



## Clinical trial results:

### A Prospective, Open-label, Long-term Safety and Efficacy Study of Teduglutide in Japanese Pediatric Subjects with Short Bowel Syndrome Who Completed SHP633-302

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2021-005404-36   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 02 November 2021 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 12 May 2022  |
| First version publication date | 12 May 2022  |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | SHP633-305 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03268811 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Shire   |
| Sponsor organisation address | 300 Shire Way, 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)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 02 November 2021 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 02 November 2021 |
| 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 long-term safety and tolerability of teduglutide treatment in Japanese pediatric participants with short bowel syndrome (SBS) who completed Study SHP633-302 (2020-005791-35).

Protection of trial subjects:

This clinical study was conducted in accordance with the study protocol and the ethical principles that have their origin in the World Medical Association Declaration of Helsinki. In addition, it was consistent with the standards stipulated in Article 14, Paragraph 3, and Article 80-2 of the Law on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices in Japan, the "Ministerial Ordinance on the Standards for the Implementation of Clinical Studies on Pharmaceutical Product" in Japan, and International Council For Harmonisation (ICH) Good Clinical Practices (GCP).

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 23 August 2017 |
| 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 | Japan: 9 |
| Worldwide total number of subjects   | 9        |
| EEA total number of subjects         | 0        |

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)  | 2 |
| Children (2-11 years)                     | 6 |
| Adolescents (12-17 years)                 | 1 |
| 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 6 centers in Japan from 23 August 2017 (first participant first visit) and 02 November 2021 (last participant last visit).

### Pre-assignment

Screening details:

A total of 9 Japanese pediatric participants who completed Study SHP633-302 (2020-005791-35) were enrolled into the extension study based on age of participants i.e., 7 children (aged 1 through 15 years of age) and 2 infants (aged 4 months through < 12 months of corrected gestational age).

### Period 1

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

### Arms

|                              |                                      |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes                                  |
| <b>Arm title</b>             | Total Children (Aged: 1 to 15 Years) |

Arm description:

Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Teduglutide      |
| Investigational medicinal product code | SHP633           |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received teduglutide 0.05 mg/kg SC injection once daily into 1 of the 4 quadrants of the abdomen or either thigh or arm.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Infants (Corrected Gestational Age: 4 to < 12 Months) |
|------------------|---|

Arm description:

Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Teduglutide      |
| Investigational medicinal product code | SHP633           |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received teduglutide 0.05 mg/kg SC injection once daily into 1 of the 4 quadrants of the abdomen or either thigh or arm.

| <b>Number of subjects in period 1</b> | Total Children<br>(Aged: 1 to 15<br>Years) | Infants (Corrected<br>Gestational Age: 4<br>to < 12 Months) |
|---------------------------------------|--|---|
| Started                               | 7  | 2   |
| Completed                             | 7  | 1   |
| Not completed                         | 0  | 1   |
| Adverse event, non-fatal              | -  | 1   |

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Total Children (Aged: 1 to 15 Years)                  |
| Reporting group description:   |   |
| Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course. |   |
| Reporting group title  | Infants (Corrected Gestational Age: 4 to < 12 Months) |
| Reporting group description:   |   |
| Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.    |   |

| Reporting group values                    | Total Children<br>(Aged: 1 to 15<br>Years) | Infants (Corrected<br>Gestational Age: 4<br>to < 12 Months) | Total |
|---|--|---|-------|
| Number of subjects                        | 7  | 2   | 9     |
| Age categorical                           |  |   |       |
| Units: Subjects                           |  |   |       |
| Aged: 1 to 15 Years                       | 7  | 0   | 7     |
| Corrected Gestation Age: 4 to < 12 months | 0  | 2   | 2     |
| Gender categorical                        |  |   |       |
| Units: Subjects                           |  |   |       |
| Male                                      | 6  | 1   | 7     |
| Female                                    | 1  | 1   | 2     |
| Race                                      |  |   |       |
| Units: Subjects                           |  |   |       |
| American Indian or Alaska Native          | 0  | 0   | 0     |
| Asian                                     | 7  | 2   | 9     |
| Native Hawaiian or Other Pacific Islander | 0  | 0   | 0     |
| Black or African American                 | 0  | 0   | 0     |
| White                                     | 0  | 0   | 0     |
| More than one race                        | 0  | 0   | 0     |
| Unknown or Not Reported                   | 0  | 0   | 0     |
| Ethnicity                                 |  |   |       |
| Units: Subjects                           |  |   |       |
| Hispanic or Latino                        | 0  | 0   | 0     |
| Not Hispanic or Latino                    | 7  | 2   | 9     |
| Unknown or Not Reported                   | 0  | 0   | 0     |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Total Children (Aged: 1 to 15 Years)                  |
| Reporting group description:<br>Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 milligram per kilogram (mg/kg) subcutaneous (SC) injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course. |   |
| Reporting group title  | Infants (Corrected Gestational Age: 4 to < 12 Months) |
| Reporting group description:<br>Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection once daily for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.    |   |

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

|   |  |
|---|--|
| End point title   | Number of Participants With Treatment-emergent Adverse Events (TEAEs) <sup>[1]</sup> |
| End point description:<br>An Adverse Event (AE) was any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. TEAEs were defined as any AEs whose onset occurred, severity worsened or intensity increased after receiving the investigational product (IP) in the core study (SHP633-302 [2020-005791-35]) or this extension study. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Number of participants with TEAEs were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). |  |
| End point type  | Primary  |
| End point timeframe:<br>From Baseline up to follow-up (up to 50 months)   |  |
| Notes:<br>[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.<br>Justification: No statistical and comparison analyses were performed for this endpoint.  |  |

| End point values            | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|-----------------------------|--------------------------------------|---|--|--|
| Subject group type          | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed | 7                                    | 2   |  |  |
| Units: Participants         | 7                                    | 2   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants With Clinically Significant Abnormalities in Vital Signs

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Abnormalities in Vital Signs <sup>[2]</sup> |
|-----------------|--|

End point description:

Vital sign assessments included pulse rate, blood pressure (systolic and diastolic blood pressure) and body temperature. Number of participants with clinically significant abnormalities in vital signs which were deemed clinically significant by the investigator were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to follow-up (up to 50 months)

Notes:

[2] - 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 analyses were performed for this endpoint.

| End point values            | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|-----------------------------|--------------------------------------|---|--|--|
| Subject group type          | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed | 7                                    | 2   |  |  |
| Units: Participants         | 0                                    | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters <sup>[3]</sup> |
|-----------------|--|

End point description:

Clinical laboratory parameters included biochemistry, hematology and urinalysis. Number of participants with clinically significant abnormalities in laboratory parameters which were deemed clinically significant by the investigator were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline up to follow-up (up to 50 months)

Notes:

[3] - 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 analyses were performed for this endpoint.



| End point values            | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed | 7  | 2   |  |  |
| Units: Participants         |  |   |  |  |
| Biochemistry                | 5  | 1   |  |  |
| Hematology                  | 1  | 0   |  |  |
| Urinalysis                  | 0  | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percent Change From Baseline in Average Total Urine Output at End of Treatment (EOT) of Last Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Percent Change From Baseline in Average Total Urine Output at End of Treatment (EOT) of Last Cycle During Teduglutide Treatment <sup>[4]</sup> |
|-----------------|--|

End point description:

Average total urine output was recorded over a 48-hour period of parental support (PS) stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The Average daily urine output milliliter per kilogram per day (mL/kg/day) was calculated as: (Total urine output over 48 hours / 2) / body weight (kilogram [kg]) where total urine output was calculated as the sum of the urine output in milliliter (mL) and the urine-only diaper weights in gram (g) (1g = 1mL) for the participant collected on the output diary form of electronic case report from (eCRF). Safety Population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[4] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 2   |  |  |
| Units: Percent Change                |  |   |  |  |
| arithmetic mean (standard deviation) | -37.228 (±<br>42.9396)                     | 146.881 (±<br>295.8061)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percent Change From Baseline in Average Number of Stools Per Day at EOT of Last Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Percent Change From Baseline in Average Number of Stools Per Day at EOT of Last Cycle During Teduglutide Treatment <sup>[5]</sup> |
|-----------------|---|

#### End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized by the average number of stools per day. The average number of stools per day was calculated as (sum of the daily data in a 48-hour period/2). The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average number of stools per day at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

#### End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

#### Notes:

[5] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 2   |  |  |
| Units: Percent Change                |  |   |  |  |
| arithmetic mean (standard deviation) | 24.37 (±<br>63.623)                        | 50.00 (±<br>0.000)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percent Change From Baseline in Average Stool/Mixed Stool Diaper Weight at EOT of Last Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Percent Change From Baseline in Average Stool/Mixed Stool Diaper Weight at EOT of Last Cycle During Teduglutide Treatment <sup>[6]</sup> |
|-----------------|--|

#### End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized by the average stool/mixed stool diaper weight (gram per kilogram per day [g/kg/day]). The body weight was used to calculate the daily stool/mixed stool diaper weight (g/kg/day). Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average stool/mixed stool diaper weight at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[6] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 1  | 2   |  |  |
| Units: Percent Change                |  |   |  |  |
| arithmetic mean (standard deviation) | -12.678 ( $\pm$<br>99999)                  | 206.017 ( $\pm$<br>332.4580)                                      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percent Change From Baseline in Average Total Ostomy Output at EOT of Last Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Percent Change From Baseline in Average Total Ostomy Output at EOT of Last Cycle During Teduglutide Treatment <sup>[7]</sup> |
|-----------------|--|

End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The body weight was used to calculate the average total ostomy output per day (mL/kg/day) using a formula analogous to that used to calculate the average daily urine output. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Percent change from baseline in average total ostomy output at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[7] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[8]</sup>                           | 2   |  |  |
| Units: Percent Change                |  |   |  |  |
| arithmetic mean (standard deviation) | ( )  | 3.143 ( $\pm$   |  |  |

Notes:

[8] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Percent Change From Baseline in Average Bristol Stool Form Score at EOT of Last Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Percent Change From Baseline in Average Bristol Stool Form Score at EOT of Last Cycle During Teduglutide Treatment <sup>[9]</sup> |
|-----------------|---|

End point description:

Fecal output was recorded over a 48-hour period of PS stability before every scheduled site visit and within 1 week of implementing any PS adjustment. The average daily fecal output was summarized the average typical stool form score using Bristol Stool Form Scale. The average typical stool form score was calculated as (sum of the daily data in a 48-hour period / 2). Typical Stool Form based on Bristol Stool Form Scale: 1 - Separate hard lumps, hard to pass, 2 - Sausage-shaped, but lumpy, 3 - Like a sausage but with cracks on the surface, 4- Like a sausage or snake, smooth and soft, 5- Soft blobs with clear-cut edges, 6- Fluffy pieces with ragged edges, a mushy stool, 7- Watery, no solid pieces, Entirely liquid. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). A negative change from baseline indicates improvement.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[9] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed          | 6                                    | 2   |  |  |
| Units: Percent Change                |                                      |   |  |  |
| arithmetic mean (standard deviation) | -7.51 (± 16.758)                     | 0.00 (± 0.000)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants With Anti-drug antibodies (ADAs) (Including Neutralizing Antibodies) at EOT of Last Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Number of Participants With Anti-drug antibodies (ADAs) (Including Neutralizing Antibodies) at EOT of Last Cycle During Teduglutide Treatment <sup>[10]</sup> |
|-----------------|---|

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**End point description:**

Number of participants with ADAs (including NABs) to teduglutide were used to summarize the presence of antibodies. The participants who tested positive for ADAs (including NABs) were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

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|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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**End point timeframe:**

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

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**Notes:**

[10] - 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 analyses were performed for this endpoint.

| End point values                           | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--|--|---|--|--|
| Subject group type                         | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed                | 6  | 2   |  |  |
| Units: Participants                        |  |   |  |  |
| Positive ADA: EOT of Last Cycle (n= 6, 2)  | 5  | 0   |  |  |
| Positive NABs: EOT of Last Cycle (n= 5, 0) | 4  | 0   |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Primary: Number of Participants With Clinically Significant Changes in Gastrointestinal (GI) Specific Testing**

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|                 |  |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Changes in Gastrointestinal (GI) Specific Testing <sup>[11]</sup> |
|-----------------|--|

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**End point description:**

GI specific testing included colonoscopy or sigmoidoscopy, abdominal ultrasound, fecal occult blood testing, upper GI series with small bowel follow-through (UGI/SBFT). Number of participants with clinically significant changes findings in gastrointestinal specific testing were reported. The safety population included all enrolled participants in the study and who received at least one dose of teduglutide (in study SHP633-302 [2020-005791-35] or SHP633-305 [2021-005404-36]). Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

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|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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**End point timeframe:**

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

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**Notes:**

[11] - 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 analyses were performed for this endpoint.

| End point values            | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed | 6  | 2   |  |  |
| Units: Participants         | 0  | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Body Weight For Age Z-Score at EOT of Last Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Body Weight For Age Z-Score at EOT of Last Cycle During Teduglutide Treatment <sup>[12]</sup> |
|-----------------|---|

End point description:

Body weight was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Change from baseline in body weight for age Z-Score at EOT of last cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of last cycle (up to Month 45) (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

Notes:

[12] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 2   |  |  |
| Units: z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.229 ( $\pm$<br>0.5636)                   | 3.982 ( $\pm$<br>3.6363)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 1 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 1 During Teduglutide Treatment <sup>[13]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq$  2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Change from baseline in height for age Z-Score at EOT of cycle 1 during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 Weeks)

Notes:

[13] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed          | 6                                    | 2   |  |  |
| Units: Z-score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | 0.002 ( $\pm$ 0.6049)                | 1.376 ( $\pm$ 0.3363)                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 2 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 2 During Teduglutide Treatment <sup>[14]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq$  2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

Notes:

[14] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.152 (±<br>0.5181)                        | 3.114 (±<br>99999)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 3 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 3 During Teduglutide Treatment <sup>[15]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

Notes:

[15] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.098 (±<br>0.3467)                        | 3.554 (±<br>99999)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 4 During



## Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 4 During Teduglutide Treatment <sup>[16]</sup> |
|-----------------|---|

### End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 4 (up to 96 weeks)

### Notes:

[16] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to $< 12$<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 5  | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.126 ( $\pm$<br>0.2622)                   | 3.542 ( $\pm$<br>99999)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 5 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 5 During Teduglutide Treatment <sup>[17]</sup> |
|-----------------|---|

### End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 5 (up to 120 weeks)

### Notes:

[17] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 3  | 0 <sup>[18]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.342 (±<br>0.1012)                        | ( )   |  |  |

Notes:

[18] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 6 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 6 During Teduglutide Treatment <sup>[19]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 6 (up to 144 weeks)

Notes:

[19] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 2  | 0 <sup>[20]</sup>   |  |  |
| Units: Z-Score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.276 (±<br>0.2593)                        | ( )   |  |  |

Notes:

[20] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 7 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 7 During Teduglutide Treatment <sup>[21]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 7 (up to 168 weeks)

Notes:

[21] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed          | 1                                    | 0 <sup>[22]</sup>                                     |  |  |
| Units: Z-Score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | 0.570 (± 99999)                      | ( )   |  |  |

Notes:

[22] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 8 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 8 During Teduglutide Treatment <sup>[23]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 8 (up to 192 weeks)

Notes:

[23] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 1  | 0 <sup>[24]</sup>   |  |  |
| Units: Z-Score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.851 (±<br>99999)                         | ( )   |  |  |

Notes:

[24] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Height For Age Z-Score at EOT of Cycle 9 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Height For Age Z-Score at EOT of Cycle 9 During Teduglutide Treatment <sup>[25]</sup> |
|-----------------|---|

End point description:

Height was measured using Age Z-Score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 9 (up to 196 weeks)

Notes:

[25] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 1  | 0 <sup>[26]</sup>   |  |  |
| Units: Z-Score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.477 (±<br>99999)                         | ( )   |  |  |

Notes:

[26] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of

## Cycle 1 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment <sup>[27]</sup> |
|-----------------|---|

### End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 weeks)

### Notes:

[27] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to $< 12$ Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[28]</sup>                    | 2   |  |  |
| Units: Z-score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | ()                                   | 2.400 ( $\pm 0.6472$ )                                  |  |  |

### Notes:

[28] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment <sup>[29]</sup> |
|-----------------|---|

### End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

### Notes:

[29] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[30]</sup>                          | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | ()   | 1.431 (±<br>99999)  |  |  |

Notes:

[30] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment <sup>[31]</sup> |
|-----------------|---|

End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

Notes:

[31] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[32]</sup>                          | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | ()   | 2.080 (±<br>99999)  |  |  |

Notes:

[32] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Head Circumference for Age Z-score at EOT of

## Cycle 4 During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Head Circumference for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment <sup>[33]</sup> |
|-----------------|---|

### End point description:

Head circumference was measured using Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 4 (up to 76 weeks)

### Notes:

[33] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to $< 12$<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 0 <sup>[34]</sup>                          | 1   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | ()   | 2.055 ( $\pm$<br>99999)   |  |  |

### Notes:

[34] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in Body Mass Index (BMI) for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Body Mass Index (BMI) for Age Z-score at EOT of Cycle 1 During Teduglutide Treatment <sup>[35]</sup> |
|-----------------|--|

### End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 1 (up to 24 weeks)

### Notes:

[35] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 0 <sup>[36]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.090 (±<br>0.6642)                        | ( )   |  |  |

Notes:

[36] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 2 During Teduglutide Treatment <sup>[37]</sup> |
|-----------------|--|

End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 2 (up to 48 weeks)

Notes:

[37] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 0 <sup>[38]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.489 (±<br>0.8474)                        | ( )   |  |  |

Notes:

[38] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 3 During



## Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 3 During Teduglutide Treatment <sup>[39]</sup> |
|-----------------|--|

### End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 3 (up to 72 weeks)

### Notes:

[39] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to $< 12$ Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group   |  |  |
| Number of subjects analysed          | 6                                    | 0 <sup>[40]</sup>                                       |  |  |
| Units: Z-score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | 0.409 ( $\pm$ 1.1688)                | ( )   |  |  |

### Notes:

[40] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 4 During Teduglutide Treatment <sup>[41]</sup> |
|-----------------|--|

### End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 4 (up to 96 weeks)

### Notes:

[41] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 5  | 0 <sup>[42]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.118 (±<br>0.8827)                        | ( )   |  |  |

Notes:

[42] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 5 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 5 During Teduglutide Treatment <sup>[43]</sup> |
|-----------------|--|

End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 5 (up to 120 weeks)

Notes:

[43] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 3  | 0 <sup>[44]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.070 (±<br>0.9770)                        | ( )   |  |  |

Notes:

[44] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 6 During

## Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 6 During Teduglutide Treatment <sup>[45]</sup> |
|-----------------|--|

End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]).

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 6 (up to 144 weeks)

Notes:

[45] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to $< 12$ Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group   |  |  |
| Number of subjects analysed          | 2                                    | 0 <sup>[46]</sup>                                       |  |  |
| Units: Z-score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | 0.925 ( $\pm$ 0.2556)                | ( )   |  |  |

Notes:

[46] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 7 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 7 During Teduglutide Treatment <sup>[47]</sup> |
|-----------------|--|

End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 7 (up to 168 weeks)

Notes:

[47] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 1  | 0 <sup>[48]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.839 (±<br>99999)                         | ( )   |  |  |

Notes:

[48] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 8 During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 8 During Teduglutide Treatment <sup>[49]</sup> |
|-----------------|--|

End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age ≥ 2 years old) and World Health Organization (age < 2 years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline, EOT of Cycle 8 (up to 192 weeks)

Notes:

[49] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 1  | 0 <sup>[50]</sup>   |  |  |
| Units: Z-score                       |  |   |  |  |
| arithmetic mean (standard deviation) | 0.015 (±<br>99999)                         | ( )   |  |  |

Notes:

[50] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Primary: Change From Baseline in BMI for Age Z-score at EOT of Cycle 9 During

## Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in BMI for Age Z-score at EOT of Cycle 9 During Teduglutide Treatment <sup>[51]</sup> |
|-----------------|--|

### End point description:

BMI Z-score was calculated by using the height and weight Age Z-score. A Z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Centers for Disease Control and Prevention (age  $\geq 2$  years old) and World Health Organization (age  $< 2$  years old) Z-score calculation charts were used for calculation. A negative Z-score indicates values lower than the mean while a positive Z-score indicates values higher than the mean. Safety population. Here, "number of participants analysed" refer to the participants evaluable for this endpoint. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

### End point timeframe:

Baseline, EOT of Cycle 9 (up to 196 weeks)

### Notes:

[51] - 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 analyses were performed for this endpoint.

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to $< 12$ Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group   |  |  |
| Number of subjects analysed          | 1                                    | 0 <sup>[52]</sup>                                       |  |  |
| Units: Z-score                       |                                      |   |  |  |
| arithmetic mean (standard deviation) | 0.480 ( $\pm$ 99999)                 | ( )   |  |  |

### Notes:

[52] - As no participant was analyzed for this arm, therefore data was not reported.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Participants Diary Parenteral Support (PS) Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Participants Diary Parenteral Support (PS) Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|--|

### End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent reduction in weight-normalized diary PS values from baseline was calculated using the formula: % reduction in PS value at the visit =  $([\text{average daily value at the scheduled visit} - \text{average daily value at baseline of the core study (SHP633-302 [2020-005791-35])}] / \text{average daily value at baseline of the core study (SHP633-302 [2020-005791-35])}) \times 100$ . Number of participants who achieved at least 20% reduction from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints.

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

### End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4

| <b>End point values</b>     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed | 6  | 2   |  |  |
| Units: Participants         |  |   |  |  |
| At EOT of Cycle 1 (n= 6, 2) | 4  | 1   |  |  |
| At EOT of Cycle 2 (n= 6, 1) | 4  | 1   |  |  |
| At EOT of Cycle 3 (n= 6, 1) | 6  | 1   |  |  |
| At EOT of Cycle 4 (n= 5, 1) | 5  | 1   |  |  |
| At EOT of Cycle 5 (n= 3, 0) | 3  | 0   |  |  |
| At EOT of Cycle 6 (n= 2, 0) | 2  | 0   |  |  |
| At EOT of Cycle 7 (n= 1, 0) | 1  | 0   |  |  |
| At EOT of Cycle 8 (n= 1, 0) | 1  | 0   |  |  |
| At EOT of Cycle 9 (n= 1, 0) | 1  | 0   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Number of Participants Who Achieved At Least 20 Percent (%) Reduction From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|--|

#### End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent reduction in weight-normalized prescribed PS values from baseline was calculated using the formula: % reduction in PS value at the visit = ([average daily value at the scheduled visit – average daily value at baseline of the core study (SHP633-302 [2020-005791-35]) / average daily value at baseline of the core study (SHP633-302 [2020-005791-35])) \*100. Number of participants who achieved at least 20% reduction from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment were reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints.

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

#### End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values            | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed | 6  | 2   |  |  |
| Units: Participants         |  |   |  |  |
| At EOT of Cycle 1 (n= 6, 2) | 5  | 1   |  |  |
| At EOT of Cycle 2 (n= 6, 1) | 5  | 1   |  |  |
| At EOT of Cycle 3 (n= 6, 1) | 6  | 1   |  |  |
| At EOT of Cycle 4 (n= 5, 1) | 5  | 1   |  |  |
| At EOT of Cycle 5 (n= 3, 0) | 3  | 0   |  |  |
| At EOT of Cycle 6 (n= 2, 0) | 2  | 0   |  |  |
| At EOT of Cycle 7 (n= 1, 0) | 1  | 0   |  |  |
| At EOT of Cycle 8 (n= 1, 0) | 1  | 0   |  |  |
| At EOT of Cycle 9 (n= 1, 0) | 1  | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|---|

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Change from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 2   |  |  |
| Units: mL/kg/day                     |  |   |  |  |
| arithmetic mean (standard deviation) |  |   |  |  |
| Change at EOT of Cycle 1 (n= 6, 2)   | -21.5 (±<br>11.83)                         | -31.9 (±<br>16.24)  |  |  |

|                                    |                 |                 |  |  |
|------------------------------------|-----------------|-----------------|--|--|
| Change at EOT of Cycle 2 (n= 6, 1) | -25.5 (± 14.38) | -54.2 (± 99999) |  |  |
| Change at EOT of Cycle 3 (n= 6, 1) | -32.1 (± 18.19) | -62.8 (± 99999) |  |  |
| Change at EOT of Cycle 4 (n= 5, 1) | -37.2 (± 24.10) | -95.8 (± 99999) |  |  |
| Change at EOT of Cycle 5 (n= 3, 0) | -54.8 (± 26.58) | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 6 (n= 2, 0) | -63.8 (± 31.57) | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 7 (n= 1, 0) | -93.8 (± 99999) | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 8 (n= 1, 0) | -80.3 (± 99999) | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 9 (n= 1, 0) | -79.1 (± 99999) | 9999 (± 9999)   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Percent Change From Baseline in Participant Diary PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|---|

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent change from baseline in participants diary PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                          | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|---|--------------------------------------|---|--|--|
| Subject group type                        | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed               | 6                                    | 2   |  |  |
| Units: Percent change                     |                                      |   |  |  |
| arithmetic mean (standard deviation)      |                                      |   |  |  |
| Percent change at EOT of Cycle 1 (n=6, 2) | -39.6 (± 34.86)                      | -32.5 (± 18.10)                                       |  |  |
| Percent change at EOT of Cycle 2 (n=6, 1) | -44.3 (± 33.11)                      | -56.6 (± 99999)                                       |  |  |
| Percent change at EOT of Cycle 3 (n=6, 1) | -52.8 (± 28.54)                      | -65.6 (± 99999)                                       |  |  |



|   |                 |                  |  |  |
|---|-----------------|------------------|--|--|
| Percent change at EOT of Cycle 4 (n=5, 1) | -62.9 (± 26.18) | -100.0 (± 99999) |  |  |
| Percent change at EOT of Cycle 5 (n=3, 0) | -73.9 (± 5.30)  | 9999 (± 9999)    |  |  |
| Percent change at EOT of Cycle 6 (n=2, 0) | -75.7 (± 0.54)  | 9999 (± 9999)    |  |  |
| Percent change at EOT of Cycle 7 (n=1, 0) | -82.9 (± 99999) | 9999 (± 9999)    |  |  |
| Percent change at EOT of Cycle 8 (n=1, 0) | -70.9 (± 99999) | 9999 (± 9999)    |  |  |
| Percent change at EOT of Cycle 9 (n=1, 0) | -69.8 (± 99999) | 9999 (± 9999)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|---|

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Change from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed          | 6                                    | 2   |  |  |
| Units: mL/kg/day                     |                                      |   |  |  |
| arithmetic mean (standard deviation) |                                      |   |  |  |
| Change at EOT of Cycle 1 (n= 6, 2)   | -20.9 (± 11.06)                      | -31.3 (± 26.77)                                       |  |  |
| Change at EOT of Cycle 2 (n= 6, 1)   | -28.0 (± 13.51)                      | -60.6 (± 99999)                                       |  |  |
| Change at EOT of Cycle 3 (n= 6, 1)   | -34.8 (± 21.13)                      | -67.5 (± 99999)                                       |  |  |
| Change at EOT of Cycle 4 (n= 5, 1)   | -36.3 (± 23.52)                      | -98.7 (± 99999)                                       |  |  |
| Change at EOT of Cycle 5 (n= 3, 0)   | -53.3 (± 26.24)                      | 9999 (± 9999)   |  |  |

|                                    |                 |               |  |  |
|------------------------------------|-----------------|---------------|--|--|
| Change at EOT of Cycle 6 (n= 2, 0) | -63.6 (± 32.10) | 9999 (± 9999) |  |  |
| Change at EOT of Cycle 7 (n= 1, 0) | -91.8 (± 99999) | 9999 (± 9999) |  |  |
| Change at EOT of Cycle 8 (n= 1, 0) | -77.3 (± 99999) | 9999 (± 9999) |  |  |
| Change at EOT of Cycle 9 (n= 1, 0) | -77.9 (± 99999) | 9999 (± 9999) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Percent Change From Baseline in Investigator Prescribed PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|---|

End point description:

PS (parenteral nutrition or intravenous fluids) was considered for managing nutritional support in terms of volume during the treatment period. Percent change from baseline in investigator prescribed PS volume at EOT of each cycle during teduglutide treatment was reported. Baseline refers to the baseline value of the core study (SHP633-302 [2020-005791-35]). Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                           | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--|--------------------------------------|---|--|--|
| Subject group type                         | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed                | 6                                    | 2   |  |  |
| Units: Percent change                      |                                      |   |  |  |
| arithmetic mean (standard deviation)       |                                      |   |  |  |
| Percent change at EOT of Cycle 1 (n= 6, 2) | -38.8 (± 35.19)                      | -32.1 (± 26.51)                                       |  |  |
| Percent change at EOT of Cycle 2 (n= 6, 1) | -46.9 (± 30.42)                      | -61.4 (± 99999)                                       |  |  |
| Percent change at EOT of Cycle 3 (n= 6, 1) | -55.4 (± 27.78)                      | -68.3 (± 99999)                                       |  |  |
| Percent change at EOT of Cycle 4 (n= 5, 1) | -62.5 (± 26.45)                      | -100.0 (± 99999)                                      |  |  |
| Percent change at EOT of Cycle 5 (n= 3, 0) | -73.3 (± 5.51)                       | 9999 (± 9999)   |  |  |
| Percent change at EOT of Cycle 6 (n= 2, 0) | -76.3 (± 2.41)                       | 9999 (± 9999)   |  |  |
| Percent change at EOT of Cycle 7 (n= 1, 0) | -83.0 (± 99999)                      | 9999 (± 9999)   |  |  |

|  |                 |               |  |  |
|--|-----------------|---------------|--|--|
| Percent change at EOT of Cycle 8 (n= 1, 0) | -69.9 (± 99999) | 9999 (± 9999) |  |  |
| Percent change at EOT of Cycle 9 (n= 1, 0) | -70.5 (± 99999) | 9999 (± 9999) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Who Achieved Enteral Autonomy PS Volume at EOT of Each Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Number of Participants Who Achieved Enteral Autonomy PS Volume at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|--|

End point description:

Enteral autonomy (completely weaned off PS) was defined as the first visit where there is no use of PS for the 7 days prior to the visit and there is no prescribed PS at that visit, and the participants remains off PS for the remainder of the treatment period of that cycle. Number of participants who achieved enteral autonomy off PS volume at EOT of each cycle during teduglutide treatment were reported. Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values            | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|-----------------------------|--------------------------------------|---|--|--|
| Subject group type          | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed | 6                                    | 2   |  |  |
| Units: Participants         |                                      |   |  |  |
| At EOT of Cycle 1 (n= 6, 2) | 1                                    | 0   |  |  |
| At EOT of Cycle 2 (n= 6, 1) | 1                                    | 0   |  |  |
| At EOT of Cycle 3 (n= 6, 1) | 1                                    | 0   |  |  |
| At EOT of Cycle 4 (n= 5, 1) | 1                                    | 1   |  |  |
| At EOT of Cycle 5 (n= 3, 0) | 0                                    | 0   |  |  |
| At EOT of Cycle 6 (n= 2, 0) | 0                                    | 0   |  |  |
| At EOT of Cycle 7 (n= 1, 0) | 0                                    | 0   |  |  |
| At EOT of Cycle 8 (n= 1, 0) | 0                                    | 0   |  |  |
| At EOT of Cycle 9 (n= 1, 0) | 0                                    | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Days Per Week of Diary PS Usage at EOT of Each Cycle During Teduglutide Treatment

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Days Per Week of Diary PS Usage at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|---|

### End point description:

Days per week of diary PS was calculated as: Days per week of actual PS = (number of days with non-zero values for PS volume within the 7 days prior to the visit / number of days for which any PS intake data was recorded within the 7 days prior to the visit) \* 7. Change from baseline in days per week of diary PS usage at EOT of each cycle during teduglutide treatment was reported. Safety population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm and "9999" indicates mean and SD could not estimated as no participant were analysed for specified arm

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

### End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                     | Total Children (Aged: 1 to 15 Years) | Infants (Corrected Gestational Age: 4 to < 12 Months) |  |  |
|--------------------------------------|--------------------------------------|---|--|--|
| Subject group type                   | Reporting group                      | Reporting group                                       |  |  |
| Number of subjects analysed          | 6                                    | 2   |  |  |
| Units: Days/week                     |                                      |   |  |  |
| arithmetic mean (standard deviation) |                                      |   |  |  |
| Change at EOT of Cycle 1 (n= 6, 2)   | -1.2 (± 2.86)                        | 0.0 (± 0.00)  |  |  |
| Change at EOT of Cycle 2 (n= 6, 1)   | -1.2 (± 2.86)                        | 0.0 (± 99999)   |  |  |
| Change at EOT of Cycle 3 (n= 6, 1)   | -1.2 (± 2.86)                        | 0.0 (± 99999)   |  |  |
| Change at EOT of Cycle 4 (n= 5, 1)   | -1.4 (± 3.13)                        | -7.0 (± 99999)  |  |  |
| Change at EOT of Cycle 5 (n= 3, 0)   | 0.0 (± 0.00)                         | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 6 (n= 2, 0)   | 0.0 (± 0.00)                         | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 7 (n= 1, 0)   | 0.0 (± 99999)                        | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 8 (n= 1, 0)   | 0.0 (± 99999)                        | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 9 (n= 1, 0)   | 0.0 (± 99999)                        | 9999 (± 9999)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Days Per Week of Prescribed PS Usage at EOT of Each Cycle During Teduglutide Treatment

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Days Per Week of Prescribed PS Usage at EOT of Each Cycle During Teduglutide Treatment |
|-----------------|--|

### End point description:

Days per week of Prescribed PS was calculated as: Days per week of actual PS = (number of days with non-zero values for PS volume within the 7 days prior to the visit / number of days for which any PS intake data was recorded within the 7 days prior to the visit) \* 7. Change from baseline in days Per week of prescribed PS usage at EOT of each cycle during teduglutide treatment was reported. Safety

population. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n" signifies to participants evaluable at given timepoints. Baseline refers to the baseline value of the core study (SHP633-302 [2021-005404-36]). Here, '99999' indicates that standard deviation could not be estimated for single subject for the specified arm and "9999" indicates mean and SD could not be estimated as no participant were analysed for specified arm.

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

End point timeframe:

Baseline, EOT of each cycle 1, 2, 3, 4, 5, 6, 7, 8 and 9 (Each Cycle 1 to 8 = 24 weeks, and Cycle 9 = 4 weeks)

| End point values                     | Total Children<br>(Aged: 1 to 15<br>Years) | Infants<br>(Corrected<br>Gestational<br>Age: 4 to < 12<br>Months) |  |  |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                            | Reporting group   |  |  |
| Number of subjects analysed          | 6  | 2   |  |  |
| Units: Days/week                     |  |   |  |  |
| arithmetic mean (standard deviation) |  |   |  |  |
| Change at EOT of Cycle 1 (n= 6, 2)   | -1.2 (± 2.86)                              | 0.0 (± 0.00)  |  |  |
| Change at EOT of Cycle 2 (n= 6, 1)   | -1.2 (± 2.86)                              | 0.0 (± 99999)   |  |  |
| Change at EOT of Cycle 3 (n= 6, 1)   | -1.2 (± 2.86)                              | 0.0 (± 99999)   |  |  |
| Change at EOT of Cycle 4 (n= 5, 1)   | -1.4 (± 3.13)                              | -7.0 (± 99999)  |  |  |
| Change at EOT of Cycle 5 (n= 3, 0)   | 0.0 (± 0.00)                               | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 6 (n= 2, 0)   | 0.0 (± 0.00)                               | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 7 (n= 1, 0)   | 0.0 (± 99999)                              | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 8 (n= 1, 0)   | 0.0 (± 99999)                              | 9999 (± 9999)   |  |  |
| Change at EOT of Cycle 9 (n= 1, 0)   | 0.0 (± 99999)                              | 9999 (± 9999)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline up to follow-up (up to 50 months)

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Infants (Corrected Gestational Age: 4 to < 12 Months) |
|-----------------------|---|

Reporting group description:

Participants (Infants) from 4 through < 12 months of corrected gestational age who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Total Children (Aged: 1 to 15 Years) |
|-----------------------|--------------------------------------|

Reporting group description:

Participants aged from 1 through 15 years who participated in the core study (SHP633-302 [2020-005791-35]) were enrolled into this extension study and received teduglutide 0.05 mg/kg SC injection for 24 weeks in each treatment cycle (Cycles 1 to 9 [Each cycle=28 weeks]) depending on the disease course.

| <b>Serious adverse events</b>                        | Infants (Corrected Gestational Age: 4 to < 12 Months) | Total Children (Aged: 1 to 15 Years) |  |
|--|---|--------------------------------------|--|
| Total subjects affected by serious adverse events    |   |                                      |  |
| subjects affected / exposed                          | 2 / 2 (100.00%)                                       | 7 / 7 (100.00%)                      |  |
| number of deaths (all causes)                        | 0   | 0                                    |  |
| number of deaths resulting from adverse events       | 0   | 0                                    |  |
| Surgical and medical procedures                      |   |                                      |  |
| Central venous catheter removal                      |   |                                      |  |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 1 / 7 (14.29%)                       |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1                                |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0                                |  |
| Nervous system disorders                             |   |                                      |  |
| Seizure  |   |                                      |  |
| subjects affected / exposed                          | 1 / 2 (50.00%)  | 0 / 7 (0.00%)                        |  |
| occurrences causally related to treatment / all      | 0 / 1   | 0 / 0                                |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0                                |  |
| General disorders and administration site conditions |   |                                      |  |
| Pyrexia  |   |                                      |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Gastrointestinal disorders</b>               |                |                |  |
| Colonic haematoma                               |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enteritis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enterocolitis                                   |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ileus   |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pancreatitis acute                              |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vomiting  |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| <b>Infections and infestations</b>              |                |                |  |
| Arthritis bacterial                             |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Beta haemolytic streptococcal                   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| infection                                       |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device related infection                        |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 4 / 7 (57.14%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 6          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastroenteritis adenovirus                      |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Medical device site infection                   |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Otitis media                                    |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Streptococcal infection                         |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Upper respiratory tract infection               |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Viral pharyngitis                               |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Viral upper respiratory tract infection         |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Product issues                                  |                |                |  |
| Device breakage                                 |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 3 / 7 (42.86%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 8          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device damage                                   |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Device occlusion                                |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| 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 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| 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>                                   | Infants (Corrected Gestational Age: 4 to < 12 Months) | Total Children (Aged: 1 to 15 Years) |  |
|---|---|--------------------------------------|--|
| Total subjects affected by non-serious adverse events               |   |                                      |  |
| subjects affected / exposed   | 2 / 2 (100.00%)                                       | 7 / 7 (100.00%)                      |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                      |  |
| Neoplasm  |   |                                      |  |
| subjects affected / exposed   | 0 / 2 (0.00%)   | 1 / 7 (14.29%)                       |  |
| occurrences (all)   | 0   | 1                                    |  |
| General disorders and administration site conditions                |   |                                      |  |

|   |                     |                     |  |
|---|---------------------|---------------------|--|
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 3 / 7 (42.86%)<br>4 |  |
| Immune system disorders<br>Food allergy<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>4 |  |
| Seasonal allergy<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Respiratory, thoracic and mediastinal disorders<br>Asthma<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 2 / 7 (28.57%)<br>2 |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Rhinitis allergic<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Upper respiratory tract inflammation<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Psychiatric disorders   |                     |                     |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| Head banging<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Product issues<br>Device damage<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Investigations<br>Alanine aminotransferase increased<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>2 | 0 / 7 (0.00%)<br>0  |  |
| Amylase increased<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Aspartate aminotransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Eosinophil count increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 1 / 7 (14.29%)<br>1 |  |
| Injury, poisoning and procedural<br>complications<br>Auricular haematoma<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 2 (50.00%)<br>1 | 0 / 7 (0.00%)<br>0  |  |
| Epiphyseal injury  |                     |                     |  |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Contusion                            |                |                |  |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                    | 1              | 0              |  |
| Fracture                             |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Fall                                 |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Gastrostomy tube site complication   |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Heat stroke                          |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Injury corneal                       |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Ligament injury                      |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Procedural pain                      |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Wound complication                   |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                    | 0              | 2              |  |
| Blood and lymphatic system disorders |                |                |  |
| Anaemia                              |                |                |  |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Eye disorders                        |                |                |  |
| Conjunctivitis allergic              |                |                |  |

|                             |               |                |  |
|-----------------------------|---------------|----------------|--|
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 2              |  |
| Eye discharge               |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Strabismus                  |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Gastrointestinal disorders  |               |                |  |
| Abdominal distension        |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 2              |  |
| Abdominal pain              |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Cheilitis                   |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 2              |  |
| Constipation                |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 2 / 7 (28.57%) |  |
| occurrences (all)           | 0             | 2              |  |
| Dental caries               |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 2 / 7 (28.57%) |  |
| occurrences (all)           | 0             | 2              |  |
| Enteritis                   |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 2 / 7 (28.57%) |  |
| occurrences (all)           | 0             | 5              |  |
| Enterocolitis               |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Gastric disorder            |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Lip dry                     |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |

|  |                |                |  |
|--|----------------|----------------|--|
| Nausea                                 |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Rectal prolapse                        |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Stomatitis                             |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                      | 0              | 2              |  |
| Hepatobiliary disorders                |                |                |  |
| Drug-induced liver injury              |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Skin and subcutaneous tissue disorders |                |                |  |
| Acne                                   |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Dermatitis allergic                    |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Dermatitis                             |                |                |  |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1              | 0              |  |
| Dermatitis diaper                      |                |                |  |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                      | 1              | 0              |  |
| Drug eruption                          |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Dry skin                               |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                      | 0              | 2              |  |
| Eczema                                 |                |                |  |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                      | 0              | 2              |  |
| Haemorrhage subcutaneous               |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                               | 0              | 2              |  |
| Miliaria  |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                               | 0              | 2              |  |
| Rash  |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 3 / 7 (42.86%) |  |
| occurrences (all)                               | 0              | 4              |  |
| Skin erosion                                    |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Skin induration                                 |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Urticaria                                       |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                               | 0              | 3              |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Joint swelling                                  |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Myalgia   |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Infections and infestations                     |                |                |  |
| Adenoviral conjunctivitis                       |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Conjunctivitis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 3              | 1              |  |
| Epididymitis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Hand-foot-and-mouth disease                     |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed             | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 0              | 1              |  |
| Gastroenteritis                         |                |                |  |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 0              | 1              |  |
| Influenza                               |                |                |  |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 2 / 7 (28.57%) |  |
| occurrences (all)                       | 0              | 2              |  |
| Infected bite                           |                |                |  |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 0              | 1              |  |
| Medical device site infection           |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 1              | 1              |  |
| Oral candidiasis                        |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                       | 1              | 0              |  |
| Periodontitis                           |                |                |  |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 0              | 2              |  |
| Upper respiratory tract infection       |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                       | 2              | 0              |  |
| Viral infection                         |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 0 / 7 (0.00%)  |  |
| occurrences (all)                       | 1              | 0              |  |
| Viral upper respiratory tract infection |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 4 / 7 (57.14%) |  |
| occurrences (all)                       | 5              | 25             |  |
| Metabolism and nutrition disorders      |                |                |  |
| Dehydration                             |                |                |  |
| subjects affected / exposed             | 1 / 2 (50.00%) | 2 / 7 (28.57%) |  |
| occurrences (all)                       | 1              | 6              |  |
| Hypomagnesaemia                         |                |                |  |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 1 / 7 (14.29%) |  |
| occurrences (all)                       | 0              | 1              |  |



|                             |               |                |  |
|-----------------------------|---------------|----------------|--|
| Hypozaemia                  |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 1              |  |
| Metabolic acidosis          |               |                |  |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 7 (14.29%) |  |
| occurrences (all)           | 0             | 5              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 26 May 2017     | <p>Amendment 1:</p> <ul style="list-style-type: none"><li>- Clarification that medical history and SBS history collected at study entry were updates to data collected at the start of the core study.</li><li>- Clarification that during the no-teduglutide treatment period, visits would take place approximately every 12 weeks.</li><li>- Clarification that PS prescription was collected at the screening visit.</li><li>- Sigmoidoscopy was added as the alternate to colonoscopy throughout the protocol.</li><li>- Clarification that unscheduled laboratory tests were performed at the investigational site laboratory, as needed.</li><li>- Clarification on visit schedule when a participant prematurely discontinues IP during a teduglutide treatment cycle.</li><li>- Clarification on handling of an investigational drug, which is for single use only and should be used within 3 hours following reconstitution.</li><li>- Removal of urine sodium from the list of urinalysis parameters to be tested.</li></ul>   |
| 24 January 2018 | <p>Amendment 2:</p> <ul style="list-style-type: none"><li>- Revised investigational product (IP) administration language to provide oversight on IP administration.</li><li>- Added direct bilirubin to the list of laboratory tests.</li><li>- Clarifications that the drug administration diary can be completed by site staff, added "guardian" to replace "legally authorized representative", and updated the emergency contact information and the product quality complaint section.</li></ul>  |
| 20 July 2018    | <p>Amendment 3:</p> <ul style="list-style-type: none"><li>- Update of the number of participants from 5 to 7.</li><li>- Addition of the study population of 2 cohorts based on age of participants at the time of entry into the core study: the infant cohort 4 to less than 12 months of corrected gestational age and children 1 to 15 years of age.</li><li>- To minimize risk to participants, a new escape criterion was added allowing those who had escaped during the follow-up period of a previous teduglutide treatment cycle to omit the follow-up period during subsequent teduglutide treatment cycles.</li><li>- Modified teduglutide treatment exclusion criterion 1 on participants body weight to accommodate younger children (exclude participants if weight less than 5 kg).</li><li>- Clarified the requirement from the study physician to observe the parent/guardian administering the IP at least twice before permitting the parent/guardian to administer teduglutide to a single observation.</li><li>- Clarified blood pressure collection to same extremity rather than same arm (arm is not used in small children).</li><li>- Clarified that IP compliance is calculated from diaries.</li><li>- Deleted the 4 hour observation period at initial dosing since participants were already exposed to teduglutide in the core study.</li><li>- Omitted saved serum samples for participants less than 10 kg.</li><li>- Updates for number of enrolled participants, corporate name change, medical monitor change, deletion of duplicate text, and other minor editorial corrections</li></ul> |

|                  |  |
|------------------|--|
| 06 November 2020 | <p>Amendment 4:</p> <ul style="list-style-type: none"> <li>- Sponsor name changed to include both Shire Human Genetic Therapies, Inc. (USA) and Takeda Pharmaceutical Company Limited.</li> <li>- Transferred back the role of in-country clinical caretaker from IQVIA Services Japan K.K to the sponsor. The sponsor is now responsible for notifying the relevant regulatory authorities of related, unexpected serious adverse events (SAEs).</li> <li>- Updated the end of the planned study period to December 2021.</li> <li>- Expanded the timing to perform a colonoscopy/sigmoidoscopy at the end of a teduglutide treatment cycle (CxW24). Participants who received 2 treatment cycles (48 weeks of teduglutide exposure) will undergo a colonoscopy/sigmoidoscopy before the next cycle of teduglutide treatment. Colonoscopy/sigmoidoscopy performed after the Visit CxW24 (<math>\pm 4</math> days) window and before the next cycle of teduglutide treatment will not be considered a protocol deviation. All other visit procedures must adhere to the (<math>\pm 4</math> days) visit window.</li> <li>- Added a new section entitled "Changes to Study Procedures Due to a Pandemic". The purpose of these changes is to maintain the participant safety, confidentiality, and study integrity in the context of healthcare delivery challenges presented by the COVID-19 pandemic.</li> <li>- Clarified the definition of an overdose as the administration of the investigational product at a dose or frequency greater than 0.05 mg/kg subcutaneous once daily. An overdose occurs if any of the following criteria are met: <ul style="list-style-type: none"> <li>* More than 0.05 mg/kg is given at any one time</li> <li>* Consecutive doses are spaced less than 12 hours apart</li> <li>* Any more than 0.05 mg/kg in one day</li> </ul> </li> <li>- Changed the data monitoring committee meeting frequency. The DMC members will review the data approximately every 6 months (previously 3 months) during the study treatment periods (date of the first participants first dose to date of the last participants last dose).</li> <li>- Updated contact information and responsible personnel.</li> </ul> |
|------------------|--|

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported