



## Clinical trial results:

**ACcomplishH: 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 |                   |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 11 April 2023 |
| First version publication date | 11 April 2023 |

### 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                                       | Interim           |
| Date of interim/final analysis                       | 20 March 2023     |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 27 September 2022 |
| Global end of trial reached?                         | 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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| 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.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | 52 Week Blinded Treatment Period (overall 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             |



## 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 mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product |                              |

### 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)          |

| End point values            | 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:

52 Week Blinded 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

| 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                       |
| 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                       |

| <b>Serious adverse events</b>                     | TransCon CNP (100 mcg/kg/wk) | Pooled Placebo |  |
|---|------------------------------|----------------|--|
| Total subjects affected by serious adverse events |                              |                |  |
| subjects affected / exposed                       | 0 / 11 (0.00%)               | 0 / 15 (0.00%) |  |
| number of deaths (all causes)                     | 0                            | 0              |  |
| number of deaths resulting from adverse events    | 0                            | 0              |  |
| Nervous system disorders                          |                              |                |  |
| Febrile convulsion                                |                              |                |  |
| subjects affected / exposed                       | 0 / 11 (0.00%)               | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0                        | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0                        | 0 / 0          |  |
| Infections and infestations                       |                              |                |  |
| Viral infection                                   |                              |                |  |
| subjects affected / exposed                       | 0 / 11 (0.00%)               | 0 / 15 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0                        | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0                        | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | 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%)           |
| Nervous system disorders                              |                            |                             |                             |
| Headache  |                            |                             |                             |
| subjects affected / exposed                           | 0 / 10 (0.00%)             | 1 / 11 (9.09%)              | 3 / 10 (30.00%)             |
| occurrences (all)                                     | 0                          | 1                           | 4                           |
| General disorders and administration site conditions  |                            |                             |                             |
| Pyrexia   |                            |                             |                             |
| subjects affected / exposed                           | 1 / 10 (10.00%)            | 4 / 11 (36.36%)             | 2 / 10 (20.00%)             |
| occurrences (all)                                     | 2                          | 7                           | 2                           |
| Injection site reaction                               |                            |                             |                             |
| subjects affected / exposed                           | 1 / 10 (10.00%)            | 1 / 11 (9.09%)              | 1 / 10 (10.00%)             |
| occurrences (all)                                     | 1                          | 1                           | 1                           |
| Fatigue   |                            |                             |                             |
| subjects affected / exposed                           | 1 / 10 (10.00%)            | 2 / 11 (18.18%)             | 0 / 10 (0.00%)              |
| occurrences (all)                                     | 1                          | 2                           | 0                           |
| Ear and labyrinth disorders                           |                            |                             |                             |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| Ear pain<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 |
| Gastrointestinal disorders<br>Vomiting<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 10 (10.00%)<br>1 | 2 / 11 (18.18%)<br>4 | 2 / 10 (20.00%)<br>3 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 2 / 10 (20.00%)<br>3 |
| Abdominal pain upper<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 |
| 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<br>subjects affected / exposed<br>occurrences (all)  | 1 / 10 (10.00%)<br>1 | 2 / 11 (18.18%)<br>2 | 1 / 10 (10.00%)<br>1 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 2 / 10 (20.00%)<br>3 |
| Snoring<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 |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | 1 / 11 (9.09%)<br>1  | 3 / 10 (30.00%)<br>7 |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 3 / 10 (30.00%)<br>4 |
| Infections and infestations   |                      |                      |                      |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 10 (30.00%)<br>3 | 1 / 11 (9.09%)<br>1  | 5 / 10 (50.00%)<br>8 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 10 (10.00%)<br>2 | 0 / 11 (0.00%)<br>0  | 5 / 10 (50.00%)<br>6 |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 10 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 | 3 / 10 (30.00%)<br>3 |
| COVID-19<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 |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 10 (10.00%)<br>1 | 2 / 11 (18.18%)<br>2 | 2 / 10 (20.00%)<br>2 |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 10 (10.00%)<br>1 | 1 / 11 (9.09%)<br>2  | 1 / 10 (10.00%)<br>4 |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 3 / 10 (30.00%)<br>5 |
| Metabolism and nutrition disorders  |                      |                      |                      |
| 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       |  |
|--|------------------------------|----------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 10 / 11 (90.91%)             | 14 / 15 (93.33%)     |  |
| Nervous system disorders   |                              |                      |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 11 (18.18%)<br>2         | 2 / 15 (13.33%)<br>8 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| General disorders and administration site conditions |                 |                 |  |
| Pyrexia  |                 |                 |  |
| subjects affected / exposed                          | 2 / 11 (18.18%) | 5 / 15 (33.33%) |  |
| occurrences (all)                                    | 4               | 8               |  |
| Injection site reaction                              |                 |                 |  |
| subjects affected / exposed                          | 1 / 11 (9.09%)  | 1 / 15 (6.67%)  |  |
| occurrences (all)                                    | 2               | 1               |  |
| Fatigue  |                 |                 |  |
| subjects affected / exposed                          | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  |  |
| occurrences (all)                                    | 0               | 1               |  |
| Ear and labyrinth disorders                          |                 |                 |  |
| Ear pain   |                 |                 |  |
| subjects affected / exposed                          | 0 / 11 (0.00%)  | 1 / 15 (6.67%)  |  |
| occurrences (all)                                    | 0               | 1               |  |
| Gastrointestinal disorders                           |                 |                 |  |
| Vomiting   |                 |                 |  |
| subjects affected / exposed                          | 3 / 11 (27.27%) | 3 / 15 (20.00%) |  |
| occurrences (all)                                    | 3               | 5               |  |
| Diarrhoea  |                 |                 |  |
| subjects affected / exposed                          | 1 / 11 (9.09%)  | 2 / 15 (13.33%) |  |
| occurrences (all)                                    | 2               | 2               |  |
| Abdominal pain upper                                 |                 |                 |  |
| subjects affected / exposed                          | 1 / 11 (9.09%)  | 2 / 15 (13.33%) |  |
| occurrences (all)                                    | 1               | 2               |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |  |
| Cough  |                 |                 |  |
| subjects affected / exposed                          | 2 / 11 (18.18%) | 3 / 15 (20.00%) |  |
| occurrences (all)                                    | 4               | 5               |  |
| Rhinorrhoea  |                 |                 |  |
| subjects affected / exposed                          | 2 / 11 (18.18%) | 1 / 15 (6.67%)  |  |
| occurrences (all)                                    | 2               | 1               |  |
| Nasal congestion                                     |                 |                 |  |
| subjects affected / exposed                          | 0 / 11 (0.00%)  | 3 / 15 (20.00%) |  |
| occurrences (all)                                    | 0               | 5               |  |
| Epistaxis  |                 |                 |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                      | 0 / 11 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                | 1 / 11 (9.09%)<br>1  | 2 / 15 (13.33%)<br>2 |  |
| Snoring<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 11 (0.00%)<br>0  | 3 / 15 (20.00%)<br>3 |  |
| Musculoskeletal and connective tissue disorders                                       |                      |                      |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 11 (27.27%)<br>3 | 1 / 15 (6.67%)<br>1  |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 11 (9.09%)<br>1  | 1 / 15 (6.67%)<br>18 |  |
| Infections and infestations   |                      |                      |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 11 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 11 (18.18%)<br>2 | 1 / 15 (6.67%)<br>3  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 11 (9.09%)<br>1  | 2 / 15 (13.33%)<br>2 |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 11 (27.27%)<br>3 | 1 / 15 (6.67%)<br>1  |  |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 11 (0.00%)<br>0  | 3 / 15 (20.00%)<br>3 |  |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 11 (0.00%)<br>0  | 2 / 15 (13.33%)<br>3 |  |
| Respiratory tract infection   |                      |                      |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 11 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |  |
| Metabolism and nutrition disorders<br>Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 0 / 11 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |  |

## 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 participants 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 participants 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