Clinical trial results:
A Long-term Study to Evaluate Growth and Development Outcomes in Patients With Infantile-Onset Pompe Disease who are Receiving Alglucosidase Alfa

Summary

EudraCT number	2021-005552-11
Trial protocol	Outside EU/EEA
Global end of trial date	23 November 2021

Results information

Result version number	v1 (current)
This version publication date	04 June 2022
First version publication date	04 June 2022

Trial information

Trial identification

Sponsor protocol code	LTS12869

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00486889
WHO universal trial number (UTN)	U1111-1163-0368
Other trial identifiers	Genzyme study code: AGLU03606

Notes:

Sponsors

Sponsor organisation name	Sanofi
Sponsor organisation address	500 Kendall Street, Cambridge, Massachusetts, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	28 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate long term growth and development of subjects with infantile onset Pompe disease who had begun treatment with alglucosidase alfa before 1 year of age.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of paediatric patients. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2008
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	United States: 12
Worldwide total number of subjects	12
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)	12
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 active sites in United States. A total of 12 subjects were screened from 26-August-2008 to 07-February-2014.

Pre-assignment

Screening details:

All 12 subjects were enrolled and treated in the 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

Arm title	Alglucosidase Alfa

Arm description:

Subjects received alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight as intravenous infusion every 2 weeks and were followed for 10 years or discontinuation from study treatment due to any reason.

Arm type	Experimental
Investigational medicinal product name	Alglucosidase Alfa
Investigational medicinal product code	
Other name	Myozyme®/Lumizyme®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Alglucosidase alfa was administered at 20 mg/kg body weight, every 2 weeks, as an intravenous infusion.

Number of subjects in period 1	Alglucosidase Alfa
Started	12
Completed	1
Not completed	11
Non-compliant	2
Death	3
Withdrawal by Subject	6

Baseline characteristics

Reporting groups	
Reporting group title	Alglucosidase Alfa
Reporting group description:	
Subjects received alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight as intravenous infusion every 2 weeks and were followed for 10 years or discontinuation from study treatment due to any reason.	

Reporting group values	Alglucosidase Alfa	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	11.558		
standard deviation	± 6.226	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	5	5	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	5	5	
White	7	7	
More than one race	0	0	
Unknown or Not Reported	0	0	
Recumbent Height/Length at Baseline Units: centimetre (cm)			
arithmetic mean	72.95		
standard deviation	± 10.24	-	
Weight at Baseline Units: kilograms (kg)			
arithmetic mean	8.42		
standard deviation	± 2.61	-	
Head Circumference at Baseline Units: cm			
arithmetic mean	45.20		
standard deviation	± 3.61	-	

End points

End points reporting groups

Reporting group title	Alglucosidase Alfa

Reporting group description:

Subjects received alglucosidase alfa 20 milligrams per kilogram (mg/kg) body weight as intravenous infusion every 2 weeks and were followed for 10 years or discontinuation from study treatment due to any reason.

Primary: Recumbent Height/Length of Subjects in Centimetres (cm)

End point title	Recumbent Height/Length of Subjects in Centimetres (cm)[1]

End point description:

Analysis was performed on full analysis set (FAS) that included all enrolled subjects who had received at least one infusion (complete or partial) of alglucosidase alfa. No summary analysis was done and subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1:Week52, Subject-2:Week82, Subject-3:Week208, Subject-4:Week208, Subject-5:Week12, Subject-6:Week365, Subject-7:Week64, Subject-8:Week156, Subject-9:Week364, Subject-10:Week52, Subject-11:Week156, Subject-12:Week520

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: cm				
number (not applicable)				
Subject-1 Baseline	80.4			
Subject-1 Week 52	93.8			
Subject-2 Baseline	67.7			
Subject-2 Week 82	91.1			
Subject-3 Baseline	69.1			
Subject-3 Week 208	107.5			
Subject-4 Baseline	67.0			
Subject-4 Week 208	110.0			
Subject-5 Baseline	71.4			
Subject-5 Week 12	71.1			
Subject-6 Baseline	83.5			
Subject-6 Week 365	131.0			
Subject-7 Baseline	57.2			
Subject-7 Week 64	80.5			
Subject-8 Baseline	70.4			
Subject-8 Week 156	110.3			
Subject-9 Baseline	61.0			
Subject-9 Week 364	117.0			
Subject-10 Baseline	76.7			
Subject-10 Week 52	83.8			

Subject-11 Baseline	95.0			
Subject-11 Week 156	115.0			
Subject-12 Baseline	76.0			
Subject-12 Week 520	139.7			

Statistical analyses

No statistical analyses for this end point

Primary: Body Weight of Subjects in Kilograms (kg)

End point title	Body Weight of Subjects in Kilograms (kg)[2]

End point description:

Analysis was performed on FAS population. No summary analysis was done and subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1:Week52, Subject-2:Week82, Subject-3:Week208, Subject-4:Week364, Subject-5:Week12, Subject-6:Week365, Subject-7:Week64, Subject-8:Week 156, Subject-9:Week364, Subject-10:Week52, Subject-11:Week156, Subject-12:Week520

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: kg				
number (not applicable)				
Subject-1 Baseline	10.0			
Subject-1 Week 52	13.8			
Subject-2 Baseline	8.0			
Subject-2 Week 82	13.1			
Subject-3 Baseline	6.5			
Subject-3 Week 208	17.4			
Subject-4 Baseline	6.2			
Subject-4 Week 364	33.3			
Subject-5 Baseline	6.5			
Subject-5 Week 12	6.7			
Subject-6 Baseline	12.8			
Subject-6 Week 365	47.5			
Subject-7 Baseline	5.0			
Subject-7 Week 64	12.2			
Subject-8 Baseline	8.9			
Subject-8 Week 156	20.3			
Subject-9 Baseline	5.2			
Subject-9 Week 364	23.1			
Subject-10 Baseline	10.5			
Subject-10 Week 52	12.8			
Subject-11 Baseline	12.1			

Subject-11 Week 156	35.0			
Subject-12 Baseline	9.3			
Subject-12 Week 520	46.3			

Statistical analyses

No statistical analyses for this end point

Primary: Head Circumference of Subjects in Centimetres (cm)

End point title	Head Circumference of Subjects in Centimetres (cm)[3]

End point description:

Analysis was performed on FAS population. No summary analysis was done and subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1:Week52, Subject-2:Week82, Subject-3:Week208, Subject-4:Week208, Subject-5:Week12, Subject-6:Week365, Subject-7:Week64, Subject-8:Week156, Subject-9:Week312, Subject-10:Week52, Subject-11:Week156, Subject-12:Week468

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: cm				
number (not applicable)				
Subject-1 Baseline	45.3			
Subject-1 Week 52	48.1			
Subject-2 Baseline	44.0			
Subject-2 Week 82	49.3			
Subject-3 Baseline	43.4			
Subject-3 Week 208	52.8			
Subject-4 Baseline	42.6			
Subject-4 Week 208	52.4			
Subject-5 Baseline	44.3			
Subject-5 Week 12	44.5			
Subject-6 Baseline	49.9			
Subject-6 Week 365	56.3			
Subject-7 Baseline	39.6			
Subject-7 Week 64	48.0			
Subject-8 Baseline	50.8			
Subject-8 Week 156	54.0			
Subject-9 Baseline	40.0			
Subject-9 Week 312	52.0			
Subject-10 Baseline	48.5			
Subject-10 Week 52	49.5			
Subject-11 Baseline	48.0			
Subject-11 Week 156	50.8			

Subject-12 Baseline	46.0			
Subject-12 Week 468	56.0			

Statistical analyses

No statistical analyses for this end point

Primary: Motor Subscale of Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) Normative Composite Scores

End point title	Motor Subscale of Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) Normative Composite Scores[4]

End point description:

Bayley-III: Instrument designed to measure developmental functioning of infants and toddlers between ages of 1 and 42 months (age adjustments for prematurity are accommodated with tool). Bayley-III administered up to 42 months of age and provides age specific norm-referenced composite scores for cognitive scales (91 items, score min 55 max 145), language scale (98 items, score min 47 max 153), motor scale (138 items, score min 46 max 154) skills. For all raw scores (for scales), higher scores indicates greater number of developmental skills credited. For norm-based composite scales for motor scale, score of 100 defines average performance of given age group, scores of 85 and 115 are 1 standard deviation (SD) below an above mean, respectively, and scores of 70 and 130 are equivalent to 2 SD from mean. Analysis was performed on FAS population. No summary analysis was one. Subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1: Week 52, Subject-2: Week 83, Subject-3: Week 104, Subject-4: Week 104, Subject-6: Week 78, Subject-7: Week 26, Subject-8: Week 26, Subject-9: Week 156, Subject-10: Week 26, Subject-11: Week 26, Subject-12: Week 104

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
number (not applicable)				
Subject-1 Baseline	94			
Subject-1 Week 52	94			
Subject-2 Baseline	94			
Subject-2 Week 83	91			
Subject-3 Baseline	46			
Subject-3 Week 104	46			
Subject-4 Baseline	46			
Subject-4 Week 104	46			
Subject-5 Baseline	58			
Subject-6 Baseline	79			
Subject-6 Week 78	100			
Subject-7 Baseline	61			
Subject-7 Week 26	46			
Subject-8 Baseline	46			

Subject-8 Week 26	46			
Subject-9 Baseline	46			
Subject-9 Week 156	70			
Subject-10 Baseline	61			
Subject-10 Week 26	73			
Subject-11 Baseline	61			
Subject-11 Week 26	58			
Subject-12 Baseline	55			
Subject-12 Week 104	61			

Statistical analyses

No statistical analyses for this end point

Primary: Gross Motor Function Measure (GMFM-88) Scores

End point title	Gross Motor Function Measure (GMFM-88) Scores[5]

End point description:

GMFM-88 is developed specifically to detect quantitative changes in gross motor function that consists of 88 items organised into 5 dimensions: lying and rolling, sitting, crawling and kneeling, standing, and walking, running and jumping. Each item is scored on a 4-point Likert scale that ranges from 0 to 3, i.e., 0=cannot do; 1=initiated (less than [<] 10 percent [%] of task); 2=partially completed (10 to <100% of task); 3=task completion. The score for each dimension is expressed as percentage of the maximum score for that dimension. Total GMFM-88 score is obtained by adding percentage score for each dimension and dividing the sum by total number of dimensions. Total score ranges from 0 to 100, where higher score indicates better gross motor functions. Analysis was performed on FAS population. No summary analysis was done and subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1: Week 52, Subject-2: Week 52, Subject-3: Week 208, Subject-4: Week 208, Subject-6: Week 359, Subject-7: Week 26, Subject-8: Week 156, Subject-9: Week 312, Subject-11: Week 156, Subject-12: Week 416

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
number (not applicable)				
Subject-1 Baseline	27.98			
Subject-1 Week 52	59.65			
Subject-2 Baseline	32.42			
Subject-2 Week 52	91.52			
Subject-3 Baseline	7.16			
Subject-3 Week 208	2.75			
Subject-4 Baseline	2.18			
Subject-4 Week 208	0.39			
Subject-5 Baseline	12.39			
Subject-6 Baseline	62.22			
Subject-6 Week 359	97.11			

Subject-7 Baseline	8.27			
Subject-7 Week 26	15.83			
Subject-8 Baseline	0.39			
Subject-8 Week 156	0.39			
Subject-9 Baseline	2.35			
Subject-9 Week 312	88.23			
Subject-10 Baseline	34.43			
Subject-11 Baseline	16.71			
Subject-11 Week 156	9.86			
Subject-12 Baseline	21.94			
Subject-12 Week 416	27.39			

Statistical analyses

No statistical analyses for this end point

Primary: Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI) Scaled Scores

End point title	Pompe Pediatric Evaluation of Disability Inventory (Pompe PEDI) Scaled Scores[6]

End point description:

Pompe PEDI:Disease specific version of PEDI developed to assess functional capabilities and performance in children with Pompe disease from 2months up to adolescence.It consists of all items of original PEDI(197-functional skill items in 3domains: self-care;mobility;social function);additional items were added to functional,mobility,functional self-care domains to reflect clinically relevant functional skills.Each domain consists of 2subdomains:functional skills,caregiver assistance. Norm-based scoring is developed for additional items and scoring algorithms for PEDI are adjusted to reflect normative data collected for Pompe PEDI.Scaled scores provide indication of performance of child along continuum of relatively easy to relatively difficult items in particular domain of PEDI.Scores on scale ranges from 0 to 100,where higher score=increased degrees of functional performance. FAS population.No summary analysis was done.Subject wise data were reported at available specified timepoint.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1: Week 52, Subject-2: Week 52, Subject-3: Week 208, Subject-4: Week 208, Subject-6: Week 359, Subject-7: Week 52, Subject-8: Week 156, Subject-9: Week 312, Subject-10: Week 26, Subject-11: Week 156, Subject-12: Week 416

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
number (not applicable)				
Subject-1 Baseline:Functional Skills-Self-Care	40.62			
Subject-1 Week 52:Functional Skills-Self-Care	50.15			
Subject1Baseline:CaregiverAssistance-Self-Care	0			
Subject1Week 52:CaregiverAssistance-Self-Care	20.1			

Subject-1 Baseline:Functional Skills-Mobility	39.68			
Subject-1 Week 52:Functional Skills-Mobility	56.31			
Subject1Baseline:CaregiverAssistance-Mobility	42.7			
Subject1Week 52:CaregiverAssistance-Mobility	47.2			
Subject-1 Baseline:Functional Skills-Social	36.1			
Subject-1 Week 52:Functional Skills-Social	45			
Subject-1 Baseline:CaregiverAssistance-Social	35.9			
Subject-1 Week 52:CaregiverAssistance-Social	31.6			
Subject-2 Baseline:Functional Skills-Self-Care	23.05			
Subject-2 Week 52:Functional Skills-Self-Care	59.79			
Subject2Week 52:CaregiverAssistance-Self-Care	32.3			
Subject-2 Baseline:Functional Skills-Mobility	28.81			
Subject-2 Week 52:Functional Skills-Mobility	62.11			
Subject2 Week 52:CaregiverAssistance-Mobility	72.7			
Subject-2 Week 52:Functional Skills-Social	52			
Subject-3 Baseline:Functional Skills-Self-Care	21.03			
Subject-3 Week 208:Functional Skills-Self-Care	34.24			
Subject3Baseline:CaregiverAssistance-Self-Care	11.6			
Subject3Week 208:CaregiverAssistance-Self-Care	0			
Subject-3 Baseline:Functional Skills-Mobility	15.06			
Subject-3 Week 208:Functional Skills-Mobility	4.53			
Subject3Baseline:CaregiverAssistance-Mobility	0			
Subject3Week 208:CaregiverAssistance-Mobility	0			
Subject-3 Baseline:Functional Skills-Social	21.6			
Subject-3 Week 208:Functional Skills-Social	40.4			
Subject-3 Baseline:CaregiverAssistance-Social	0			
Subject-3 Week 208:CaregiverAssistance-Social	11.3			
Subject-4 Baseline:Functional Skills-Self-Care	4.92			
Subject-4 Week 208:Functional Skills-Self-Care	23.05			
Subject4Baseline:CaregiverAssistance-Self-Care	0			
Subject4Week 208:CaregiverAssistance-Self-Care	0			

Subject-4 Baseline:Functional Skills-Mobility	4.53			
Subject-4 Week 208:Functional Skills-Mobility	0			
Subject4Baseline:CaregiverAssistance-Mobility	0			
Subject4Week 208:CaregiverAssistance-Mobility	0			
Subject-4 Baseline:Functional Skills-Social	14.7			
Subject-4 Week 208:Functional Skills-Social	40.4			
Subject-4 Baseline:CaregiverAssistance-Social	0			
Subject-4 Week 208:CaregiverAssistance-Social	11.3			
Subject-5 Baseline:Functional Skills-Self-Care	36.16			
Subject5Baseline:CaregiverAssistance-Self-Care	0			
Subject-5 Baseline:Functional Skills-Mobility	19.75			
Subject5Baseline:CaregiverAssistance-Mobility	0			
Subject-5 Baseline:Functional Skills-Social	32.9			
Subject-5 Baseline:CaregiverAssistance-Social	0			
Subject-6 Baseline:Functional Skills-Self-Care	45.7			
Subject-6 Week 359:Functional Skills-Self-Care	81.36			
Subject6Baseline:CaregiverAssistance-Self-Care	44.4			
Subject6Week 359:CaregiverAssistance-Self-Care	100			
Subject-6 Baseline:Functional Skills-Mobility	52.44			
Subject-6 Week 359:Functional Skills-Mobility	76.46			
Subject6Baseline:CaregiverAssistance-Mobility	61.8			
Subject6Week 359:CaregiverAssistance-Mobility	100			
Subject-6 Baseline:Functional Skills-Social	40.4			
Subject-6 Week 359:Functional Skills-Social	100			
Subject-6 Baseline:CaregiverAssistance-Social	57.3			
Subject-6 Week 359:CaregiverAssistance-Social	100			
Subject-7 Baseline:Functional Skills-Self-Care	12.7			
Subject-7 Week 52:Functional Skills-Self-Care	33.1			
Subject7Week 52:CaregiverAssistance-Self-Care	11.6			
Subject-7 Baseline:Functional Skills-Mobility	4.53			
Subject-7 Week 52:Functional Skills-Mobility	25.12			

Subject7Baseline:CaregiverAssistance-Mobility	0			
Subject7Week 52:CaregiverAssistance-Mobility	0			
Subject-7 Baseline:Functional Skills-Social	6.6			
Subject-7 Week 52:Functional Skills-Social	27.7			
Subject-7 Baseline:CaregiverAssistance-Social	0			
Subject-7 Week 52:CaregiverAssistance-Social	0			
Subject-8 Baseline:Functional Skills-Self-Care	0.01			
Subject-8 Week 156:Functional Skills-Self-Care	12.7			
Subject8Baseline:CaregiverAssistance-Self-Care	0			
Subject8Week 156:CaregiverAssistance-Self-Care	0			
Subject-8 Baseline:Functional Skills-Mobility	0.01			
Subject-8 Week 156:Functional Skills-Mobility	0			
Subject8Baseline:CaregiverAssistance-Mobility	0			
Subject8Week 156:CaregiverAssistance-Mobility	0			
Subject-8 Baseline:Functional Skills-Social	3.1			
Subject-8 Week 156:Functional Skills-Social	35.1			
Subject-8 Baseline:CaregiverAssistance-Social	0			
Subject-8 Week 156:CaregiverAssistance-Social	20.4			
Subject-9 Baseline:Functional Skills-Self-Care	16.09			
Subject-9 Week 312:Functional Skills-Self-Care	77.1			
Subject9Baseline:CaregiverAssistance-Self-Care	0			
Subject9Week 312:CaregiverAssistance-Self-Care	100			
Subject-9 Baseline:Functional Skills-Mobility	4.53			
Subject-9 Week 312:Functional Skills-Mobility	63.25			
Subject9Baseline:CaregiverAssistance-Mobility	0			
Subject9Week 312:CaregiverAssistance-Mobility	100			
Subject-9 Baseline:Functional Skills-Social	10.5			
Subject-9 Week 312:Functional Skills-Social	73.4			
Subject-9 Baseline:CaregiverAssistance-Social	0			
Subject-9 Week 312:CaregiverAssistance-Social	100			
Subject10 Baseline:Functional Skills-Self-Care	35.25			

Subject-10 Week 26:Functional Skills-Self-Care	49.18			
Subject10Baseline:CaregiverAssistanceSelf-Care	11.6			
Subject10 Week26:CaregiverAssistance-Self-Care	42.8			
Subject-10 Baseline:Functional Skills-Mobility	34.55			
Subject-10 Week 26:Functional Skills-Mobility	49.26			
Subject10Baseline:CaregiverAssistance-Mobility	31.9			
Subject10 Week26:CaregiverAssistance-Mobility	48.5			
Subject-10 Baseline:Functional Skills-Social	31.6			
Subject-10 Week 26:Functional Skills-Social	44.4			
Subject-10 Baseline:CaregiverAssistance-Social	11.3			
Subject-10 Week 26:CaregiverAssistance-Social	50.9			
Subject-11Baseline:Functional Skills-Self-Care	43.58			
Subject-11 Week156:Functional Skills-Self-Care	43			
Subject11Baseline:CaregiverAssistance-SelfCare	25.4			
Subject11Week156:CaregiverAssistance-SelfCare	25.4			
Subject-11 Baseline:Functional Skills-Mobility	28.15			
Subject-11 Week 156:Functional Skills-Mobility	25.93			
Subject11Baseline:CaregiverAssistance-Mobility	0			
Subject11Week 156:CaregiverAssistance-Mobility	11.7			
Subject-11 Baseline:Functional Skills-Social	37			
Subject-11 Week 156:Functional Skills-Social	51.4			
Subject-11 Baseline:CaregiverAssistance-Social	11.3			
Subject-11 Week 156:CaregiverAssistance-Social	39.6			
Subject-12Baseline:Functional Skills-Self-Care	31.8			
Subject-12 Week416:Functional Skills-Self-Care	64.08			
Subject12Baseline:CaregiverAssistance-SelfCare	11.6			
Subject12Week416:CaregiverAssistance-Self-Care	55.7			
Subject-12 Baseline:Functional Skills-Mobility	26.71			
Subject-12 Week 416:Functional Skills-Mobility	48.06			
Subject12Baseline:CaregiverAssistance-Mobility	11.7			
Subject12Week 416:CaregiverAssistance-Mobility	40.9			

Subject-12 Baseline:Functional Skills-Social	37.9			
Subject-12 Week 416:Functional Skills-Social	73.4			
Subject-12 Baseline:CaregiverAssistance-Social	11.3			
Subject-12 Week 416:CaregiverAssistance-Social	63.3			

Statistical analyses

No statistical analyses for this end point

Primary: Cognitive and Language Subscales of Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) Normative Composite Scores

End point title	Cognitive and Language Subscales of Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) Normative Composite Scores[7]

End point description:

Bayley-III: Instrument designed to measure developmental functioning of infants and toddlers between ages of 1 and 42 months (age adjustments for prematurity are accommodated with tool). Bayley-III administered up to 42 months of age and provides age specific norm-referenced composite scores for cognitive scales (91 items, score min 55 max 145), language scale (98 items, score min 47 max 153), motor scale (138 items, score min 46 max 154) skills. For all raw scores (for scales), higher scores indicates greater number of developmental skills credited. For norm-based composite scales for cognitive and language, score of 100 defines average performance of given age group, scores of 85 and 115 are 1 standard deviation (SD) below an above mean, respectively, and scores of 70 and 130 are equivalent to 2 SD from mean. Analysis was performed on FAS population. No summary analysis was one. Subject wise data were reported at available specified timepoints.

End point type	Primary

End point timeframe:

Subjects 1-12: Baseline, Subject-1: Week 52, Subject-2: Week 83, Subject-3: Week 104, Subject-4: Week 104, Subject-6: Week 78, Subject-7: Week 26, Subject-8: Week 26, Subject-9: Week 156, Subject-10: Week 26, Subject-11: Week 26, Subject-12: Week 104

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
number (not applicable)				
Subject-1 Baseline: Cognitive	90			
Subject-1 Week 52: Cognitive	100			
Subject-2 Baseline: Cognitive	85			
Subject-2 Week 83: Cognitive	100			
Subject-3 Baseline: Cognitive	65			
Subject-3 Week 104: Cognitive	55			
Subject-4 Baseline: Cognitive	55			
Subject-4 Week 104: Cognitive	55			
Subject-5 Baseline: Cognitive	60			
Subject-6 Baseline: Cognitive	75			

Subject-6 Week 78: Cognitive	105			
Subject-7 Baseline: Cognitive	65			
Subject-7 Week 26: Cognitive	60			
Subject-8 Baseline: Cognitive	55			
Subject-8 Week 26: Cognitive	55			
Subject-9 Baseline: Cognitive	55			
Subject-9 Week 156: Cognitive	65			
Subject-10 Baseline: Cognitive	85			
Subject-10 Week 26: Cognitive	85			
Subject-11 Baseline: Cognitive	75			
Subject-11 Week 26: Cognitive	75			
Subject-12 Baseline: Cognitive	80			
Subject-12 Week 104: Cognitive	85			
Subject-1 Baseline: Language	103			
Subject-1 Week 52: Language	103			
Subject-2 Baseline: Language	79			
Subject-2 Week 83: Language	103			
Subject-3 Baseline: Language	59			
Subject-3 Week 104: Language	53			
Subject-4 Baseline: Language	47			
Subject-4 Week 104: Language	47			
Subject-5 Baseline: Language	71			
Subject-6 Baseline: Language	71			
Subject-6 Week 78: Language	91			
Subject-7 Baseline: Language	65			
Subject-7 Week 26: Language	50			
Subject-8 Baseline: Language	47			
Subject-8 Week 26: Language	47			
Subject-9 Baseline: Language	53			
Subject-9 Week 156: Language	74			
Subject-10 Baseline: Language	94			
Subject-10 Week 26: Language	86			
Subject-11 Baseline: Language	68			
Subject-11 Week 26: Language	71			
Subject-12 Baseline: Language	86			
Subject-12 Week 104: Language	65			

Statistical analyses

No statistical analyses for this end point

Primary: Brief Intelligence Quotient (IQ) Score of the Leiter International Performance Scale-Revised (Leiter-R)

End point title	Brief Intelligence Quotient (IQ) Score of the Leiter International Performance Scale-Revised (Leiter-R)[8]

End point description:

Leiter Scale:Designed as nonverbal measure of intellectual function, memory and attention for subjects with communication disorders, hearing impairments, motor impairments, certain types of learning disabilities.Leiter-R was administered to subjects after aging out of Bayley-III and before Leiter-3 utilisation.Leiter-R scale consists of 2groups of subtests,Visualisation-Reasoning Battery,Attention-Memory Battery. Subtests in Leiter-R were Figure Ground,Form Completion,Sequential Order,Repeated

Patterns using that ‘Brief Scale IQ’ was scored for estimation of intellectual ability.Brief-IQ scores range is 30-170,where higher scores=higher intelligence.Score of 100 is expected mean standard score at each age interval. 95% children in each age group(based on normative sample) are expected to score within 2 SD of mean.FAS.No summary analysis was done.Subject wise data were reported at available specified timepoint."Number of subjects analysed"=subjects who were evaluated for this endpoint.

End point type	Primary

End point timeframe:

Subject-1: Week 156, Subject-2: Week 156, Subject-3: Week 260, Subject-4: Week 156, Subject-5: Week 208

Notes:

[8] - 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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
number (not applicable)				
Subject-1 Week 156	54			
Subject-2 Week 156	50			
Subject-3 Week 260	100			
Subject-4 Week 156	98			
Subject-5 Week 208	97			

Statistical analyses

No statistical analyses for this end point

Primary: Nonverbal Intelligence Quotient (IQ) Score of Leiter International Performance Scale - 3rd Edition (Leiter-3)

End point title	Nonverbal Intelligence Quotient (IQ) Score of Leiter International Performance Scale - 3rd Edition (Leiter-3)[9]

End point description:

Leiter Scale: Designed as nonverbal measure of intellectual function, memory and attention for subjects with communication disorders, hearing impairments, motor impairments, certain types of learning disabilities. Leiter-3 has 2groups of subtests: cognitive battery, attention/memory battery. Nonverbal intelligence estimates global intellectual ability. 4cognitive battery subtests are: Figure Ground, Form Completion, Sequential Order, Classification-analogies along with 1 optional subset,Visual Patterns. Nonverbal IQ scores range is 30-170,which encompass 'severe delay' to 'extremely high/gifted', higher numbers=higher intelligence. Score of 100 is expected mean standard score at each age interval. 95% children in each age group (based on normative sample) are expected to score within 2 SD of mean. FAS population. No summary analysis was done. Subject wise data were reported at available specified timepoints. "Number of subjects analysed"=subjects who were evaluated for this endpoints.

End point type	Primary

End point timeframe:

Subject-1: Week 156, Subject-2: Week 312, Subject-3: Week 416

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: As the endpoint was descriptive in nature, no statistical analysis was performed.

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: score on a scale				
number (not applicable)				
Subject-1 Week 156	87			
Subject-2 Week 312	78			
Subject-3 Week 416	70			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

Adverse event (AE): any undesirable physical, psychological or behavioral effect experienced by subjects during their participation in an investigational study, in conjunction with use of drug or biologic, whether or not product-related. Any untoward signs or symptoms experienced by subject from time of signing of informed consent until completion of study. Serious AE (SAE): any AE that resulted in any of the following outcomes: death, life-threatening experience, required hospitalisation or prolonged inpatient hospitalisation, persistent or significant disability/incapacity, congenital anomaly, and important medical events. TEAEs: AEs that developed, worsened, or became serious during the treatment-emergent period (defined as the period from first study drug administration until last study assessment). Analysis was performed on FAS population.

End point type	Secondary

End point timeframe:

From Baseline up to 13.25 years

End point values	Alglucosidase Alfa			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: subjects				
TEAEs	11			
TESAEs	9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From administration of first dose of study drug up to 13.25 years

Adverse event reporting additional description:

Reported AEs and deaths are TEAEs that developed, worsened, or became serious during the treatment period (from the first administration of study drug in the study to the last study assessment, i.e., 13.25 years). Analysis was performed on FAS population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Alglucosidase Alfa

Reporting group description:

Subjects received alglucosidase alfa 20 mg/kg body weight as intravenous infusion every 2 weeks and were followed for 10 years or discontinuation from study treatment due to any reason.

Serious adverse events	Alglucosidase Alfa		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Investigations			
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Glycogen Storage Disease Type Ii			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-Respiratory Arrest			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neurological Decompensation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemic Seizure			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchial Secretion Retention			

subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	4 / 12 (33.33%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Apnoea				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercapnia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic Respiratory Failure				

subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Failure				
subjects affected / exposed	5 / 12 (41.67%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 1			
Respiratory Distress				
subjects affected / exposed	4 / 12 (33.33%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Velopharyngeal Incompetence				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Hypertension				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wheezing				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis Contact				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Catheter Site Infection				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				

subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Aspiration				
subjects affected / exposed	3 / 12 (25.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	7 / 12 (58.33%)			
occurrences causally related to treatment / all	0 / 18			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Device Related Sepsis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia Bacterial				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudomonas Infection				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Medical Device Site Infection				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				

subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular Device Infection				
subjects affected / exposed	5 / 12 (41.67%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Respiratory Syncytial Virus Bronchiolitis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acidosis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetes Mellitus				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Feeding Disorder				
subjects affected / exposed	1 / 12 (8.33%)			
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	Alglucosidase Alfa		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Flushing			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
General disorders and administration site conditions			
Unevaluable Event			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Mass			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Catheter Site Rash			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Swelling Face			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	9 / 12 (75.00%)		
occurrences (all)	42		
Pain			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	6		
Vascular Device Occlusion			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Immune system disorders			
Allergy To Animal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Multiple Allergies			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Bronchial Secretion Retention			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Atelectasis			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	7		
Cough			
subjects affected / exposed	8 / 12 (66.67%)		
occurrences (all)	28		
Asthma			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hypoventilation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Aspiration			

subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Increased Upper Airway Secretion				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Dyspnoea				
subjects affected / exposed	3 / 12 (25.00%)			
occurrences (all)	5			
Epistaxis				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Hypercapnia				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	3			
Pleural Effusion				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Nasal Congestion				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Hypoxia				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Respiratory Tract Congestion				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Oropharyngeal Pain				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Productive Cough				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Respiratory Distress				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Pulmonary Oedema				

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory Failure			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Rhonchi			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Sinus Congestion			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Velopharyngeal Incompetence			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	16		
Upper Respiratory Tract Congestion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Wheezing			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Sneezing			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Stridor			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Product issues			
Device Malfunction			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	4		
Investigations			
Clostridium Test Positive			

subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	2			
Electrocardiogram Qrs Complex Prolonged				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Blood Urine Present				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Body Temperature Increased				
subjects affected / exposed	2 / 12 (16.67%)			
occurrences (all)	2			
Audiogram Abnormal				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Electrocardiogram Qt Prolonged				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Pseudomonas Test Positive				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Blood Potassium Decreased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Oxygen Saturation Decreased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	5			
Tympanometry Abnormal				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Urine Output Decreased				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			
Bacterial Test Positive				
subjects affected / exposed	1 / 12 (8.33%)			
occurrences (all)	1			

Haemoglobin Decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Haematocrit Decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Fungal Test Positive			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Electrocardiogram T Wave Inversion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Procedural Pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Anaesthetic Complication			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Stoma Site Haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Joint Dislocation			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	17		
Sinus Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Right Ventricular Hypertrophy			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Focal Dyscognitive Seizures			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypotonia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Encephalopathy			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Areflexia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
White Matter Lesion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Iron Deficiency Anaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
External Ear Disorder			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Deafness Neurosensory			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	4		
Middle Ear Effusion			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Eye disorders			
Papilloedema			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Eyelid Ptosis			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Visual Acuity Reduced			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Eye Discharge			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Chalazion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Eye Swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Mouth Ulceration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Post-Tussive Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Gingival Swelling			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	6		
Dental Caries			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Swollen Tongue			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Salivary Hypersecretion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Teething			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	11		
Skin and subcutaneous tissue disorders			
Dermatitis Diaper			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	5		
Decubitus Ulcer			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Angioedema			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Dry Skin			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hair Growth Abnormal			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Papule			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Erythema			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	20		
Rash Papular			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin Disorder			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	19		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	3		
Extremity Contracture			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Pain In Extremity			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Scoliosis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Spinal Deformity			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Foot Deformity			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Muscular Weakness			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Myopathy			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Joint Contracture			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Infections and infestations			
Ear Infection			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Rash Pustular			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Respiratory Tract Infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Fungal Skin Infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pharyngitis Streptococcal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	9		
Oral Candidiasis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		

Influenza			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Otitis Media			
subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	11		
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Viral Pharyngitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	13		
Vulvovaginal Candidiasis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Urinary Tract Infection			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Feeding Disorder			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hypoglycaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	5		
Hypophosphataemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hyponatraemia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Diabetes Mellitus			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2007	•Updated Study Manager and Medical Monitor titles•Expanded types of data collected from this long-term study•Added urinary oligosaccharides analysis as exploratory objective.•Added cross-reacting immunologic material (CRIM) status and T cells analysis for research purposes only•New citation added that was not available at time original protocol•Study design:Added "multinational" to clarify that study was multinational•Clarified independent data safety monitoring board (DSMB) would review safety information•Subject population and selection:Clarified that only subjects with Pompe disease might participate•Subject withdrawal:Clarified that in this 10-year study, subject might be lost to follow-up before EOS period•"Package insert" was changed to "full prescribing information"•Revised text to indicate that actual infusion schedule was to be determined by investigator•Revised section title to reflect exploratory variables•Updated that non-baseline assessments had window of +/-60 days; immunoglobulin G (IgG collection-Baseline and Months 3,6,9,12,15,18,21,24, annually thereafter;vital signs-monitored at Baseline and at end of each infusion;•Modified Leiter-R scale assessment -not performed at Baseline;•Length, height, weight measurements description were made consistent;•Clarified procedures for CRIM, T cell assays, blood collection,vital signs,infusions•Revised schedule for new T cell assay at Months 1,3,6,9,12,15,18,21,24 only•Table reflected new exploratory assessments.•Vital signs-monitored at end of each infusion at Months 6,12,18,24, annually thereafter•Serum IgG,vital signs assessments were updated to be performed at Month 12 and every 12 months thereafter (or on study withdrawal)•Procedures for urinary oligosaccharides, CRIM and T cell assays were described•Revised details of hearing test procedures•Vital signs-recorded if subject had recurrent IAR•Clarified circumstances to report SAEs to regulatory agencies•Updated definition of Center for Disease Control (CDC).
18 October 2007	•Study duration-'over a 10-year period' was added.•Enrollment period was not limited prospectively to allow enrollment of sufficient numbers of subjects.•Study was opened up to allow subjects who had received Myozyme before their first birthday to bolster enrollment. Investigational 2000 Litre Myozyme was provided by Sponsor until approval of this product.•Frequency of efficacy assessments was based on subject's age or time in study, rather than yearly.•Bayley-III test-measured cognitive language and motor development,each subscale of Bayley-III was assessed until subject reached 42months of age or maximum score for that subscale, if earlier.•Cognition-assessed by Leiter-R concurrently with last administration of Bayley-III cognitive subscale and annually thereafter.•GMFM-66 and Pompe PEDI was performed.•Magnetic resonance imaging (MRI) assessment-performed at discretion of Investigator.•T cell assessment-removed.•Clarified appropriate hearing tests for subjects of various ages.•Added gross motor ability estimator (GMAE) for gross motor function measure (GMFM) scores analysis.•Updated current investigator's brochure with risks associated with Myozyme use.•Clarified this was a study and not sub-registry program.•Updated definition of "ongoing" in context of AEs continuing at time subject withdrew or study completion.•Concomitant therapies-not recorded.•Vital signs-recorded before and at end of each infusion.•Medical/surgical history-added to allow collection of retrospective AEs.•IgG collection assessment-performed every 3 months and every 12months and urine oligosaccharide assessment-performed every 6months and every 12months, both with delimiters of Study Month specified.•Physical Growth-performed by same individual at each subject visit (as far as possible).•Leiter-R wording revised to emphasize its role as measure of intellectual ability.•Neuroimaging assessments-performed by MRI at discretion of Investigator.•Clarified requirements to follow and report AEs/SAEs.

20 October 2009	•Tradename "Myozyme" was replaced globally with nonproprietary name "alglucosidase alfa" that applied regardless of manufacturing scale.•Urine oligosaccharides indicated specific oligomer measured in assay.•GMFM-66 was replaced by GMFM-88.•Updated department name with exception of pharmacovigilancesafety@genzyme.com e-mail address;•Added date of Amendment 3 on title page.•Change in responsible study personnel and to include Medical Monitor signature on cover page to comply with global standards.•Reflected that cap on number of sites that might participate was not needed; •Clarified that subjects must receive their first infusion of Myozyme before 1 year of age to be included in study;•Expanded the pool of eligible subjects;•Emphasize that subjects participated in study were treated with Myozyme commercially outside of protocol, and provided study requirements for investigators who might chosen to implement home infusions to treat subject participating instudy;•Provideddetailed example of when inhibitory antibody testing was clinically indicated.•Allowed acid alpha-glucosidase(GAA) mutation analysis, beyond documentation of diagnosis of Pompe disease based on deficient endogenous GAA activity or GAA mutation analysis, for use in interpreting the outcomes of the study.•Safety information on anaphylaxis and allergic reactions reflected changes in current Myozyme (alglucosidase alfa) label was added.•Added new safety information from the current label.•Highlighted important information on risks.•Subjects received commercial Myozyme during study; hence,pharmacy manual does not apply.•Concomitant therapies were collected along with concomitant medications for duration of study.•Only 4 subtests were administered estimated brief IQ.•Visual screening-clinically significant changes in vision as compared to Baseline results were noted as AEs.•Relevant changes were made within schedule of assessment and its footnotes.•Updated list to include new
28 September 2010	•Updated department name; •Updated Section 9.1 Schedule of Assessments; •For subjects on home infusion, some assessments might be allowed to be conducted in the home setting and were not required to be conducted in the clinic.
15 September 2011	•Updated cover page and protocol synopsis; •Exclusion criteria: clarifiedy that subjects cannot be enrolled in any clinical trial utilizing an investigational therapy as that could interfere with efficacy or safety of Myozyme and skew observational results of the AGLU03606 study. •Treatment administration-Myozyme would be administered at 20 mg/kg body weight as prescribed by the treating physician every 2 weeks as an intravenous infusion. •Serum IgE antibody testing-in the event that subject experienced a moderate, severe, or recurrent IAR, the subject should return to the study centre at least 72 hours after the infusion ends.
06 February 2013	• Changed "Global Subject Safety and Risk Management" to "Global Pharmacovigilance and Epidemiology" to reflect recent department name change. • Title Page: Added date of Protocol Amendment 6; •Updated Study Manager, Medical Monitor and Statistician information; • Updated protocol synopsis; •1) Treatments administered was updated with 'If clinically feasible, all subjects would continue at the same dose throughout the study. Any modification to the dose and/or frequency of dosing is not permitted unless it is due to disease progression or to an AE, in which case it is not a protocol deviation, but the Investigator must consult with the Sponsor's Medical Monitor and Global Safety Officer in the event of a dose change. The dosing change and the reasons for it will be documented on the appropriate CRFs.' 2) •Complement Activation Testing and Serum Tryptase Testing- plasma sample should be drawn within 1 to 3 hours of the event for complement activation testing, when clinically indicated.

02 December 2014	•Change to the inclusion/exclusion criteria, •Addition of Leiter-3, •Updated potential risks and potential benefits •Updated product name as 'Myozyme®/Lumizyme® (alglucosidase alfa). •Updated cognitive development with change in Brief IQ score of the Leiter International Performance Scale – Revised (Leiter-R) and/or the change in the Nonverbal IQ score of the Leiter International Performance Scale – 3rd Edition (Leiter-3) (starting at the final assessment of the Bayley-III before 42 months of age). •Updated information within Summary of Potential Risks and Summary of Potential Benefits. •GAA mutation analysis was to be conducted only if written results were not available. •Updated infusion-associated reactions (IAR) definition as AEs that occur during the infusion or within up to 24 hours after the start of infusion and were considered as related or possibly related to the ERT by the Investigator or the Sponsor. •An event occurring >=24 hours after the start of an infusion might be judged an IAR if a delayed reaction was considered possible by Investigator or Sponsor. •Copies of score sheets for cognitive function and motor development assessments would be sent to central Genzyme representative for centralised scoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No summary analysis was done and subject wise data were reported at available specified timepoints. Reporting of subject numbers is per-endpoint and not consistent between assessments to maintain subject's privacy.

Notes: