Clinical trial results:
A Long-Term, Open-Label, Multicenter, Phase IV Study to Assess Longitudinal Changes on Height and Weight in Patients with MPS II Who Are Receiving Elaprase and Started Treatment with Elaprase at < 6 Years of Age

Summary

EudraCT number	2014-004804-31
Trial protocol	DE
Global end of trial date	29 July 2025

Results information

Result version number	v2 (current)
This version publication date	24 May 2026
First version publication date	13 February 2026
Version creation reason	• New data added to full data set information updated

Trial information

Trial identification

Sponsor protocol code	SHP-ELA-401

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02455622
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, MA, United States, 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 July 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study was to assess longitudinal changes in the following parameters in patients with MPS II who began Elaprase treatment at <6 years of age and who are receiving treatment with Elaprase:
• height
• weight

Protection of trial subjects:

Each participant or their legally authorized representative signed an informed consent form (ICF) before participating in the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Dominican Republic: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	Malaysia: 2
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Serbia: 1
Country: Number of subjects enrolled	Philippines: 2
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Viet Nam: 10
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	66
EEA total number of subjects	16

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)	19
Children (2-11 years)	47
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 28 October 2015 to 29 July 2025.

Pre-assignment

Screening details:

Treatment-naïve participants with mucopolysaccharidosis II(MPS II) were enrolled to receive weekly intravenous(IV) infusions of Elaprase starting at less than(<)6 years of age. Data for primary growth analyses was utilized from the Hunter Outcome Survey (HOS) registry participants for this study.

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
Arm title	Prospective Set

Arm description:

Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

Arm type	Experimental
Investigational medicinal product name	Elaprase
Investigational medicinal product code	
Other name	Idursulfase
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Weekly Elaprase infusion from Week 1 till minimum of 5 years or until they reach their 10th birthday, whichever is longer.

Arm title	Hunter Outcome Survey (HOS) Treated Set

Arm description:

Participants in the HOS patient registry, who were treated, were combined with the Prospective Set in the Primary Growth Analysis for this study using their height and weight data.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	HOS Untreated Set

Arm description:

Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Prospective Set	Hunter Outcome Survey (HOS) Treated Set	HOS Untreated Set
Started	21	19	26
Completed	17	19	26
Not completed	4	0	0
Adverse event, serious fatal	1	-	-
Reason Not Specified	1	-	-
Non-compliance with study drug	2	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Prospective Set
Reporting group description:	
Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.	
Reporting group title	Hunter Outcome Survey (HOS) Treated Set
Reporting group description:	
Participants in the HOS patient registry, who were treated, were combined with the Prospective Set in the Primary Growth Analysis for this study using their height and weight data.	
Reporting group title	HOS Untreated Set
Reporting group description:	
Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data.	

Reporting group values	Prospective Set	Hunter Outcome Survey (HOS) Treated Set	HOS Untreated Set
Number of subjects	21	19	26
Age Categorical Units: Subjects			
Less than (<)2 years	2	2	15
Greater than equal to (>=) 2 years	19	17	11
Gender categorical Units: Subjects			
Female	0	0	0
Male	21	19	26
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	15	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	2
White	4	14	23
More than one race	0	0	0
Unknown or Not Reported	2	3	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	0	0
Not Hispanic or Latino	9	0	0
Unknown or Not Reported	10	19	26

Reporting group values	Total		
Number of subjects	66		
Age Categorical Units: Subjects			
Less than (<)2 years	19		
Greater than equal to (>=) 2 years	47		

Gender categorical Units: Subjects			
Female	0		
Male	66		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	17		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	3		
White	41		
More than one race	0		
Unknown or Not Reported	5		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2		
Not Hispanic or Latino	9		
Unknown or Not Reported	55		

End points

End points reporting groups

Reporting group title	Prospective Set

Reporting group description:

Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

Reporting group title	Hunter Outcome Survey (HOS) Treated Set

Reporting group description:

Participants in the HOS patient registry, who were treated, were combined with the Prospective Set in the Primary Growth Analysis for this study using their height and weight data.

Reporting group title	HOS Untreated Set

Reporting group description:

Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data.

Subject analysis set title	Combined Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. Efficacy Set includes participants who received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

Primary: Height Overall

End point title	Height Overall[1]

End point description:

The effect of treatment on growth evaluated in terms of height. As pre-specified in the statistical analysis plan (SAP), descriptive analysis for this outcome measure was planned for the Combined Set and HOS Untreated Set arms and the assessment for Primary Growth Analysis was considered for the Combined Set in comparison to the HOS Untreated Set. The Combined Set included treated participants enrolled in this study (prospective participants) as well as treated participants from the HOS registry. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. The HOS Treated Set included all participants enrolled in the HOS registry that met the criteria. The HOS Untreated Set included untreated participants from the HOS registry that met the criteria.

End point type	Primary

End point timeframe:

Prospective participants: From Baseline through End-of-Study (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	HOS Untreated Set	Combined Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	40		
Units: centimeter (cm)				
least squares mean (standard error)	108.143 (± 1.7668)	113.759 (± 1.211)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	HOS Untreated Set v Combined Set
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011
Method	Linear mixed model
Parameter estimate	LS Mean Difference
Point estimate	5.616
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.329
upper limit	9.903
Variability estimate	Standard error of the mean
Dispersion value	2.1497

Primary: Weight Overall

End point title	Weight Overall[2]

End point description:

The effect of treatment on growth was evaluated, in terms of weight. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned for the Combined Set and HOS Untreated Set arms and the assessment for Primary Growth Analysis was considered for the Combined Set in comparison to the HOS Untreated Set. The Combined Set included treated participants enrolled in this study (prospective participants) as well as treated participants from the HOS registry. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. The HOS Treated Patients included all participants enrolled in the HOS registry that met the criteria. The HOS Untreated Set included untreated participants from the HOS registry that met the criteria.

End point type	Primary

End point timeframe:

Prospective participants: From Baseline through End-of-Study (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	HOS Untreated Set	Combined Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	40		
Units: kilograms (kg)				
least squares mean (standard error)	26.11 (± 1.1647)	25.164 (± 0.8382)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	HOS Untreated Set v Combined Set
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5106
Method	Linear mixed model
Parameter estimate	LS Mean Difference
Point estimate	-0.946
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	1.908
Variability estimate	Standard error of the mean
Dispersion value	1.4308

Primary: Change from Baseline in Height Measured by Z- score

End point title	Change from Baseline in Height Measured by Z- score[3][4]

End point description:

Z-score(standard score) for height was calculated as number of standard deviations(SD) by which mean height(MH) of each arm was above/below MH of reference population. Z-scores were calculated based on World Health Organization Drug Dictionary(WHO-DD) growth charts(for age less or equal to[≤] 24 months(m))& Centers for Disease Control & Prevention(CDC) growth charts(for age more than[>]24 m)normal height-for-age data. Normal growth Z-score range:-1 to +1.Z-score:0 represents reference mean & 50th percentile. Z-score of more than or equal to(≥)+2=above normal range & taller than average (avg.) & Z-score ≤-2=shorter stature than avg. & may indicate growth issues. Score is calculated as Z=(Actual value for participant in study-Mean value of healthy population(HP))/(SD of HP). Combined & HOS Untreated Set was utilized. Subjects analysed=number of participants with data available for analysis for this end point.

End point type	Primary

End point timeframe:

Prospective participants: From Baseline through End-of-Study (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

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: Only descriptive statistics is provided for this end point.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	HOS Untreated Set	Combined Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	22	39		
Units: height z score				
arithmetic mean (standard deviation)	-4.228 (± 1.4616)	-1.135 (± 1.3480)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Weight Measured by Z-score

End point title	Change from Baseline in Weight Measured by Z-score[5][6]

End point description:

Z-score (standard score) for weight was calculated as number of SDs by which mean weight (MW) of each arm was above or below the MW of the reference population. Z-scores were calculated based on WHO-DD growth charts (for age ≤ 24 m) & CDC growth charts (for age > 24 m) normal weight-for-age data. Normal range for growth Z score is defined as -1 to +1. Z-score: 0 represents reference population mean & 50th percentile. Positive Z-score of ≥ +2= above avg. weight (overweight). Negative Z-score of ≤ -2= below avg. weight (underweight). Score is calculated as Z=(Actual value for participant in study-Mean value of HP)/ (SD of HP). As per SAP, descriptive analysis was planned for Combined & HOS Untreated Set arms, with Primary Growth Analysis assessed for Combined Set compared to HOS Untreated Set. Combined and HOS untreated set was utilized. Subjects analysed is the number of participants with data available for analysis for this outcome measure.

End point type	Primary

End point timeframe:

Prospective participants: From Baseline through End-of-Study (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

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: Only descriptive statistics is provided for this end point.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	HOS Untreated Set	Combined Set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	26	39		
Units: weight z score				
arithmetic mean (standard deviation)	-2.337 (± 1.9014)	-1.161 (± 1.3259)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinical Significant Abnormal Neurological Examination

End point title	Number of Participants With Clinical Significant Abnormal Neurological Examination[7][8]

End point description:

A full physical examination will be performed with a thorough review of body systems. Physical examinations will include a review of the patient's general appearance, neurological examination, as well as evaluation of the body systems. Any abnormal change in findings will be recorded as an adverse event (AE). The Safety Analysis Set consisted of all prospective participants who received any amount of investigational product (IP). As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all treated participants in this study.

End point type	Primary

End point timeframe:

From Screening to End-of-Study (approximately 9.75 years)

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: Only descriptive statistics is provided for this end point.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormal Urinalysis Values

End point title	Number of Participants With Clinically Significant Abnormal Urinalysis Values[9][10]

End point description:

Reported here is the number of participants with clinically significant abnormal values in urinalysis tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all treated participants in this study.

End point type	Primary

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

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: Only descriptive statistics is provided for this end point.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all

the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
Bacteria (/High-power field (HPF))	5			
Erythrocytes (/HPF)	1			
Glucose (milligrams per deciliter (mg/dl))	1			
Leukocyte Esterase	1			
Mucous Threads	1			
Nitrite	4			
Occult Blood	1			
Protein (mg/dL)	3			
Specimen Appearance	6			
Squamous Epithelial Cells (/HPF)	2			
Squamous Transitional Epithelial Cells (/HPF)	1			
Triple Phosphate Crystals (/HPF)	2			
Yeast Cells	1			
pH (pH)	3			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAE)[11][12]

End point description:

An AE is any noxious, pathologic, or unintended change in anatomical, physiologic, or metabolic function as indicated by physical signs, symptoms, or laboratory changes occurring in any phase of a clinical study, whether or not considered product-related. This includes an exacerbation of a pre-existing condition. A TEAE is defined as an AE with an onset that occurs after receiving study drug. The Safety Analysis Set consisted of all prospective participants who received any amount of IP. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all treated participants in this study.

End point type	Primary

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

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: Only descriptive statistics is provided for this end point.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants	21			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormal Serum Chemistry Values

End point title	Number of Participants With Clinically Significant Abnormal Serum Chemistry Values[13][14]

End point description:

Reported here is the number of participants with clinically significant abnormal values in serum chemistry tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all treated participants in this study.

End point type	Primary

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

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: Only descriptive statistics is provided for this end point.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
Alanine Aminotransferase (units per liter (U/L))	1			
Aspartate Aminotransferase (U/L)	1			
Gamma Glutamyl Transferase (U/L)	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormal Hematology Values

End point title	Number of Participants With Clinically Significant Abnormal Hematology Values[15][16]

End point description:

Reported here is the number of participants with clinically significant abnormal values in haematological tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all treated participants in this study.

End point type	Primary

End point timeframe:

Screening to End-of-Study (approximately 9.75 years)

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: Only descriptive statistics is provided for this end point.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
Ery. Mean Corpuscular Hemoglobin (picogram (pg))	1			
Ery. Mean Corpuscular Volume (femtoliter (fL))	1			
Hemoglobin (gram per litre (g/L))	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Value of Height Velocity From Baseline to End of Study

End point title	Observed Value of Height Velocity From Baseline to End of Study[17]

End point description:

Height velocity was calculated as the difference in height, divided by the difference in age between consecutive study visits. BL denotes Baseline, HV denotes Height Velocity, EOS denotes End-of-Study and Y denotes Years for the reported categories. Efficacy Set: all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Combined Set included data from all participants in both Efficacy Set and HOS Treated Set. HOS Treated Set included all participants enrolled in HOS registry that meet the criteria. HOS Untreated Set included untreated participants from HOS registry that meet the criteria. Number analysed (n) is the number of participants with data available for the specified categories.

End point type	Secondary

End point timeframe:

Prospective participants: From Baseline till End-of-Study Treatment (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is

reported.

End point values	Prospective Set	HOS Untreated Set	Combined Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	21	26	40	
Units: centimeters (cm)/year				
arithmetic mean (standard deviation)				
Overall HV:BL to <6Y of Age (n=16,22,32)	5.401 (± 2.5815)	6.557 (± 2.5902)	6.556 (± 2.6803)	
Overall HV:6Y of Age to EOS (n=20,18,38)	2.699 (± 1.7610)	1.761 (± 1.2178)	3.571 (± 1.8064)	

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Value of Weight Velocity From Baseline to End of Study

End point title	Observed Value of Weight Velocity From Baseline to End of Study[18]

End point description:

Weight velocity was be calculated as the difference in weight, divided by the difference in age between consecutive study visits. Efficacy Set: all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Combined Set included data from all participants in both Efficacy Set and HOS Treated Set. HOS Treated Set included all participants enrolled in HOS registry that meet the criteria. HOS Untreated Set included untreated participants from HOS registry that meet criteria. BL denotes baseline, Y denotes Years and V denotes Velocity for the reported categories. Number analyzed (n) is the number of participants with data available for the specified categories.

End point type	Secondary

End point timeframe:

Prospective participants: From Baseline till End-of-Study Treatment (approximately 9.75 years); HOS participants followed up to a maximum of 9.5 years where participant data were accessed from the registry between the period of 08/01/07 to 02/06/22

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set	HOS Untreated Set	Combined Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	21	26	40	
Units: kilograms (kg)/year				
arithmetic mean (standard deviation)				
Overall V:BL to <6Y of Age (n=16,22,32)	1.772 (± 1.2029)	3.670 (± 2.0005)	2.475 (± 1.4550)	
Overall V: 6Y of Age to EOS (n=20,19,38)	1.573 (± 1.3198)	1.445 (± 0.8324)	2.305 (± 1.7134)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline for Urinary glycosaminoglycans (uGAG) Levels Normalized to Urine Creatinine

End point title	Percent Change From Baseline for Urinary glycosaminoglycans (uGAG) Levels Normalized to Urine Creatinine [19]

End point description:

Urinary GAG levels were normalized to urine creatinine (normalized uGAG) and reported as mg uGAG/ millimoles (mmol) creatinine. The Efficacy Set is defined as all prospective participants who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analysed is the number of participants with data available for analysis for this outcome measure at the end-of-study. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set in this study.

End point type	Secondary

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: percent change				
arithmetic mean (standard deviation)				
Normalized uGAG (mg/mmol)	-70.446 (± 17.8741)			

Statistical analyses

No statistical analyses for this end point

Secondary: Normalized uGAG Divided by Upper Llimit of Normal for Age (uGAG/ULN) Every 12 Months

End point title	Normalized uGAG Divided by Upper Llimit of Normal for Age (uGAG/ULN) Every 12 Months[20]

End point description:

Normalized uGAG was divided by the upper limit of normal for age (uGAG/ULN), where the ULN for uGAG was obtained from Mayo Clinic. The Efficacy Set is defined as all prospective participants who had a baseline and at least 1 post-baseline efficacy assessment. Number analyzed (n) is the number of participants with data available for analysis for this outcome measure at the end-of-study. 9999 denotes Standard Deviation (SD) was not estimable for a single participant. As pre-specified in the SAP,

descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set in this study.

End point type	Secondary

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Normalized uGAG/ULN				
arithmetic mean (standard deviation)				
Normalized uGAG/ULN: Baseline(n=20)	5.052 (± 1.0376)			
Normalized uGAG/ULN: 12 Months(n=20)	2.315 (± 0.7655)			
Normalized uGAG/ULN: 24 Months(n=19)	2.096 (± 0.7657)			
Normalized uGAG/ULN: 36 Months(n=17)	2.182 (± 0.9339)			
Normalized uGAG/ULN: 48 Months(n=17)	2.063 (± 0.6853)			
Normalized uGAG/ULN: 60 Months(n=7)	2.197 (± 0.8870)			
Normalized uGAG/ULN: 72 Months(n=3)	2.190 (± 1.0945)			
Normalized uGAG/ULN: 84 Months(n=1)	0.830 (± 9999)			
Normalized uGAG/ULN: End of Study(n=21)	2.055 (± 1.1866)			

Statistical analyses

No statistical analyses for this end point

Secondary: Spleen Volume

End point title	Spleen Volume[21]

End point description:

Spleen volume was assessed using abdominal ultrasonography. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analysed is the number of participants with data available for analysis. Number analyzed (n) is the number of participants with data available for analysis at the specified time points. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set.

End point type	Secondary

End point timeframe:

Baseline up to 24 Months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: mL				
arithmetic mean (standard deviation)				
Spleen Volume: Baseline (n=8)	104.593 (± 29.9658)			
Spleen Volume: 24 Months (n=14)	98.427 (± 47.8022)			

Statistical analyses

No statistical analyses for this end point

Secondary: Liver Volume

End point title	Liver Volume[22]

End point description:

Liver volume was assessed using abdominal ultrasonography. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analysed is the number of participants with data available for analysis. Number analyzed (n) is the number of participants with data available for analysis at the specified time points. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set.

End point type	Secondary

End point timeframe:

Baseline up to 24 Months

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: milliliters (mL)				
arithmetic mean (standard deviation)				
Liver Volume: Baseline (n=8)	105.855 (± 16.8925)			
Liver Volume: 24 Months (n=14)	87.811 (± 7.0147)			

Statistical analyses

No statistical analyses for this end point

Secondary: Joint Mobility, as Measured by Joint Range of Motion (JROM) Scores, Including Upper-Limb and Lower-Limb Joint Scores

End point title	Joint Mobility, as Measured by Joint Range of Motion (JROM) Scores, Including Upper-Limb and Lower-Limb Joint Scores[23]

End point description:

Global JROM(% normal range of motion [ROM]) = average (avg.) of 11 ratios multiplied by 100. Ratios are Left/Right means of passive ROM in Shoulder(Flexion [flex]/Extension [ext],Abduction,Internal/External Rotation (I/ER)),Elbow (flex/ext),Wrist (flex/ext),Index Finger(flex/ext [Combined Metacarpophalangeal joint, Proximal interphalangeal joint, Distal interphalangeal joint motion]),Hip(flex/ext,Abduction, I/ER),Knee(flex/ext) & Ankle(Dorsiflexion)divided by normal range(reference: American Academy of Orthopedic Surgeons & American Medical Association).For reported values of upper limb(UL) & lower limb(LL) scores,UL score=avg. of 3 joint scores in UL(shoulder-elbow-wrist) & LL score=avg. of 3 joint scores in LL(hip-knee-ankle).JM(in degrees) was avg. across both sides,divided by normal value & multiplied by 100 to yield a % score. Score >100% occurs when measured JM exceeds normal reference values. Subjects analysed=participants with data available for analysis for this end point at

End point type	Secondary

End point timeframe:

From Baseline to End-of-Study (approximately 9.75 years)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: score on a scale				
arithmetic mean (standard deviation)				
Lower Limb	94.50 (± 31.634)			
Upper Limb	104.24 (± 21.471)			

Statistical analyses

No statistical analyses for this end point

Secondary: Distance Walked, as Measured by Six Minute Walk Test (6MWT)

End point title	Distance Walked, as Measured by Six Minute Walk Test

End point description:

The 6MWT was conducted according to the American Thoracic Society guidelines for the 6MWT in participants who were able to walk. The distance achieved in meters was recorded. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set in this study.

End point type	Secondary

End point timeframe:

From Baseline to End-of-Study (approximately 9.75 years)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: meters				
arithmetic mean (standard deviation)				
End of Study	224.2 (± 178.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life, as Measured by Hunter-Syndrome Functional Outcome in Clinical Understanding Scale (HS-FOCUS)

End point title	Quality of Life, as Measured by Hunter-Syndrome Functional Outcome in Clinical Understanding Scale (HS-FOCUS) [25]

End point description:

The participant's QoL was assessed using the HS-FOCUS (shortened version) questionnaire. The HS-FOCUS (shortened version) questionnaire has 5 function domains (walking/standing, grip/reach, schooling/work, activities, and breathing). The scale of the 5 function domains ranges from 0 to 3, with a 3-score denoting highest disability: 0: with no difficulty;1: with some difficulty; 2: with much difficulty; 3: unable to do; Missing: Does not apply. The response option "Does not apply" is treated as "missing" with no score, the same as if the item had not been completed in the questionnaire. Higher scores indicate worse functional outcomes/greater disability. Efficacy Set was utilized.n=number of participants with data available for the specified categories.As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set in this study.

End point type	Secondary

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: score on a scale				
arithmetic mean (standard deviation)				
End of Study: Walking/Standing (n=21)	1.19 (± 1.042)			
End of Study: Grip/Reach (n=21)	1.83 (± 0.986)			
End of Study: School/Work (n=17)	1.97 (± 1.166)			
End of Study: Activities (n=20)	1.68 (± 1.238)			
End of Study: Breathing (n=21)	1.00 (± 0.929)			

Statistical analyses

No statistical analyses for this end point

Secondary: Impact of Illness on Ability to Function in Daily Life, as Measured by Childhood Health Assessment Questionnaire (CHAQ Parent Report)

End point title	Impact of Illness on Ability to Function in Daily Life, as Measured by Childhood Health Assessment Questionnaire (CHAQ Parent Report)[26]

End point description:

Impact on ability to function in daily life was measured by the CHAQ (Parent Report).CHAQ includes 30 items measured on a scale of 0-3: 0=without any difficulty; 1=with some difficulty; 2=with much difficulty; 3=Unable to do; Missing: Does not apply. It evaluates functional abilities across 8 domains (dressing, hygiene, arising, eating, walking, reach, grip & activities). Result=Disability Index. Highest scoring item in each category determines the score for that category with higher scores= worse functioning/higher disability. Discomfort Index & Health Status Index are measured on separate 15 cm scales. Distance from the left end of the scale to the respondent's mark is measured and multiplied by 0.2 to calculate the score (range 0-3). Discomfort & Health Status Index scores were rescaled to 0-100 scales. Higher scores= greater discomfort/worse health status. Efficacy Set was utilized.

End point type	Secondary

End point timeframe:

Baseline to End-of-Study (approximately 9.75 years)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: score on a scale				
arithmetic mean (standard deviation)				
Disability Index	2.143 (± 0.7334)			
Discomfort Index	16.4 (± 25.57)			
Health Status Index	51.9 (± 33.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Adaptive Behavior, as Measured by the Vineland Adaptive Behavior Scales (VABS II)

End point title	Adaptive Behavior, as Measured by the Vineland Adaptive Behavior Scales (VABS II)[27]

End point description:

Adaptive behavior was assessed using parent/caregiver report on VABS-II, a standardized norm-referenced tool to evaluate adaptive behavior for ages 0-90. VABS-II has 1 composite score(Adaptive Behavior Composite [ABC]),reflecting overall adaptive ability. ABC comprises 4 domain scores(DS) in participants <7years old(Communication(CM),Daily Living Skills(DLS),Socialization(SC),&Motor Skills(MS))& 3 DS in participants ≥7years of age(CM,DLS,&SC).ABC standard score(SS) is derived from domain SS per VABS-II manual(not a simple sum/avg. of reported SS).DS are SS derived from combination of 11 subdomain scores according to VABS-II scoring rules/manual. Scale for ABC & domain SS ranges between 20 & 160.ABC & DS have a normative mean=100, with SD=15 & subdomain scores are normed with a mean=15 & SD=3.Higher scores=better, while lower scores=worse adaptive functioning. Efficacy Set was utilized. Subjects analysed=participants with data available for analysis for this outcome measure at the EOS.

End point type	Secondary

End point timeframe:

Baseline to End-of-Study (approximately 9.75 years)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: score on a scale				
arithmetic mean (standard deviation)				
EOS:Adaptive Behavior Composite Standard Score	48.1 (± 19.07)			
EOS:Communication Domain Standard Score	44.4 (± 15.19)			
EOS:Daily Living Domain Standard Score	51.6 (± 22.53)			
EOS:Motor Skills Domain Standard Score	28.5 (± 13.22)			
EOS: Social Domain Standard Score	53.6 (± 19.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Idursulfase Antibodies (ADA) in Serum

End point title	Anti-Idursulfase Antibodies (ADA) in Serum[28]

End point description:

Blood samples were collected and analyzed for determination of anti-idursulfase antibodies every 6 months in SHP-ELA-401. Analysis of anti-idursulfase antibodies including neutralizing antibodies (NAb) was conducted using validated 3-tier immunoassay methods (screening, confirmatory, and titer). Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. As pre-specified in the SAP, descriptive analysis for this outcome measure was planned only for the reported arm, which included all prospective participants in the Efficacy Set in this study.

End point type	Secondary

End point timeframe:

From Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

End point values	Prospective Set			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
ADA Positive (ADA+)	21			
NAb Positive (NAb+)	15			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline until the end of study (up to approximately 9.75 years)

Adverse event reporting additional description:

The Safety Analysis Set consisted of all prospective participants who received any amount of IP. Adverse Event data only for participants receiving study drug in this study was collected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Prospective Set

Reporting group description:

Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

Serious adverse events	Prospective Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 21 (52.38%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hydrocephalus			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Sudden death			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Chills			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Papilloedema			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			

subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Hypernatraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Prospective Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 21 (100.00%)		
Injury, poisoning and procedural complications			
Skin abrasion			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Procedural pain			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Head injury			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Ear injury			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Thermal burn			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Skin laceration			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	5		
Mitral valve incompetence			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	5		

Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Seizure			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 21 (52.38%)		
occurrences (all)	48		
Gait disturbance			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Eye disorders			
Blepharitis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	13 / 21 (61.90%)		
occurrences (all)	21		
Constipation			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Anal fissure			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Wheezing			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Rhinitis allergic			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	11		
Rhinorrhoea			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	227		
Dermatitis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Dermatitis allergic			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	4		
Dermatitis atopic			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Dermatitis diaper			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Erythema			

subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Rash macular			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	4		
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Infections and infestations			
Carbuncle			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Conjunctivitis			
subjects affected / exposed	5 / 21 (23.81%)		
occurrences (all)	8		
Ear infection			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	3		
Furuncle			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	4 / 21 (19.05%)		
occurrences (all)	8		
COVID-19			
subjects affected / exposed	7 / 21 (33.33%)		
occurrences (all)	8		
Bronchitis			
subjects affected / exposed	11 / 21 (52.38%)		
occurrences (all)	24		
Otitis media			

subjects affected / exposed	2 / 21 (9.52%)			
occurrences (all)	7			
Nasopharyngitis				
subjects affected / exposed	14 / 21 (66.67%)			
occurrences (all)	96			
Influenza				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	3			
Impetigo				
subjects affected / exposed	2 / 21 (9.52%)			
occurrences (all)	2			
Viral infection				
subjects affected / exposed	7 / 21 (33.33%)			
occurrences (all)	11			
Varicella				
subjects affected / exposed	4 / 21 (19.05%)			
occurrences (all)	4			
Urinary tract infection				
subjects affected / exposed	6 / 21 (28.57%)			
occurrences (all)	6			
Upper respiratory tract infection				
subjects affected / exposed	13 / 21 (61.90%)			
occurrences (all)	38			
Tonsillitis				
subjects affected / exposed	5 / 21 (23.81%)			
occurrences (all)	5			
Sinusitis				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	5			
Rhinitis				
subjects affected / exposed	7 / 21 (33.33%)			
occurrences (all)	16			
Pneumonia				
subjects affected / exposed	4 / 21 (19.05%)			
occurrences (all)	5			
Pharyngotonsillitis				

subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	6 / 21 (28.57%)		
occurrences (all)	8		
Parotitis			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		
Otitis media acute			
subjects affected / exposed	3 / 21 (14.29%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	2 / 21 (9.52%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2015	The following changes were made as per Amendment 01: 1) Added section regarding benefit/risk assessment of participants treated with Elaprase in completed clinical studies. 2) Added a section regarding monitoring of burden/risk to participants in this study (SHP-ELA-401). 3) Added a Visit window of 48 hours for completion of study activities for all visits. 4) Added Exclusion criterion regarding hypersensitivity to active substance or excipients for Group 1: Prospective Patient Group. 5) Allowed home infusion of Elaprase by a trained healthcare provider, with Sponsor approval.
05 August 2016	The following changes were made as per Amendment 02: 1) Changed planned enrollment and Primary Growth Analysis. 2) Added CRIM status evaluation and interpretation. 3) Changed study objectives. 4) Changed study outcome measures. 5) Added visit to the study schedule of events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported