



## Clinical trial results:

### A Randomized, Open-label, 24-Week Safety, Efficacy, and Pharmacokinetic Study of Teduglutide in Infants 4 to 12 Months of Age with Short Bowel Syndrome Who are Dependent on Parenteral Support

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-003606-40    |
| Trial protocol           | GB FI IT FR       |
| Global end of trial date | 24 September 2020 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 28 March 2021 |
| First version publication date | 28 March 2021 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | SHP633-301 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03571516 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                           |
|------------------------------|---------------------------------------------------------------------------|
| Sponsor organisation name    | Shire                                                                     |
| Sponsor organisation address | 300 ShireWay, Lexington, United States, MA 02421                          |
| Public contact               | Study Director, Shire, +1 866 842 5335,<br>ClinicalTransparency@shire.com |
| Scientific contact           | Study Director, Shire, +1 866 842 5335,<br>ClinicalTransparency@shire.com |

Notes:

#### Paediatric regulatory details

|                                                                      |                     |
|----------------------------------------------------------------------|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000482-PIP01-08 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|                                                      |                   |
|------------------------------------------------------|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 24 September 2020 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 24 September 2020 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the safety, efficacy/pharmacodynamics(PD) and pharmacokinetics (PK) of teduglutide treatment in infants with short bowel syndrome (SBS) dependent on parenteral support.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and in compliance with all applicable industry regulations, International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guideline E6 (1996), European Union (EU) Directive 2001/20/EC, as well as all applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

|                                                           |                |
|-----------------------------------------------------------|----------------|
| Actual start date of recruitment                          | 31 August 2018 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | Yes            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Finland: 2        |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Worldwide total number of subjects   | 10                |
| EEA total number of subjects         | 2                 |

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)  | 10 |
| Children (2-11 years)                     | 0  |
| 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:

The study was conducted at Finland and United Kingdom between 31 August 2018 (first subject first visit) and 24 September 2020 (last subject last visit).

### Pre-assignment

Screening details:

A total of 10 subjects were enrolled into the study, of which 8 subjects completed the study.

### Period 1

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

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | Teduglutide (TED) |

Arm description:

Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks.

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Revestive        |
| Investigational medicinal product code | A16AX08          |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Subjects (infants) received 0.05 mg/kg of teduglutide SC injection into abdomen or into either the thigh or arm.

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Standard of Care (SOC) |
|------------------|------------------------|

Arm description:

Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Arm type                                                  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| <b>Number of subjects in period 1</b> | Teduglutide (TED) | Standard of Care (SOC) |
|---------------------------------------|-------------------|------------------------|
| Started                               | 5                 | 5                      |
| Completed                             | 4                 | 4                      |
| Not completed                         | 1                 | 1                      |
| Consent withdrawn by subject          | -                 | 1                      |
| Severe diarrhea                       | 1                 | -                      |



## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Teduglutide (TED) |
|-----------------------|-------------------|

Reporting group description:

Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Standard of Care (SOC) |
|-----------------------|------------------------|

Reporting group description:

Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.

| Reporting group values             | Teduglutide (TED) | Standard of Care (SOC) | Total |
|------------------------------------|-------------------|------------------------|-------|
| Number of subjects                 | 5                 | 5                      | 10    |
| Age Categorical<br>Units: Subjects |                   |                        |       |

|                                                                          |               |               |    |
|--------------------------------------------------------------------------|---------------|---------------|----|
| Age Continuous<br>Units: months<br>arithmetic mean<br>standard deviation | 8.5<br>± 3.09 | 8.3<br>± 2.65 | -  |
| Gender Categorical<br>Units: Subjects                                    |               |               |    |
| Female                                                                   | 1             | 2             | 3  |
| Male                                                                     | 4             | 3             | 7  |
| Ethnicity<br>Units: Subjects                                             |               |               |    |
| Hispanic or Latino                                                       | 0             | 0             | 0  |
| Not Hispanic or Latino                                                   | 5             | 5             | 10 |
| Race<br>Units: Subjects                                                  |               |               |    |
| White                                                                    | 4             | 4             | 8  |
| Asian                                                                    | 1             | 1             | 2  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                               |                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Reporting group title                                                                                                                                                                                                                                         | Teduglutide (TED)      |
| Reporting group description:<br>Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 milligram per kilogram (mg/kg) of teduglutide subcutaneous (SC) injection once daily (QD) in addition to standard medical therapy for 24 weeks. |                        |
| Reporting group title                                                                                                                                                                                                                                         | Standard of Care (SOC) |
| Reporting group description:<br>Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.                                                                                                               |                        |

### Primary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)

|                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                             | Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET) <sup>[1]</sup> |
| End point description:<br>Number of subjects who achieved at least 20% reduction from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. Intent-to-Treat (ITT) set consisted of all subjects randomized in the study. |                                                                                                                                                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                              | Primary                                                                                                                                                                                           |
| End point timeframe:<br>Baseline, EOT/ET (up to Week 24)                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                   |

Notes:

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

Justification: No statistical and comparison analysis were performed for this endpoint.

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 5                 | 5                      |  |  |
| Units: Subjects             |                   |                        |  |  |
| Dairy Data: EOT/ET          | 3                 | 1                      |  |  |
| Prescribed Data: EOT/ET     | 3                 | 3                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Plasma Concentration of Teduglutide at Nominal Time Points (Baseline at Pre-dose, and 1 Hour and 4 Hours Post-dose; 2 Hours Post-dose at Week 7)

|                 |                                                                                                                                                                 |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Plasma Concentration of Teduglutide at Nominal Time Points (Baseline at Pre-dose, and 1 Hour and 4 Hours Post-dose; 2 Hours Post-dose at Week 7) <sup>[2]</sup> |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Mean plasma concentration of teduglutide at nominal time points was reported. Pharmacokinetic (PK) set included all subjects who received at least one dose of teduglutide and have at least one evaluable and interpretable post-dose PK concentration value. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint and n=number of subjects analysed refer to the subjects evaluable for this specific time points. Data was not planned to be collected and analysed for SOC arm.

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

End point timeframe:

Baseline: Pre-dose, 1, 4 hours post-dose, and 2 hours post-dose on Week 7

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was only planned to be analysed for the reporting group of "Teduglutide" arm.

| End point values                       | Teduglutide (TED)       |  |  |  |
|----------------------------------------|-------------------------|--|--|--|
| Subject group type                     | Reporting group         |  |  |  |
| Number of subjects analysed            | 4                       |  |  |  |
| Units: Nanogram per milliliter (ng/mL) |                         |  |  |  |
| median (full range (min-max))          |                         |  |  |  |
| Baseline: At Pre-dose (n=4)            | 0.00 (0.000 to 0.00)    |  |  |  |
| Baseline: At 1 hour (n=3)              | 16.300 (7.25 to 25.70)  |  |  |  |
| Baseline: At 4 hour (n=4)              | 8.385 (3.86 to 22.5)    |  |  |  |
| Week 7: At 2 hours (n=2)               | 16.950 (14.80 to 19.10) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Number of Subjects With Treatment-emergent Adverse Events (TEAEs) |
|-----------------|-------------------------------------------------------------------|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. TEAEs are defined as AEs that start or deteriorate on or after the date of the first dose of investigational product. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment.

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

End point timeframe:

From start of study treatment up to end of study (EOS) (up to Week 28)

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 5                 | 5                      |  |  |
| Units: Subjects             | 5                 | 5                      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Body Weight Z-score at Week 24

|                 |                                                        |
|-----------------|--------------------------------------------------------|
| End point title | Change From Baseline in Body Weight Z-score at Week 24 |
|-----------------|--------------------------------------------------------|

End point description:

Body weight was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in body weight Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline, Week 24

| End point values                     | Teduglutide (TED)     | Standard of Care (SOC) |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 4                     | 3                      |  |  |
| Units: Z-score                       |                       |                        |  |  |
| arithmetic mean (standard deviation) | -0.408 ( $\pm$ 0.377) | -0.289 ( $\pm$ 0.278)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Length Z-Score at Week 24

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | Change From Baseline in Length Z-Score at Week 24 |
|-----------------|---------------------------------------------------|

End point description:

Length was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in length Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline, Week 24

| End point values                     | Teduglutide (TED)     | Standard of Care (SOC) |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 4                     | 2                      |  |  |
| Units: Z-Score                       |                       |                        |  |  |
| arithmetic mean (standard deviation) | -0.274 ( $\pm$ 1.258) | -0.422 ( $\pm$ 0.384)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Head Circumference Z-Score at Week 24

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change From Baseline in Head Circumference Z-Score at Week 24 |
|-----------------|---------------------------------------------------------------|

End point description:

Head circumference was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in head circumference Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline, Week 24

| End point values                     | Teduglutide (TED)     | Standard of Care (SOC) |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 4                     | 2                      |  |  |
| Units: Z-Score                       |                       |                        |  |  |
| arithmetic mean (standard deviation) | -0.544 ( $\pm$ 0.446) | -0.167 ( $\pm$ 0.690)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Weight-for-Length Z-Score at Week 24

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Change From Baseline in Weight-for-Length Z-Score at Week |
|-----------------|-----------------------------------------------------------|

## End point description:

Weight-for-length was measured using Z-score. Z-score was calculated as (observed value - median value of the reference population)/standard deviation value of reference population. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Change from baseline in weight-for-length Z-score at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline, Week 24

| End point values                     | Teduglutide (TED)     | Standard of Care (SOC) |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 4                     | 3                      |  |  |
| Units: Z-Score                       |                       |                        |  |  |
| arithmetic mean (standard deviation) | -0.447 ( $\pm$ 1.042) | -0.058 ( $\pm$ 0.992)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Average Total Urine Output at Week 24

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change From Baseline in Average Total Urine Output at Week 24 |
|-----------------|---------------------------------------------------------------|

## End point description:

Average total urine output was recorded over a 48-hour period of nutritional stability at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint. Here, milliliter per kilogram per day is abbreviated as mL/kg/day.

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

End point timeframe:

Baseline, Week 24

| End point values                     | Teduglutide (TED)     | Standard of Care (SOC) |  |  |
|--------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                   | Reporting group       | Reporting group        |  |  |
| Number of subjects analysed          | 3                     | 3                      |  |  |
| Units: mL/kg/day                     |                       |                        |  |  |
| arithmetic mean (standard deviation) | -0.61 ( $\pm$ 14.548) | 10.25 ( $\pm$ 17.383)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Fecal Output at Week 24

|                 |                                                 |
|-----------------|-------------------------------------------------|
| End point title | Change From Baseline in Fecal Output at Week 24 |
|-----------------|-------------------------------------------------|

End point description:

Change from baseline in the fecal output (Average number of stools per day) at Week 24 was reported. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed refer to the subjects evaluable for this endpoint.

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

End point timeframe:

Baseline, Week 24

| End point values                        | Teduglutide (TED)    | Standard of Care (SOC) |  |  |
|-----------------------------------------|----------------------|------------------------|--|--|
| Subject group type                      | Reporting group      | Reporting group        |  |  |
| Number of subjects analysed             | 3                    | 3                      |  |  |
| Units: Average number of stools per day |                      |                        |  |  |
| arithmetic mean (standard deviation)    | -3.33 ( $\pm$ 3.547) | 1.67 ( $\pm$ 1.756)    |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Positive Specific Antibodies to Teduglutide

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Number of Subjects With Positive Specific Antibodies to Teduglutide <sup>[3]</sup> |
|-----------------|------------------------------------------------------------------------------------|

End point description:

Number of subjects with positive specific antibodies to teduglutide were used to summarize the presence of antibodies. Safety set consisted of all subjects who met the following criteria: Teduglutide treatment arm: subjects who received at least 1 dose of teduglutide and had undergone at least 1 post baseline safety assessment; Standard of care treatment arm: subjects who had undergone at least 1 post baseline safety assessment. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analyzed for SOC group.

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

End point timeframe:

Baseline, EOS (up to week 28)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was only planned to be analysed for the reporting group of "Teduglutide" arm.

| End point values            | Teduglutide (TED) |  |  |  |
|-----------------------------|-------------------|--|--|--|
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 3                 |  |  |  |
| Units: Subjects             | 0                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Who Achieved At least 20 Percent (%) Reduction From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of subjects who achieved at least 20% reduction from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 5                 | 5                      |  |  |
| Units: Subjects             |                   |                        |  |  |
| Dairy Data: EOT/ET          | 3                 | 1                      |  |  |
| Prescribed Data: EOT/ET     | 3                 | 3                      |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at Week 24

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Number of Subjects Who Achieved 100 Percent (%) Reduction |
|-----------------|-----------------------------------------------------------|

End point description:

Number of subjects who achieved 100% reduction in complete weaning off (enteral autonomy) PS volume at Week 24 were reported. ITT set consisted of all subjects randomized in the study. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint.

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

End point timeframe:

Week 24

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 4                 | 4                      |  |  |
| Units: Subjects             | 0                 | 0                      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at End of Study (EOS)

|                 |                                                                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Who Achieved 100 Percent (%) Reduction in Complete Weaning Off (Enteral Autonomy) Parenteral Support (PS) Volume at End of Study (EOS) |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of subjects who achieved 100% reduction in complete weaning off (enteral autonomy) PS volume at EOS (up to Week 28) were reported. ITT set consisted of all subjects randomized in the study. Here, the number of subjects analysed signifies subjects who were evaluable for this endpoint.

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

End point timeframe:

EOS (up to Week 28)

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 4                 | 5                      |  |  |
| Units: Subjects             | 0                 | 0                      |  |  |

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)**

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|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

---

| End point values                     | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|--------------------------------------|-------------------|------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed          | 5                 | 5                      |  |  |
| Units: mL/kg/day                     |                   |                        |  |  |
| arithmetic mean (standard deviation) |                   |                        |  |  |
| Dairy Data: EOT/ET (n=5, 3)          | -21.54 (± 28.909) | -9.51 (± 7.497)        |  |  |
| Prescribed Data: EOT/ET (n=5, 5)     | -22.90 (± 26.940) | -14.90 (± 12.323)      |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET)**

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|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Volume at End of Treatment/Early Termination (EOT/ET) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Percent change from baseline in weight-normalized PS volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

---

| End point values                     | Teduglutide (TED)      | Standard of Care (SOC) |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 5                      | 5                      |  |  |
| Units: Percent change                |                        |                        |  |  |
| arithmetic mean (standard deviation) |                        |                        |  |  |
| Dairy Data: EOT/ET (n=5, 3)          | -24.77 ( $\pm$ 34.723) | -16.75 ( $\pm$ 16.392) |  |  |
| Prescribed Data: EOT/ET (n=5, 5)     | -27.28 ( $\pm$ 33.518) | -22.39 ( $\pm$ 17.198) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. Here, kilo-calories per kilogram per day was abbreviated as (kcal/kg/day). ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values                     | Teduglutide (TED)      | Standard of Care (SOC) |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 5                      | 5                      |  |  |
| Units: kcal/kg/day                   |                        |                        |  |  |
| arithmetic mean (standard deviation) |                        |                        |  |  |
| Dairy Data: EOT/ET (n=5, 3)          | -16.14 ( $\pm$ 17.547) | -6.10 ( $\pm$ 10.386)  |  |  |
| Prescribed Data: EOT/ET (n=5, 5)     | -15.31 ( $\pm$ 17.839) | -20.40 ( $\pm$ 21.024) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline in Weight-normalized Parenteral Support (PS) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Percent Change From Baseline in Weight-normalized Parenteral |
|-----------------|--------------------------------------------------------------|

## End point description:

Percent change from baseline in weight-normalized PS caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values                     | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|--------------------------------------|-------------------|------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed          | 5                 | 5                      |  |  |
| Units: Percent change                |                   |                        |  |  |
| arithmetic mean (standard deviation) |                   |                        |  |  |
| Dairy Data: EOT/ET (n=5, 3)          | -27.00 (± 29.473) | -13.68 (± 21.873)      |  |  |
| Prescribed Data: EOT/ET (n=5, 5)     | -27.81 (± 30.777) | -38.86 (± 39.893)      |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Change From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)**

|                 |                                                                                                                        |
|-----------------|------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET) |
|-----------------|------------------------------------------------------------------------------------------------------------------------|

## End point description:

Change from baseline in weight-normalized EN volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values                     | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|--------------------------------------|-------------------|------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed          | 5                 | 5                      |  |  |
| Units: mL/kg/day                     |                   |                        |  |  |
| arithmetic mean (standard deviation) |                   |                        |  |  |

|                                  |                  |                   |  |  |
|----------------------------------|------------------|-------------------|--|--|
| Dairy Data: EOT/ET (n=4, 3)      | 16.14 (± 18.683) | -15.25 (± 31.496) |  |  |
| Prescribed Data: EOT/ET (n=4, 5) | -1.28 (± 2.563)  | 2.27 (± 22.232)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) volume at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) volume at End of Treatment/Early Termination (EOT/ET) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

Percent change from baseline in weight-normalized EN volume at EOT/ET (up to Week 24) was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, '99999' indicates that standard deviation was not analysed for this category as there were only one subjects available at specified time points. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values                     | Teduglutide (TED)  | Standard of Care (SOC) |  |  |
|--------------------------------------|--------------------|------------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group        |  |  |
| Number of subjects analysed          | 5                  | 5                      |  |  |
| Units: Percent change                |                    |                        |  |  |
| arithmetic mean (standard deviation) |                    |                        |  |  |
| Dairy Data: EOT/ET (n=2, 2)          | 273.20 (± 246.784) | -44.25 (± 78.847)      |  |  |
| Prescribed Data: EOT/ET (n=1, 4)     | -16.40 (± 99999)   | 14.80 (± 69.834)       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in weight-normalized EN caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects

randomized in the study. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

|                                  |           |
|----------------------------------|-----------|
| End point type                   | Secondary |
| End point timeframe:             |           |
| Baseline, EOT/ET (up to Week 24) |           |

| End point values                     | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|--------------------------------------|-------------------|------------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed          | 5                 | 5                      |  |  |
| Units: kcal/kg/day                   |                   |                        |  |  |
| arithmetic mean (standard deviation) |                   |                        |  |  |
| Dairy Data: EOT/ET (n=4, 3)          | 9.08 (± 10.662)   | -9.38 (± 21.402)       |  |  |
| Prescribed Data: EOT/ET (n=4, 5)     | -1.15 (± 2.306)   | 3.11 (± 16.285)        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                        |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Percent change from baseline in weight-normalized EN caloric intake at EOT/ET (up to Week 24) were reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study. Here, '99999' indicates that standard deviation was not analysed for this category as there were only one subjects available at specified time points. Here, n=number of subjects analysed refer to the subjects evaluable for this specific time points.

|                                  |           |
|----------------------------------|-----------|
| End point type                   | Secondary |
| End point timeframe:             |           |
| Baseline, EOT/ET (up to Week 24) |           |

| End point values                     | Teduglutide (TED)  | Standard of Care (SOC) |  |  |
|--------------------------------------|--------------------|------------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group        |  |  |
| Number of subjects analysed          | 5                  | 5                      |  |  |
| Units: Percent change                |                    |                        |  |  |
| arithmetic mean (standard deviation) |                    |                        |  |  |
| Dairy Data: EOT/ET (n=2, 2)          | 207.06 (± 153.159) | -44.25 (± 78.847)      |  |  |
| Prescribed Data: EOT/ET (n=1, 4)     | -16.40 (± 99999)   | 24.18 (± 78.115)       |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                                                                  |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Volume at End of Treatment/Early Termination (EOT/ET) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of subjects who achieved at least 20% increase from baseline in weight-normalized EN volume at EOT/ET was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

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

End point timeframe:

Baseline, EOT/ET (up to Week 24)

| End point values            | Teduglutide (TED) | Standard of Care (SOC) |  |  |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type          | Reporting group   | Reporting group        |  |  |
| Number of subjects analysed | 5                 | 5                      |  |  |
| Units: Subjects             |                   |                        |  |  |
| Dairy Data: EOT/ET          | 2                 | 0                      |  |  |
| Prescribed Data: EOT/ET     | 0                 | 2                      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET)

|                 |                                                                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Who Achieved At least 20 Percent (%) Increase From Baseline in Weight-normalized Enteral Nutrition (EN) Caloric Intake at End of Treatment/Early Termination (EOT/ET) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Number of subjects who achieved at least 20% increase from baseline in weight-normalized EN caloric intake at EOT/ET was reported. EOT/ET was defined as the last available visit after the date of first dose (or randomization in standard of care treatment group) during the 24-week treatment period. ITT set consisted of all subjects randomized in the study.

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

---

End point timeframe:

Baseline, EOT/ET (up to Week 24)

---

| <b>End point values</b>     | Teduglutide<br>(TED) | Standard of<br>Care (SOC) |  |  |
|-----------------------------|----------------------|---------------------------|--|--|
| Subject group type          | Reporting group      | Reporting group           |  |  |
| Number of subjects analysed | 5                    | 5                         |  |  |
| Units: Subjects             |                      |                           |  |  |
| Dairy Data: EOT/ET          | 2                    | 0                         |  |  |
| Prescribed Data: EOT/ET     | 0                    | 2                         |  |  |

### Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of study treatment up to end of study (EOS) (up to Week 28)

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Teduglutide |
|-----------------------|-------------|

Reporting group description:

Subjects (infants) 4 to 12 months of corrected gestational aged received 0.05 mg/kg of teduglutide SC injection once daily for 24 weeks.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Standard of Care (SOC) |
|-----------------------|------------------------|

Reporting group description:

Subjects (infants) 4 to 12 months of corrected gestational aged received standard medical therapy for 24 weeks.

| Serious adverse events                               | Teduglutide    | Standard of Care (SOC) |  |
|------------------------------------------------------|----------------|------------------------|--|
| Total subjects affected by serious adverse events    |                |                        |  |
| subjects affected / exposed                          | 4 / 5 (80.00%) | 3 / 5 (60.00%)         |  |
| number of deaths (all causes)                        | 0              | 0                      |  |
| number of deaths resulting from adverse events       | 0              | 0                      |  |
| Investigations                                       |                |                        |  |
| Transaminases increased                              |                |                        |  |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 1 / 5 (20.00%)         |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1                  |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0                  |  |
| Nervous system disorders                             |                |                        |  |
| Ataxia                                               |                |                        |  |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 1 / 5 (20.00%)         |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1                  |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0                  |  |
| General disorders and administration site conditions |                |                        |  |
| Pyrexia                                              |                |                        |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)          |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 0                  |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0                  |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Immune system disorders                         |                |                |  |
| Immunisation reaction                           |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Device related infection                        |                |                |  |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 2 / 5 (40.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Product issues                                  |                |                |  |
| Device breakage                                 |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device leakage                                  |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device occlusion                                |                |                |  |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 5 (20.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Metabolic acidosis                              |                |                |  |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 5 (20.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| 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>                     | Teduglutide     | Standard of Care (SOC) |  |
|-------------------------------------------------------|-----------------|------------------------|--|
| Total subjects affected by non-serious adverse events |                 |                        |  |
| subjects affected / exposed                           | 5 / 5 (100.00%) | 5 / 5 (100.00%)        |  |

|                                                                                        |                     |                     |  |
|----------------------------------------------------------------------------------------|---------------------|---------------------|--|
| Investigations                                                                         |                     |                     |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>2 | 0 / 5 (0.00%)<br>0  |  |
| Blood iron decreased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Faecal volume increased<br>subjects affected / exposed<br>occurrences (all)            | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Respiratory rate increased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Serum ferritin decreased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>2 |  |
| Injury, poisoning and procedural complications                                         |                     |                     |  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Lip injury<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Skin abrasion<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Vascular disorders                                                                     |                     |                     |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Blood and lymphatic system disorders                                                   |                     |                     |  |
| Anaemia                                                                                |                     |                     |  |

|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| Iron deficiency anaemia                              |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia                                              |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 1 / 5 (20.00%) |  |
| occurrences (all)                                    | 1              | 1              |  |
| Secretion discharge                                  |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| Gastrointestinal disorders                           |                |                |  |
| Abdominal discomfort                                 |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 2              | 0              |  |
| Abdominal distension                                 |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 3              | 0              |  |
| Abnormal faeces                                      |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| Constipation                                         |                |                |  |
| subjects affected / exposed                          | 0 / 5 (0.00%)  | 1 / 5 (20.00%) |  |
| occurrences (all)                                    | 0              | 1              |  |
| Diarrhoea                                            |                |                |  |
| subjects affected / exposed                          | 2 / 5 (40.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 3              | 0              |  |
| Faeces discoloured                                   |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| Flatulence                                           |                |                |  |
| subjects affected / exposed                          | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                                    | 1              | 0              |  |
| Frequent bowel movements                             |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 2 / 5 (40.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 2              | 0              |  |
| Gastrointestinal sounds abnormal                |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Mucous stools                                   |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Retching                                        |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Teething                                        |                |                |  |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 2 / 5 (40.00%) |  |
| occurrences (all)                               | 0              | 3              |  |
| Vomiting                                        |                |                |  |
| subjects affected / exposed                     | 3 / 5 (60.00%) | 1 / 5 (20.00%) |  |
| occurrences (all)                               | 8              | 2              |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Cough                                           |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 1 / 5 (20.00%) |  |
| occurrences (all)                               | 1              | 1              |  |
| Rhinorrhoea                                     |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 1 / 5 (20.00%) |  |
| occurrences (all)                               | 1              | 1              |  |
| Skin and subcutaneous tissue disorders          |                |                |  |
| Dermatitis diaper                               |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 2              | 0              |  |
| Eczema                                          |                |                |  |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 5 (0.00%)  |  |
| occurrences (all)                               | 1              | 0              |  |
| Rash papular                                    |                |                |  |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 5 (20.00%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Psychiatric disorders                           |                |                |  |

|                                                                                                              |                     |                     |  |
|--------------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| Irritability<br>subjects affected / exposed<br>occurrences (all)                                             | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                                           | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Infections and infestations<br>Gastroenteritis norovirus<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Hand-foot-and-mouth disease<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Medical device site infection<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                          | 2 / 5 (40.00%)<br>2 | 0 / 5 (0.00%)<br>0  |  |
| Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 5 (20.00%)<br>2 | 0 / 5 (0.00%)<br>0  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 5 (20.00%)<br>1 | 2 / 5 (40.00%)<br>2 |  |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 5 (20.00%)<br>1 | 1 / 5 (20.00%)<br>1 |  |
| Product issues<br>Device breakage<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 5 (20.00%)<br>1 | 1 / 5 (20.00%)<br>1 |  |
| Device occlusion<br>subjects affected / exposed<br>occurrences (all)                                         | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |
| Metabolism and nutrition disorders                                                                           |                     |                     |  |

|                                                                        |                     |                     |  |
|------------------------------------------------------------------------|---------------------|---------------------|--|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 5 (20.00%)<br>2 | 0 / 5 (0.00%)<br>0  |  |
| Hypoglycaemia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 5 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |  |
| Hypophagia<br>subjects affected / exposed<br>occurrences (all)         | 1 / 5 (20.00%)<br>1 | 0 / 5 (0.00%)<br>0  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18 January 2018  | Protocol Amendment 1:<br>- Clarification that subjects must have been 4 to 12 months corrected gestational age at screening.<br>- Pharmacokinetic sampling on Week 6 was moved to Week 7 so that samples could be collected without exceeding the weekly/monthly total blood volume restrictions. Clarification that blood for post-dose PK samples might be taken within $\pm 10$ minutes of the time pre-specified.<br>- Teduglutide dose adjustments were changed to Week 12 rather than at every clinic visit to reduce the site burden.<br>- Assessment of the 5-level EuroQol five dimensions questionnaire was removed to reduce the caregiver burden. |
| 04 December 2018 | Protocol Amendment 2:<br>- The dose selection rationale was updated with results from a simulation work using the previous population PK model. Based on the totality of clinical data, 0.05 mg/kg once daily was expected to provide comparable C <sub>max</sub> concentrations in infants as compared to pediatric subjects with SBS and was recommended as an evaluation dosing regimen in Study SHP633-301.                                                                                                                                                                                                                                               |
| 24 May 2019      | Amendment 3:<br>- The significant change in this amendment included the deletion of inclusion criterion 6: "Lack of terminal ileum and ileocecal valve." due to difficulties in enrollment.                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 17 December 2019 | Protocol Amendment 4: - Specification that the pre-dose PK sample was not to be collected from subjects who weighed lesser than ( $<$ ) 7 kilograms (kg). The optional PK measurement at Week 12 was removed; postbaseline PK samples were to be performed at Week 7. The information to be collected for PK assessments was clarified. - Clarification that subjects might enroll in an extension study at EOS if that study was open to enrollment at the time of the SHP633-301 EOS.                                                                                                                                                                       |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported