



## Clinical trial results:

**ACcomplish: A Phase 2, multicenter, double-blind, randomized, placebo-controlled, dose escalation trial evaluating safety, efficacy, and pharmacokinetics of subcutaneous doses of TransCon CNP administered once weekly for 52 weeks in prepubertal children with achondroplasia followed by an Open-Label Extension Period**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2019-002754-22    |
| Trial protocol           | IE GB DE AT DK PT |
| Global end of trial date | 01 October 2024   |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 24 May 2025   |
| First version publication date | 11 April 2023   |
| Version creation reason        | • New data added to full data set update to include OLE safety data |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | TCC-201 |
|-----------------------|---------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04085523 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Ascendis Pharma Growth Disorders A/S   |
| Sponsor organisation address | Tuborg Blvd 12, Hellerup, Denmark, DK 2900   |
| Public contact               | Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com |
| Scientific contact           | Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.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                       | 19 February 2025 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 October 2024  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

In prepubertal children with achondroplasia (ACH) at 52 weeks

- To determine the safety of once weekly subcutaneous (SC) doses of TransCon CNP
- To evaluate the effect of once weekly SC doses of TransCon CNP on annualized height velocity (AHV).

Protection of trial subjects:

Written informed consent was obtained from all subjects prior to enrollment into the trial, as dictated by the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 May 2020      |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 2 Years          |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 9      |
| Country: Number of subjects enrolled | New Zealand: 2    |
| Country: Number of subjects enrolled | United States: 29 |
| Country: Number of subjects enrolled | Portugal: 1       |
| Country: Number of subjects enrolled | Austria: 3        |
| Country: Number of subjects enrolled | Denmark: 6        |
| Country: Number of subjects enrolled | Germany: 1        |
| Country: Number of subjects enrolled | Ireland: 6        |
| Worldwide total number of subjects   | 57                |
| EEA total number of subjects         | 17                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

|  |    |
|--|----|
| Newborns (0-27 days)                     | 0  |
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 57 |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 0  |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Overall, 57 subjects were enrolled and dosed. Enrollment of subjects occurred in eight countries: Australia, Austria, Denmark, Germany, Ireland, Portugal, New Zealand, and the United States.

### Pre-assignment

Screening details:

A total of 60 subjects were screened and 57 of these met eligibility criteria and were enrolled into the study. All 57 subjects completed the 52-week double-blind period and entered the 104-week open-label extension (OLE), where they received TransCon CNP. All subjects received up to a maximum dose level of 100-mcg dose of TransCon CNP during OLE.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | 52 Week Blinded Treatment Period                              |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |                            |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes                        |
| <b>Arm title</b>             | TransCon CNP (6 mcg/kg/wk) |

Arm description:

Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TransCon CNP                                  |
| Investigational medicinal product code | ACP-015                                       |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | TransCon CNP (20 mcg/kg/wk) |
|------------------|-----------------------------|

Arm description:

Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TransCon CNP                                  |
| Investigational medicinal product code | ACP-015                                       |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | TransCon CNP (50 mcg/kg/wk) |
|------------------|-----------------------------|

Arm description:

Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |   |
|--|---|
| Investigational medicinal product name | TransCon CNP                                  |
| Investigational medicinal product code | ACP-015                                       |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | TransCon CNP (100 mcg/kg/wk) |
|------------------|------------------------------|

Arm description:

Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TransCon CNP                                  |
| Investigational medicinal product code | ACP-015                                       |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

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

Arm description:

Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.

|  |   |
|--|---|
| Arm type                               | Placebo                                       |
| Investigational medicinal product name | Placebo                                       |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

Dosage and administration details:

Placebo for TransCon CNP is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

| <b>Number of subjects in period 1</b> | TransCon CNP (6 mcg/kg/wk) | TransCon CNP (20 mcg/kg/wk) | TransCon CNP (50 mcg/kg/wk) |
|---------------------------------------|----------------------------|-----------------------------|-----------------------------|
| Started                               | 10                         | 11                          | 10                          |
| Completed                             | 10                         | 11                          | 10                          |

| <b>Number of subjects in period 1</b> | TransCon CNP (100 mcg/kg/wk) | Pooled Placebo |
|---------------------------------------|------------------------------|----------------|
| Started                               | 11                           | 15             |
| Completed                             | 11                           | 15             |

## Period 2

|                              |                                     |
|------------------------------|-------------------------------------|
| Period 2 title               | Open-Label Period (Weeks 52 to 156) |
| Is this the baseline period? | No                                  |
| Allocation method            | Randomised - controlled             |
| Blinding used                | Not blinded                         |

## Arms

|                  |   |
|------------------|---|
| <b>Arm title</b> | Open-Label Extension Period: TransCon CNP |
|------------------|---|

### Arm description:

Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegritide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection.

|  |   |
|--|---|
| Arm type                               | Experimental                                  |
| Investigational medicinal product name | TransCon CNP                                  |
| Investigational medicinal product code | ACP-015                                       |
| Other name                             |   |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Subcutaneous use                              |

### Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

| <b>Number of subjects in period 2</b> | Open-Label<br>Extension Period:<br>TransCon CNP |
|---------------------------------------|---|
| Started                               | 57  |
| Completed                             | 55  |
| Not completed                         | 2   |
| Consent withdrawn by subject          | 2   |

## Baseline characteristics

### Reporting groups

|  |                              |
|--|------------------------------|
| Reporting group title  | TransCon CNP (6 mcg/kg/wk)   |
| Reporting group description:   |                              |
| Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.   |                              |
| Reporting group title  | TransCon CNP (20 mcg/kg/wk)  |
| Reporting group description:   |                              |
| Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.  |                              |
| Reporting group title  | TransCon CNP (50 mcg/kg/wk)  |
| Reporting group description:   |                              |
| Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.  |                              |
| Reporting group title  | TransCon CNP (100 mcg/kg/wk) |
| Reporting group description:   |                              |
| Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.   |                              |
| Reporting group title  | Pooled Placebo               |
| Reporting group description:   |                              |
| Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product. |                              |

| Reporting group values | TransCon CNP (6 mcg/kg/wk) | TransCon CNP (20 mcg/kg/wk) | TransCon CNP (50 mcg/kg/wk) |
|------------------------|----------------------------|-----------------------------|-----------------------------|
| Number of subjects     | 10                         | 11                          | 10                          |
| Age categorical        |                            |                             |                             |
| Units: Subjects        |                            |                             |                             |

|   |         |         |         |
|---|---------|---------|---------|
| Age continuous                            |         |         |         |
| Units: years                              |         |         |         |
| arithmetic mean                           | 6.52    | 6.29    | 5.20    |
| standard deviation                        | ± 2.593 | ± 2.896 | ± 2.991 |
| Gender categorical                        |         |         |         |
| Units: Subjects                           |         |         |         |
| Female                                    | 7       | 3       | 3       |
| Male                                      | 3       | 8       | 7       |
| Race                                      |         |         |         |
| Units: Subjects                           |         |         |         |
| American Indian or Alaskan Native         | 0       | 0       | 0       |
| Asian                                     | 2       | 1       | 1       |
| Black or African American                 | 0       | 0       | 0       |
| Native Hawaiian or Other Pacific Islander | 0       | 0       | 1       |
| White                                     | 8       | 10      | 8       |
| Other                                     | 0       | 0       | 0       |
| Ethnicity                                 |         |         |         |
| Units: Subjects                           |         |         |         |
| Hispanic or Latino                        | 1       | 0       | 2       |
| Not Hispanic or Latino                    | 9       | 11      | 6       |
| Unknown/Not Reported                      | 0       | 0       | 2       |
| Region                                    |         |         |         |
| Units: Subjects                           |         |         |         |

|   |         |          |          |
|---|---------|----------|----------|
| North America                             | 4       | 4        | 4        |
| Europe                                    | 2       | 5        | 4        |
| Oceania                                   | 4       | 2        | 2        |
| Height                                    |         |          |          |
| Units: cm                                 |         |          |          |
| arithmetic mean                           | 90.63   | 92.29    | 86.61    |
| standard deviation                        | ± 8.973 | ± 12.103 | ± 12.967 |
| Height SDS                                |         |          |          |
| Units: Standard deviation score (SDS)     |         |          |          |
| arithmetic mean                           | -5.45   | -4.87    | -4.85    |
| standard deviation                        | ± 1.046 | ± 0.673  | ± 0.801  |
| Weight                                    |         |          |          |
| Units: kg                                 |         |          |          |
| arithmetic mean                           | 17.49   | 19.67    | 15.67    |
| standard deviation                        | ± 3.677 | ± 6.602  | ± 4.399  |
| Body Mass Index                           |         |          |          |
| Units: kg^m2                              |         |          |          |
| arithmetic mean                           | 21.10   | 22.52    | 20.61    |
| standard deviation                        | ± 1.664 | ± 2.599  | ± 1.496  |
| Baseline AHV                              |         |          |          |
| Baseline annualized height velocity (AHV) |         |          |          |
| Units: cm/year                            |         |          |          |
| arithmetic mean                           | 5.04    | 5.29     | 5.76     |
| standard deviation                        | ± 2.157 | ± 1.619  | ± 3.147  |

| <b>Reporting group values</b> | TransCon CNP (100 mcg/kg/wk) | Pooled Placebo | Total |
|-------------------------------|------------------------------|----------------|-------|
| Number of subjects            | 11                           | 15             | 57    |
| Age categorical               |                              |                |       |
| Units: Subjects               |                              |                |       |

|   |         |         |    |
|---|---------|---------|----|
| Age continuous                            |         |         |    |
| Units: years                              |         |         |    |
| arithmetic mean                           | 5.79    | 5.89    |    |
| standard deviation                        | ± 2.613 | ± 3.109 | -  |
| Gender categorical                        |         |         |    |
| Units: Subjects                           |         |         |    |
| Female                                    | 6       | 5       | 24 |
| Male                                      | 5       | 10      | 33 |
| Race                                      |         |         |    |
| Units: Subjects                           |         |         |    |
| American Indian or Alaskan Native         | 0       | 0       | 0  |
| Asian                                     | 0       | 2       | 6  |
| Black or African American                 | 1       | 1       | 2  |
| Native Hawaiian or Other Pacific Islander | 0       | 0       | 1  |
| White                                     | 10      | 12      | 48 |
| Other                                     | 0       | 0       | 0  |
| Ethnicity                                 |         |         |    |
| Units: Subjects                           |         |         |    |
| Hispanic or Latino                        | 2       | 1       | 6  |
| Not Hispanic or Latino                    | 9       | 14      | 49 |



|   |          |          |    |
|---|----------|----------|----|
| Unknown/Not Reported                      | 0        | 0        | 2  |
| Region                                    |          |          |    |
| Units: Subjects                           |          |          |    |
| North America                             | 8        | 9        | 29 |
| Europe                                    | 3        | 3        | 17 |
| Oceania                                   | 0        | 3        | 11 |
| Height                                    |          |          |    |
| Units: cm                                 |          |          |    |
| arithmetic mean                           | 89.23    | 90.85    |    |
| standard deviation                        | ± 12.822 | ± 14.920 | -  |
| Height SDS                                |          |          |    |
| Units: Standard deviation score (SDS)     |          |          |    |
| arithmetic mean                           | -4.92    | -4.85    |    |
| standard deviation                        | ± 0.829  | ± 0.958  | -  |
| Weight                                    |          |          |    |
| Units: kg                                 |          |          |    |
| arithmetic mean                           | 17.03    | 17.99    |    |
| standard deviation                        | ± 4.699  | ± 5.542  | -  |
| Body Mass Index                           |          |          |    |
| Units: kg^m2                              |          |          |    |
| arithmetic mean                           | 21.11    | 21.39    |    |
| standard deviation                        | ± 1.612  | ± 1.853  | -  |
| Baseline AHV                              |          |          |    |
| Baseline annualized height velocity (AHV) |          |          |    |
| Units: cm/year                            |          |          |    |
| arithmetic mean                           | 4.73     | 6.17     |    |
| standard deviation                        | ± 1.133  | ± 1.394  | -  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | TransCon CNP (6 mcg/kg/wk)                |
| Reporting group description:<br>Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.  |   |
| Reporting group title   | TransCon CNP (20 mcg/kg/wk)               |
| Reporting group description:<br>Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.   |   |
| Reporting group title   | TransCon CNP (50 mcg/kg/wk)               |
| Reporting group description:<br>Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.   |   |
| Reporting group title   | TransCon CNP (100 mcg/kg/wk)              |
| Reporting group description:<br>Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.  |   |
| Reporting group title   | Pooled Placebo                            |
| Reporting group description:<br>Once weekly subcutaneous administration of placebo for TransCon CNP to mimic the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.   |   |
| Reporting group title   | Open-Label Extension Period: TransCon CNP |
| Reporting group description:<br>Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegritide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection. |   |

### Primary: Annualized Height Velocity

|  |                            |
|--|----------------------------|
| End point title  | Annualized Height Velocity |
| End point description:<br>The primary efficacy analysis compared the difference in the primary efficacy endpoint between the TransCon CNP treatment group and the pooled placebo group using an ANCOVA model with the annualized height velocity (AHV) at Week 52 as the response variable, treatment (TransCon CNP dose groups and placebo) and sex as factors, baseline age and baseline height SDS as the covariates, and based on the Full Analysis Set. |                            |
| End point type   | Primary                    |
| End point timeframe:<br>52 weeks   |                            |

| End point values                             | TransCon CNP (6 mcg/kg/wk) | TransCon CNP (20 mcg/kg/wk) | TransCon CNP (50 mcg/kg/wk) | TransCon CNP (100 mcg/kg/wk) |
|--|----------------------------|-----------------------------|-----------------------------|------------------------------|
| Subject group type                           | Reporting group            | Reporting group             | Reporting group             | Reporting group              |
| Number of subjects analysed                  | 10                         | 11                          | 10                          | 11                           |
| Units: cm/year                               |                            |                             |                             |                              |
| least squares mean (confidence interval 95%) | 4.09 (3.34 to 4.84)        | 4.52 (3.82 to 5.22)         | 5.16 (4.43 to 5.90)         | 5.42 (4.74 to 6.11)          |

|  |                     |  |  |  |
|--|---------------------|--|--|--|
| <b>End point values</b>                      | Pooled Placebo      |  |  |  |
| Subject group type                           | Reporting group     |  |  |  |
| Number of subjects analysed                  | 15                  |  |  |  |
| Units: cm/year                               |                     |  |  |  |
| least squares mean (confidence interval 95%) | 4.35 (3.75 to 4.94) |  |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Primary efficacy endpoint                   |
| Statistical analysis description:<br>ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates. |   |
| Comparison groups  | TransCon CNP (6 mcg/kg/wk) v Pooled Placebo |
| Number of subjects included in analysis  | 25  |
| Analysis specification   | Pre-specified                               |
| Analysis type  | superiority                                 |
| P-value  | = 0.6004                                    |
| Method   | ANCOVA                                      |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Primary efficacy endpoint                    |
| Statistical analysis description:<br>ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates. |  |
| Comparison groups  | TransCon CNP (20 mcg/kg/wk) v Pooled Placebo |
| Number of subjects included in analysis  | 26   |
| Analysis specification   | Pre-specified                                |
| Analysis type  | superiority                                  |
| P-value  | = 0.7022                                     |
| Method   | ANCOVA                                       |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Primary efficacy endpoint                    |
| Statistical analysis description:<br>ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates. |  |
| Comparison groups  | TransCon CNP (50 mcg/kg/wk) v Pooled Placebo |
| Number of subjects included in analysis  | 25   |
| Analysis specification   | Pre-specified                                |
| Analysis type  | superiority                                  |
| P-value  | = 0.0849                                     |
| Method   | ANCOVA                                       |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Primary efficacy endpoint                     |
| Statistical analysis description:<br>ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates. |   |
| Comparison groups  | TransCon CNP (100 mcg/kg/wk) v Pooled Placebo |
| Number of subjects included in analysis  | 26  |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | superiority                                   |
| P-value  | = 0.0218                                      |
| Method   | ANCOVA  |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Week 0 to Week 52 for double-blind treatment period and up to Week 156 for OLE Period

Adverse event reporting additional description:

Analysis was performed on safety analysis set that included all randomised subjects who received at least one dose of trial drug. Subjects were analysed according to trial treatment as treated. Adverse Events were reported as per MedDRA version 24.1 for double-blind treatment period and MedDRA version 26.0 for OLE period.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | TransCon CNP (6 mcg/kg/wk) |
|-----------------------|----------------------------|

Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | TransCon CNP (20 mcg/kg/wk) |
|-----------------------|-----------------------------|

Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | TransCon CNP (50 mcg/kg/wk) |
|-----------------------|-----------------------------|

Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | TransCon CNP (100 mcg/kg/wk) |
|-----------------------|------------------------------|

Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.

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

Reporting group description:

Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.

|                       |   |
|-----------------------|---|
| Reporting group title | Open-Label Extension Period: TransCon CNP |
|-----------------------|---|

Reporting group description:

Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegitide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection.

| Serious adverse events                            | TransCon CNP (6 mcg/kg/wk) | TransCon CNP (20 mcg/kg/wk) | TransCon CNP (50 mcg/kg/wk) |
|---|----------------------------|-----------------------------|-----------------------------|
| Total subjects affected by serious adverse events |                            |                             |                             |
| subjects affected / exposed                       | 1 / 10 (10.00%)            | 0 / 11 (0.00%)              | 1 / 10 (10.00%)             |
| number of deaths (all causes)                     | 0                          | 0                           | 0                           |
| number of deaths resulting from adverse events    | 0                          | 0                           | 0                           |
| Nervous system disorders                          |                            |                             |                             |
| Febrile convulsion                                |                            |                             |                             |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| 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                                  |                 |                |                 |
| Obstructive sleep apnoea syndrome<br>alternative dictionary used:<br>MedDRA 26.0 |                 |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0          | 0 / 0           |
| Tonsillar hypertrophy  |                 |                |                 |
| alternative dictionary used:<br>MedDRA 26.0                                      |                 |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0          | 0 / 0           |
| Infections and infestations  |                 |                |                 |
| Viral infection  |                 |                |                 |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Influenza  |                 |                |                 |
| alternative dictionary used:<br>MedDRA 26.0                                      |                 |                |                 |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 10 (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>Serious adverse events</b>                     | TransCon CNP (100 mcg/kg/wk) | Pooled Placebo | Open-Label Extension Period:<br>TransCon CNP |
|---|------------------------------|----------------|--|
| Total subjects affected by serious adverse events |                              |                |  |
| subjects affected / exposed                       | 0 / 11 (0.00%)               | 0 / 15 (0.00%) | 2 / 57 (3.51%)                               |
| number of deaths (all causes)                     | 0                            | 0              | 0  |
| number of deaths resulting from adverse events    | 0                            | 0              | 0  |
| Nervous system disorders                          |                              |                |  |
| Febrile convulsion                                |                              |                |  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 15 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Obstructive sleep apnoea syndrome               |                |                |                |
| alternative dictionary used: MedDRA 26.0        |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 15 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tonsillar hypertrophy                           |                |                |                |
| alternative dictionary used: MedDRA 26.0        |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 15 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Viral infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 15 (0.00%) | 0 / 57 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza                                       |                |                |                |
| alternative dictionary used: MedDRA 26.0        |                |                |                |
| subjects affected / exposed                     | 0 / 11 (0.00%) | 0 / 15 (0.00%) | 1 / 57 (1.75%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| Non-serious adverse events                            | TransCon CNP (6 mcg/kg/wk) | TransCon CNP (20 mcg/kg/wk) | TransCon CNP (50 mcg/kg/wk) |
|---|----------------------------|-----------------------------|-----------------------------|
| Total subjects affected by non-serious adverse events |                            |                             |                             |
| subjects affected / exposed                           | 9 / 10 (90.00%)            | 11 / 11 (100.00%)           | 10 / 10 (100.00%)           |
| General disorders and administration site conditions  |                            |                             |                             |
| Pyrexia   |                            |                             |                             |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 10 (10.00%)<br>2 | 4 / 11 (36.36%)<br>7 | 2 / 10 (20.00%)<br>2 |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)  | 1 / 10 (10.00%)<br>1 | 1 / 11 (9.09%)<br>1  | 1 / 10 (10.00%)<br>1 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 1 / 10 (10.00%)<br>1 | 2 / 11 (18.18%)<br>2 | 0 / 10 (0.00%)<br>0  |
| Influenza like illness<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Injection site pain<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Injection site swelling<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Immune system disorders<br>Seasonal allergy<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)                                   | 4 / 10 (40.00%)<br>7 | 3 / 11 (27.27%)<br>7 | 4 / 10 (40.00%)<br>6 |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 | 2 / 10 (20.00%)<br>4 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)   | 1 / 10 (10.00%)<br>1 | 3 / 11 (27.27%)<br>4 | 2 / 10 (20.00%)<br>3 |



|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Epistaxis                                      |                 |                 |                 |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 2 / 11 (18.18%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 1               | 2               | 1               |
| Oropharyngeal pain                             |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                              | 0               | 0               | 3               |
| Snoring  |                 |                 |                 |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                              | 1               | 1               | 1               |
| Obstructive sleep apnoea syndrome              |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0               | 0               | 0               |
| Sleep apnoea syndrome                          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0               | 1               | 0               |
| Tonsillar hypertrophy                          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0               | 0               | 0               |
| Investigations                                 |                 |                 |                 |
| Vitamin D decreased                            |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0               | 0               | 0               |
| Injury, poisoning and procedural complications |                 |                 |                 |
| Fall   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 1               | 0               | 0               |
| Skin abrasion                                  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0    |                 |                 |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0               | 0               | 0               |

|  |  |   |   |
|--|--|---|---|
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1   | 3 / 10 (30.00%)<br>4  |
| Blood and lymphatic system disorders<br>Lymphadenopathy<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0   |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypoacusis<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)<br><br>Middle ear effusion<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 10 (10.00%)<br>1<br><br>0 / 10 (0.00%)<br>0<br><br>0 / 10 (0.00%)<br>0                             | 1 / 11 (9.09%)<br>1<br><br>0 / 11 (0.00%)<br>0<br><br>0 / 11 (0.00%)<br>0                             | 1 / 10 (10.00%)<br>1<br><br>1 / 10 (10.00%)<br>1<br><br>1 / 10 (10.00%)<br>1                            |
| Gastrointestinal disorders<br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>alternative dictionary used: | 1 / 10 (10.00%)<br>1<br><br>1 / 10 (10.00%)<br>1<br><br>0 / 10 (0.00%)<br>0<br><br>0 / 10 (0.00%)<br>0 | 2 / 11 (18.18%)<br>4<br><br>0 / 11 (0.00%)<br>0<br><br>1 / 11 (9.09%)<br>1<br><br>1 / 11 (9.09%)<br>1 | 2 / 10 (20.00%)<br>3<br><br>2 / 10 (20.00%)<br>3<br><br>1 / 10 (10.00%)<br>1<br><br>0 / 10 (0.00%)<br>0 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| MedDRA 26.0                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Skin and subcutaneous tissue disorders          |                 |                 |                 |
| Rash  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Pain in extremity                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 1 / 11 (9.09%)  | 3 / 10 (30.00%) |
| occurrences (all)                               | 1               | 1               | 7               |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                               | 1               | 0               | 4               |
| Back pain                                       |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Knee deformity                                  |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Infections and infestations                     |                 |                 |                 |
| Upper respiratory tract infection               |                 |                 |                 |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 1 / 11 (9.09%)  | 5 / 10 (50.00%) |
| occurrences (all)                               | 3               | 1               | 8               |
| Nasopharyngitis                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 5 / 10 (50.00%) |
| occurrences (all)                               | 2               | 0               | 6               |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 2 / 11 (18.18%) | 3 / 10 (30.00%) |
| occurrences (all)                               | 0               | 2               | 3               |
| COVID-19  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 1               | 1               |
| Otitis media                                |                 |                 |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)                           | 1               | 2               | 2               |
| Viral infection                             |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 2               | 4               |
| Respiratory tract infection                 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                           | 0               | 0               | 5               |
| Conjunctivitis                              |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Ear infection                               |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Gastroenteritis viral                       |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 0               | 0               | 0               |
| Influenza                                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                           | 1               | 0               | 0               |
| Otitis media acute                          |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Pharyngitis                                 |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Pharyngitis streptococcal<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)               | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Rhinitis<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 10 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1 | 1 / 10 (10.00%)<br>1 |
| Sinusitis<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Viral upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 10 (10.00%)<br>1 | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |

| <b>Non-serious adverse events</b>   | TransCon CNP (100 mcg/kg/wk) | Pooled Placebo       | Open-Label Extension Period:<br>TransCon CNP |
|---|------------------------------|----------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                | 10 / 11 (90.91%)             | 14 / 15 (93.33%)     | 57 / 57 (100.00%)                            |
| General disorders and administration site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 2 / 11 (18.18%)<br>4         | 5 / 15 (33.33%)<br>8 | 23 / 57 (40.35%)<br>56                       |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)   | 1 / 11 (9.09%)<br>2          | 1 / 15 (6.67%)<br>1  | 5 / 57 (8.77%)<br>24                         |
| Fatigue   |                              |                      |  |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  | 0 / 57 (0.00%)   |
| occurrences (all)                               | 0               | 1               | 0                |
| Influenza like illness                          |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                  |
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 3 / 57 (5.26%)   |
| occurrences (all)                               | 0               | 0               | 3                |
| Injection site pain                             |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                  |
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 6 / 57 (10.53%)  |
| occurrences (all)                               | 0               | 0               | 26               |
| Injection site swelling                         |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                  |
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 4 / 57 (7.02%)   |
| occurrences (all)                               | 0               | 0               | 6                |
| Immune system disorders                         |                 |                 |                  |
| Seasonal allergy                                |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0     |                 |                 |                  |
| subjects affected / exposed                     | 1 / 11 (9.09%)  | 0 / 15 (0.00%)  | 6 / 57 (10.53%)  |
| occurrences (all)                               | 1               | 0               | 8                |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                  |
| Cough   |                 |                 |                  |
| subjects affected / exposed                     | 2 / 11 (18.18%) | 3 / 15 (20.00%) | 21 / 57 (36.84%) |
| occurrences (all)                               | 4               | 5               | 51               |
| Rhinorrhoea                                     |                 |                 |                  |
| subjects affected / exposed                     | 2 / 11 (18.18%) | 1 / 15 (6.67%)  | 11 / 57 (19.30%) |
| occurrences (all)                               | 2               | 1               | 18               |
| Nasal congestion                                |                 |                 |                  |
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 3 / 15 (20.00%) | 13 / 57 (22.81%) |
| occurrences (all)                               | 0               | 5               | 31               |
| Epistaxis                                       |                 |                 |                  |
| subjects affected / exposed                     | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 3 / 57 (5.26%)   |
| occurrences (all)                               | 0               | 0               | 3                |
| Oropharyngeal pain                              |                 |                 |                  |
| subjects affected / exposed                     | 1 / 11 (9.09%)  | 2 / 15 (13.33%) | 10 / 57 (17.54%) |
| occurrences (all)                               | 1               | 2               | 14               |

|  |                                 |                                   |
|--|---------------------------------|-----------------------------------|
| <p>Snoring</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  | <p>3 / 15 (20.00%)</p> <p>3</p> | <p>7 / 57 (12.28%)</p> <p>9</p>   |
| <p>Obstructive sleep apnoea syndrome</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                          | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>6 / 57 (10.53%)</p> <p>6</p>   |
| <p>Sleep apnoea syndrome</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                      | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>4 / 57 (7.02%)</p> <p>5</p>    |
| <p>Tonsillar hypertrophy</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>                                      | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>3 / 57 (5.26%)</p> <p>3</p>    |
| <p>Investigations</p> <p>Vitamin D decreased</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>1 / 11 (9.09%)</p> <p>occurrences (all)</p> <p>1</p>                  | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>5 / 57 (8.77%)</p> <p>5</p>    |
| <p>Injury, poisoning and procedural complications</p> <p>Fall</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> | <p>1 / 15 (6.67%)</p> <p>2</p>  | <p>5 / 57 (8.77%)</p> <p>6</p>    |
| <p>Skin abrasion</p> <p>alternative dictionary used:<br/>MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>0 / 11 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  | <p>0 / 15 (0.00%)</p> <p>0</p>  | <p>3 / 57 (5.26%)</p> <p>3</p>    |
| <p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>2 / 11 (18.18%)</p> <p>occurrences (all)</p> <p>2</p>  | <p>2 / 15 (13.33%)</p> <p>8</p> | <p>17 / 57 (29.82%)</p> <p>40</p> |
| Blood and lymphatic system disorders   |                                 |                                   |

|   |  |  |   |
|---|--|--|---|
| Lymphadenopathy<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 4 / 57 (7.02%)<br>4   |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypoacusis<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)<br><br>Middle ear effusion<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)  | 0 / 11 (0.00%)<br>0<br><br>0 / 11 (0.00%)<br>0<br><br>0 / 11 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0  | 10 / 57 (17.54%)<br>22<br><br>7 / 57 (12.28%)<br>10<br><br>5 / 57 (8.77%)<br>6  |
| Gastrointestinal disorders<br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all) | 3 / 11 (27.27%)<br>3<br><br>1 / 11 (9.09%)<br>2<br><br>1 / 11 (9.09%)<br>1<br><br>0 / 11 (0.00%)<br>0<br><br>1 / 11 (9.09%)<br>1 | 3 / 15 (20.00%)<br>5<br><br>2 / 15 (13.33%)<br>2<br><br>2 / 15 (13.33%)<br>2<br><br>0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0 | 16 / 57 (28.07%)<br>25<br><br>6 / 57 (10.53%)<br>8<br><br>4 / 57 (7.02%)<br>7<br><br>3 / 57 (5.26%)<br>4<br><br>3 / 57 (5.26%)<br>3 |
| Skin and subcutaneous tissue disorders  |  |  |   |



|   |   |  |  |
|---|---|--|--|
| Rash<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)   | 1 / 11 (9.09%)<br>1   | 1 / 15 (6.67%)<br>1  | 4 / 57 (7.02%)<br>7  |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br>Back pain<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all)<br>Knee deformity<br>alternative dictionary used:<br>MedDRA 26.0<br>subjects affected / exposed<br>occurrences (all) | 3 / 11 (27.27%)<br>3<br><br>1 / 11 (9.09%)<br>1<br><br>0 / 11 (0.00%)<br>0<br><br>0 / 11 (0.00%)<br>0                             | 1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>18<br><br>0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>1                              | 7 / 57 (12.28%)<br>8<br><br>9 / 57 (15.79%)<br>14<br><br>9 / 57 (15.79%)<br>10<br><br>3 / 57 (5.26%)<br>3                                      |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br>Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br>Otitis media<br>subjects affected / exposed<br>occurrences (all)<br>Viral infection       | 0 / 11 (0.00%)<br>0<br><br>2 / 11 (18.18%)<br>2<br><br>1 / 11 (9.09%)<br>1<br><br>3 / 11 (27.27%)<br>3<br><br>0 / 11 (0.00%)<br>0 | 2 / 15 (13.33%)<br>2<br><br>1 / 15 (6.67%)<br>3<br><br>2 / 15 (13.33%)<br>2<br><br>1 / 15 (6.67%)<br>1<br><br>3 / 15 (20.00%)<br>3 | 14 / 57 (24.56%)<br>22<br><br>20 / 57 (35.09%)<br>35<br><br>10 / 57 (17.54%)<br>13<br><br>20 / 57 (35.09%)<br>22<br><br>14 / 57 (24.56%)<br>18 |

|   |                 |                 |                  |
|---|-----------------|-----------------|------------------|
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 2 / 15 (13.33%) | 8 / 57 (14.04%)  |
| occurrences (all)                           | 0               | 3               | 17               |
| Respiratory tract infection                 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 0 / 57 (0.00%)   |
| occurrences (all)                           | 0               | 0               | 0                |
| Conjunctivitis                              |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 4 / 57 (7.02%)   |
| occurrences (all)                           | 0               | 0               | 5                |
| Ear infection                               |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  | 14 / 57 (24.56%) |
| occurrences (all)                           | 0               | 1               | 27               |
| Gastroenteritis viral                       |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 2 / 11 (18.18%) | 0 / 15 (0.00%)  | 7 / 57 (12.28%)  |
| occurrences (all)                           | 2               | 0               | 11               |
| Influenza                                   |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 10 / 57 (17.54%) |
| occurrences (all)                           | 0               | 0               | 10               |
| Otitis media acute                          |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  | 7 / 57 (12.28%)  |
| occurrences (all)                           | 0               | 3               | 15               |
| Pharyngitis                                 |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 5 / 57 (8.77%)   |
| occurrences (all)                           | 0               | 0               | 5                |
| Pharyngitis streptococcal                   |                 |                 |                  |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                  |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 5 / 57 (8.77%)   |
| occurrences (all)                           | 0               | 0               | 6                |
| Rhinitis                                    |                 |                 |                  |
| alternative dictionary used:                |                 |                 |                  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| MedDRA 26.0                                 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 0 / 15 (0.00%)  | 6 / 57 (10.53%) |
| occurrences (all)                           | 0               | 0               | 6               |
| Sinusitis                                   |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 2 / 11 (18.18%) | 0 / 15 (0.00%)  | 4 / 57 (7.02%)  |
| occurrences (all)                           | 3               | 0               | 4               |
| Viral upper respiratory tract infection     |                 |                 |                 |
| alternative dictionary used:<br>MedDRA 26.0 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 2 / 15 (13.33%) | 6 / 57 (10.53%) |
| occurrences (all)                           | 0               | 2               | 8               |
| Metabolism and nutrition disorders          |                 |                 |                 |
| Vitamin D deficiency                        |                 |                 |                 |
| subjects affected / exposed                 | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  | 5 / 57 (8.77%)  |
| occurrences (all)                           | 0               | 1               | 6               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 01 September 2020 | Protocol Version 2.0 summary of changes: <ul style="list-style-type: none"><li>- increase enrollment to include approximately 14 subjects in Cohorts 2-5</li><li>- add allowance for select visits to be conducted off-site</li><li>- remove BMI as a secondary efficacy endpoint</li><li>- modify the placebo comparator and dosing procedure for Cohort 1</li><li>- add availability of home health nurse to give weekly injections</li><li>- update contact information for SAE reporting</li><li>- update the definition of AE</li></ul> |
| 08 January 2021   | Protocol Version 3.0 added a 2 year Open-Label Extension period to assess long term safety and efficacy following the Randomized Period.   |
| 12 August 2021    | Protocol Version 4.0 added implementation of unblinding per cohort after completion of the Randomized Treatment Period.  |
| 28 December 2022  | Protocol Version 5.0 summary of changes: <ul style="list-style-type: none"><li>- Added information of a new separate long-term open-label extension study for subjects completing treatment in the TCC-201 protocol</li><li>- Updated SAE reporting</li></ul>  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported