0.43 (± 0.65)  |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -1.24                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -2.97                             |
| upper limit                             | 0.48                              |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -1.38                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -3.11                             |
| upper limit                             | 0.36                              |

## Secondary: Change from baseline in sitting diastolic blood pressure at Week 52

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Change from baseline in sitting diastolic blood pressure at Week 52 |
|-----------------|---------------------------------------------------------------------|

### End point description:

The change from baseline is the Week 52 diastolic blood pressure minus the Week 0 diastolic blood pressure. Sitting blood pressure was measured in triplicate. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one diastolic blood pressure measurement (baseline or post-baseline).

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

### End point timeframe:

Baseline and Week 52

| <b>End point values</b>             | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                  | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed         | 156                | 153                 | 153             |  |
| Units: mmHg                         |                    |                     |                 |  |
| least squares mean (standard error) |                    |                     |                 |  |
| Baseline                            | 78.44 (± 0.36)     | 78.44 (± 0.36)      | 78.44 (± 0.36)  |  |
| Change from baseline                | -1.52 (± 0.61)     | -1.38 (± 0.62)      | -0.53 (± 0.73)  |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 309                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.99                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -2.82                             |
| upper limit                             | 0.84                              |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 306                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.85                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -2.69                             |
| upper limit                             | 0.99                              |

## Secondary: Percentage of participants receiving glycemic rescue medication by Week 26

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Percentage of participants receiving glycemic rescue medication by Week 26 |
|-----------------|----------------------------------------------------------------------------|

End point description:

Glycemic rescue medication was initiated for participants who met progressively more stringent glycemic rescue criteria. Rescue medication included glimepiride (or insulin glargine if glimepiride was not considered appropriate for the participant). Analysis population included all randomized participants who took at least one dose of study medication.

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

End point timeframe:

Week 26

| End point values                  | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 1.3                | 2                   | 16.3            |  |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| Parameter estimate                      | Difference in percent        |
| Point estimate                          | -15.1                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -21.9                        |
| upper limit                             | -9.4                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison      |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo |
| Number of subjects included in analysis | 306                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| Parameter estimate                      | Difference in percent         |
| Point estimate                          | -14.4                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -21.3                         |
| upper limit                             | -8.5                          |

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**Secondary: Percentage of participants receiving glycemic rescue medication by Week 52**

---

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Percentage of participants receiving glycemic rescue medication by Week 52 |
|-----------------|----------------------------------------------------------------------------|

End point description:

Glycemic rescue medication was initiated for participants who met progressively more stringent glycemic rescue criteria. Rescue medication included glimepiride (or insulin glargine if glimepiride was not considered appropriate for the participant). Analysis population included all randomized participants who took at least one dose of study medication.

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

End point timeframe:

Week 52

---

| End point values                  | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed       | 156                | 153                 | 153             |  |
| Units: Percentage of participants |                    |                     |                 |  |
| number (not applicable)           | 12.8               | 13.7                | 41.8            |  |

**Statistical analyses**

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison     |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo |
| Number of subjects included in analysis | 309                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           |                              |
| Parameter estimate                      | Difference in percentage     |
| Point estimate                          | -29                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -38.3                        |
| upper limit                             | -19.4                        |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Between group comparison      |
| Comparison groups                 | Ertugliflozin 15 mg v Placebo |

|                                         |                          |
|-----------------------------------------|--------------------------|
| Number of subjects included in analysis | 306                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| Parameter estimate                      | Difference in percentage |
| Point estimate                          | -28.1                    |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | -37.5                    |
| upper limit                             | -18.4                    |

### Secondary: Time to initiation of glycemic rescue by Week 26

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Time to initiation of glycemic rescue by Week 26 |
| End point description:<br>Glycemic rescue medication was initiated for participants who met progressively more stringent glycemic rescue criteria. Rescue medication included glimepiride (or insulin glargine if glimepiride was not considered appropriate for the participant). Data presented are the minimum and maximum times to the initiation of rescue therapy in days. Analysis population included all randomized participants who took at least one dose of study medication. |                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Secondary                                        |
| End point timeframe:<br>Up to week 26                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                  |

| End point values                              | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                            | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed                   | 156                | 153                 | 153             |  |
| Units: Days                                   |                    |                     |                 |  |
| Minimum time to initiation of glycemic rescue | 135                | 43                  | 26              |  |
| Maximum time to initiation of glycemic rescue | 141                | 147                 | 212             |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to initiation of glycemic rescue by Week 52

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Time to initiation of glycemic rescue by Week 52 |
| End point description:<br>Glycemic rescue medication was initiated for participants who met progressively more stringent glycemic rescue criteria. Rescue medication included glimepiride (or insulin glargine if glimepiride was not considered appropriate for the participant). Data presented are the minimum and maximum times to the initiation of rescue therapy in days. Analysis population included all randomized participants who took at least one dose of study medication. |                                                  |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Secondary                                        |

End point timeframe:

Up to week 52

| End point values                              | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|-----------------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                            | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed                   | 156                | 153                 | 153             |  |
| Units: Days                                   |                    |                     |                 |  |
| Minimum time to initiation of glycemic rescue | 135                | 43                  | 26              |  |
| Maximum time to initiation of glycemic rescue | 295                | 299                 | 327             |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Baseline homeostasis model assessment of $\beta$ -cell function (HOMA-% $\beta$ ) value

|                 |                                                                                         |
|-----------------|-----------------------------------------------------------------------------------------|
| End point title | Baseline homeostasis model assessment of $\beta$ -cell function (HOMA-% $\beta$ ) value |
|-----------------|-----------------------------------------------------------------------------------------|

End point description:

HOMA-% $\beta$  is a well-accepted means of assessing fasting  $\beta$ -cell function, and is calculated using measured C-peptide and glucose levels and is measured as a percentage of a normal reference population.  $\text{HOMA-\%}\beta = [20 \times \text{fasting insulin } (\mu\text{U/mL})] / [\text{fasting plasma glucose (mmol/L)} - 3.5]$ . Analysis population included all randomized participants who took at least one dose of study medication and had HOMA-% $\beta$  measurement at baseline.

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

End point timeframe:

Baseline

| End point values                     | Ertugliflozin 5 mg   | Ertugliflozin 15 mg   | Placebo               |  |
|--------------------------------------|----------------------|-----------------------|-----------------------|--|
| Subject group type                   | Reporting group      | Reporting group       | Reporting group       |  |
| Number of subjects analysed          | 140                  | 131                   | 127                   |  |
| Units: Percentage                    |                      |                       |                       |  |
| arithmetic mean (standard deviation) | 47.99 ( $\pm$ 23.89) | 48.54 ( $\pm$ 34.782) | 48.04 ( $\pm$ 30.733) |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in HOMA-% $\beta$ at Week 26

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Change from baseline in HOMA-%β at Week 26 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                            |
| HOMA-%β is a well-accepted means of assessing fasting β-cell function, and is calculated using measured C-peptide and glucose levels and is measured as a percentage of a normal reference population. $HOMA\text{-}\% \beta = [20 \times \text{fasting insulin } (\mu\text{U/mL})] / [\text{fasting plasma glucose (mmol/L)} - 3.5]$ . Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one HOMA-%β measurement (baseline or post-baseline). |                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                  |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                            |
| Baseline and Week 26                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                            |

| End point values                             | Ertugliflozin 5 mg    | Ertugliflozin 15 mg   | Placebo              |  |
|----------------------------------------------|-----------------------|-----------------------|----------------------|--|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group      |  |
| Number of subjects analysed                  | 153                   | 151                   | 147                  |  |
| Units: Percentage                            |                       |                       |                      |  |
| least squares mean (confidence interval 95%) | 13.28 (8.87 to 17.68) | 12.43 (7.94 to 16.93) | 0.52 (-4.08 to 5.12) |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 300                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 12.75                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 6.83                              |
| upper limit                             | 18.68                             |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| <b>Statistical analysis title</b>       | Between group comparison          |
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 298                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 11.91                             |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 5.94    |
| upper limit         | 17.88   |

## Secondary: Change from baseline in HOMA-%β at Week 52

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Change from baseline in HOMA-%β at Week 52 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                            |
| HOMA-%β is a well-accepted means of assessing fasting β-cell function, and is calculated using measured C-peptide and glucose levels and is measured as a percentage of a normal reference population. $HOMA\text{-}\% \beta = [20 \times \text{fasting insulin } (\mu\text{U/mL})] / [\text{fasting plasma glucose (mmol/L)} - 3.5]$ . Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one HOMA-%β measurement (baseline or post-baseline). |                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                  |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                            |
| Baseline and Week 52                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                            |

| End point values                             | Ertugliflozin 5 mg    | Ertugliflozin 15 mg   | Placebo               |  |
|----------------------------------------------|-----------------------|-----------------------|-----------------------|--|
| Subject group type                           | Reporting group       | Reporting group       | Reporting group       |  |
| Number of subjects analysed                  | 155                   | 152                   | 152                   |  |
| Units: Percentage                            |                       |                       |                       |  |
| least squares mean (confidence interval 95%) | 10.85 (6.29 to 15.41) | 10.93 (6.24 to 15.61) | -1.93 (-6.88 to 3.02) |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Statistical analysis title              | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 307                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 12.78                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 6.54                              |
| upper limit                             | 19.03                             |

|                            |                          |
|----------------------------|--------------------------|
| Statistical analysis title | Between group comparison |
|----------------------------|--------------------------|

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 304                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 12.86                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 6.54                              |
| upper limit                             | 19.18                             |

### Secondary: Baseline EQ-5D 3-level version (EQ-5D-3L) Questionnaire Score

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                               |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Baseline EQ-5D 3-level version (EQ-5D-3L) Questionnaire Score |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                               |
| <p>The EQ-5D-3L is a health profile questionnaire that assesses quality of life along 5 dimensions. Participants rate 5 aspects of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) by choosing from 3 answering options (1=no problems; 2=some problems; 3=extreme problems). The summed score ranges from 1-15 with "3" corresponding to no problems and "15" corresponding to severe problems in the 5 dimensions. EQ-5D-3L also includes an EQ visual analogue score (VAS) that ranges between 100 (best imaginable health) and 0 (worst imaginable health). Total index summary score is weighted with a range of -0.594 (worst) to 1.0 (best). Analysis population included all randomized participants who took at least one dose of study medication and had a baseline EQ-5D-3L measurement.</p> |                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Secondary                                                     |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                               |
| Baseline                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                               |

| End point values                     | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo         |  |
|--------------------------------------|--------------------|---------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group     | Reporting group |  |
| Number of subjects analysed          | 150                | 150                 | 152             |  |
| Units: Score on a scale              |                    |                     |                 |  |
| arithmetic mean (standard deviation) | 0.88 (± 0.166)     | 0.89 (± 0.182)      | 0.9 (± 0.144)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in EQ-5D-3L Questionnaire Score at Week 26

|                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                       | Change from baseline in EQ-5D-3L Questionnaire Score at Week 26 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                |                                                                 |
| <p>The EQ-5D-3L is a health profile questionnaire that assesses quality of life along 5 dimensions. Participants rate 5 aspects of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) by choosing from 3 answering options (1=no problems; 2=some problems; 3=extreme problems). The summed score ranges from 3-15 with "3" corresponding to no problems and</p> |                                                                 |

"15" corresponding to severe problems in the 5 dimensions. EQ-5D-3L also includes an EQ VAS that ranges between 100 (best imaginable health) and 0 (worst imaginable health). Total index summary score is weighted with a range of -0.594 (worst) to 1.0 (best). Decrease from baseline in EQ-5D-3L signifies improvement. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one EQ-5D-3L measurement (baseline or post-baseline).

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Week 26 |           |

| End point values                             | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo              |  |
|----------------------------------------------|--------------------|---------------------|----------------------|--|
| Subject group type                           | Reporting group    | Reporting group     | Reporting group      |  |
| Number of subjects analysed                  | 155                | 151                 | 153                  |  |
| Units: Score on a scale                      |                    |                     |                      |  |
| least squares mean (confidence interval 95%) | 0 (-0.02 to 0.03)  | 0.02 (0 to 0.04)    | 0.01 (-0.01 to 0.04) |  |

## Statistical analyses

| Statistical analysis title              | Between group comparison          |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 308                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.01                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -0.04                             |
| upper limit                             | 0.02                              |

| Statistical analysis title              | Between group comparison          |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | Ertugliflozin 15 mg v Placebo     |
| Number of subjects included in analysis | 304                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 0.01                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -0.02                             |
| upper limit                             | 0.04                              |

## Secondary: Change from baseline in EQ-5D-3L score at Week 52

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Change from baseline in EQ-5D-3L score at Week 52 |
|-----------------|---------------------------------------------------|

End point description:

The EQ-5D-3L is a health profile questionnaire that assesses quality of life along 5 dimensions. Participants rate 5 aspects of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) by choosing from 3 answering options (1=no problems; 2=some problems; 3=extreme problems). The summed score ranges from 3-15 with "3" corresponding to no problems and "15" corresponding to severe problems in the 5 dimensions. EQ-5D-3L also includes an EQ VAS that ranges between 100 (best imaginable health) and 0 (worst imaginable health). Total index summary score is weighted with a range of -0.594 (worst) to 1.0 (best). Decrease from baseline in EQ-5D-3L signifies improvement. Data presented exclude data following the initiation of rescue therapy. Analysis population included all randomized participants who took at least one dose of study medication and had at least one EQ-5D-3L measurement (baseline or post-baseline).

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

End point timeframe:

Baseline and Week 52

| End point values                             | Ertugliflozin 5 mg | Ertugliflozin 15 mg | Placebo              |  |
|----------------------------------------------|--------------------|---------------------|----------------------|--|
| Subject group type                           | Reporting group    | Reporting group     | Reporting group      |  |
| Number of subjects analysed                  | 155                | 151                 | 153                  |  |
| Units: Score on a scale                      |                    |                     |                      |  |
| least squares mean (confidence interval 95%) | 0.03 (0 to 0.05)   | 0 (-0.03 to 0.03)   | 0.02 (-0.01 to 0.06) |  |

## Statistical analyses

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Statistical analysis title              | Between group comparison          |
| Comparison groups                       | Ertugliflozin 5 mg v Placebo      |
| Number of subjects included in analysis | 308                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | 0                                 |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -0.04                             |
| upper limit                             | 0.04                              |

|                            |                               |
|----------------------------|-------------------------------|
| Statistical analysis title | Between group comparison      |
| Comparison groups          | Ertugliflozin 15 mg v Placebo |

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Number of subjects included in analysis | 304                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Difference in least squares means |
| Point estimate                          | -0.02                             |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -0.07                             |
| upper limit                             | 0.02                              |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 54 weeks

Adverse event reporting additional description:

Data presented below includes data following the initiation of rescue therapy for the entire study (ie, all data after randomization, with no upper limit on the follow-up window for participants who discontinued study drug). Two participants randomized to ertugliflozin 15 mg didn't receive any study medication & aren't included in the below tables

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

### Dictionary used

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

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

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Ertugliflozin 5 mg (Phase A+B) |
|-----------------------|--------------------------------|

Reporting group description:

Ertugliflozin, 5 mg, oral, once daily for 52 weeks

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Placebo (Phase A+B) |
|-----------------------|---------------------|

Reporting group description:

Matching placebo to ertugliflozin, oral, once daily for 52 weeks

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Ertugliflozin 15 mg (Phase A+B) |
|-----------------------|---------------------------------|

Reporting group description:

Ertugliflozin, 15 mg, oral, once daily for 52 weeks

| Serious adverse events                                              | Ertugliflozin 5 mg<br>(Phase A+B) | Placebo (Phase A+B) | Ertugliflozin 15 mg<br>(Phase A+B) |
|---------------------------------------------------------------------|-----------------------------------|---------------------|------------------------------------|
| Total subjects affected by serious adverse events                   |                                   |                     |                                    |
| subjects affected / exposed                                         | 13 / 156 (8.33%)                  | 8 / 153 (5.23%)     | 3 / 153 (1.96%)                    |
| number of deaths (all causes)                                       | 0                                 | 1                   | 0                                  |
| number of deaths resulting from adverse events                      | 0                                 | 0                   | 0                                  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                   |                     |                                    |
| Benign ear neoplasm                                                 |                                   |                     |                                    |
| subjects affected / exposed                                         | 1 / 156 (0.64%)                   | 0 / 153 (0.00%)     | 0 / 153 (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                              |
| Bladder cancer                                                      |                                   |                     |                                    |
| subjects affected / exposed                                         | 0 / 156 (0.00%)                   | 1 / 153 (0.65%)     | 0 / 153 (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                              |
| Invasive ductal breast carcinoma                                    |                                   |                     |                                    |

|                                                       |                 |                 |                 |
|-------------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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>Injury, poisoning and procedural complications</b> |                 |                 |                 |
| Femur fracture                                        |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Spinal compression fracture                           |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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>Vascular disorders</b>                             |                 |                 |                 |
| Hypertension                                          |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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>Cardiac disorders</b>                              |                 |                 |                 |
| Acute myocardial infarction                           |                 |                 |                 |
| subjects affected / exposed                           | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |
| Angina pectoris                                       |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Angina unstable                                       |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Coronary artery disease                               |                 |                 |                 |
| subjects affected / exposed                           | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |

|                                                      |                 |                 |                 |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| Nervous system disorders                             |                 |                 |                 |
| Cerebral haemorrhage                                 |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 0 / 153 (0.00%) | 1 / 153 (0.65%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Hemiplegia                                           |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 0 / 153 (0.00%) | 1 / 153 (0.65%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                 |                 |                 |
| Non-cardiac chest pain                               |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |
| Gastrointestinal disorders                           |                 |                 |                 |
| Abdominal pain lower                                 |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                              |                 |                 |                 |
| Cholelithiasis                                       |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |
| Liver disorder                                       |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 0 / 153 (0.00%) | 1 / 153 (0.65%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |                 |
| Chronic obstructive pulmonary disease                |                 |                 |                 |
| subjects affected / exposed                          | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |
| Renal and urinary disorders                          |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Urge incontinence                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Urinary retention                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 156 (0.00%) | 0 / 153 (0.00%) | 1 / 153 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endocrine disorders                             |                 |                 |                 |
| Goitre                                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Infections and infestations                     |                 |                 |                 |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Bone tuberculosis                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Lymphangitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Meningitis tuberculous                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Osteomyelitis                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Pyelonephritis acute                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 156 (0.64%) | 0 / 153 (0.00%) | 0 / 153 (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           |
| Subcutaneous abscess                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 156 (0.00%) | 1 / 153 (0.65%) | 0 / 153 (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           |

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

| <b>Non-serious adverse events</b>                     | Ertugliflozin 5 mg<br>(Phase A+B) | Placebo (Phase A+B) | Ertugliflozin 15 mg<br>(Phase A+B) |
|-------------------------------------------------------|-----------------------------------|---------------------|------------------------------------|
| Total subjects affected by non-serious adverse events |                                   |                     |                                    |
| subjects affected / exposed                           | 24 / 156 (15.38%)                 | 29 / 153 (18.95%)   | 18 / 153 (11.76%)                  |
| Musculoskeletal and connective tissue disorders       |                                   |                     |                                    |
| Back pain                                             |                                   |                     |                                    |
| subjects affected / exposed                           | 8 / 156 (5.13%)                   | 6 / 153 (3.92%)     | 3 / 153 (1.96%)                    |
| occurrences (all)                                     | 8                                 | 6                   | 3                                  |
| Infections and infestations                           |                                   |                     |                                    |
| Nasopharyngitis                                       |                                   |                     |                                    |
| subjects affected / exposed                           | 8 / 156 (5.13%)                   | 5 / 153 (3.27%)     | 6 / 153 (3.92%)                    |
| occurrences (all)                                     | 8                                 | 6                   | 6                                  |
| Urinary tract infection                               |                                   |                     |                                    |
| subjects affected / exposed                           | 2 / 156 (1.28%)                   | 8 / 153 (5.23%)     | 5 / 153 (3.27%)                    |
| occurrences (all)                                     | 2                                 | 9                   | 5                                  |
| Metabolism and nutrition disorders                    |                                   |                     |                                    |

|                                                                   |                       |                        |                       |
|-------------------------------------------------------------------|-----------------------|------------------------|-----------------------|
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all) | 7 / 156 (4.49%)<br>16 | 11 / 153 (7.19%)<br>18 | 5 / 153 (3.27%)<br>11 |
|-------------------------------------------------------------------|-----------------------|------------------------|-----------------------|

## **More information**

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

Were there any global substantial amendments to the protocol? No

---

### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported