Clinical trial results:
An open, non-controlled, parallel, ascending multiple-dose, multicenter study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of SOBI003 in pediatric MPS IIIA patients

Summary

EudraCT number	2017-002806-10
Trial protocol	DE NL
Global end of trial date	25 October 2019

Results information

Result version number	v1 (current)
This version publication date	22 April 2023
First version publication date	22 April 2023

Trial information

Trial identification

Sponsor protocol code	SOBI003-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03423186
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Swedish Orphan Biovitrum AB
Sponsor organisation address	Tomtebodavägen 23A, Stockholm, Sweden, 11276
Public contact	Anders Bröijersen MD, Medical Information, Swedish Orphan Biovitrum AB, +46 86972000, medical.info@sobi.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002380-PIP01-18
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2019
Global end of trial reached?	Yes
Global end of trial date	25 October 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety and tolerability of SOBI003 at different dose levels.

Protection of trial subjects:

This study was conducted in compliance with the protocol, the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP), applicable regulatory requirements, and in accordance with the latest revision of the Ethical Principles for Medical Research Involving Human Subjects (the Declaration of Helsinki).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2018
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	Turkey: 3
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	6
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	2
Children (2-11 years)	4
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 in 3 sites from 19 June, 2018 to 25 October, 2019.

Pre-assignment

Screening details:

A total of 6 participants were enrolled and treated with Sobi003 in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental: SOBI003 3 mg/kg

Arm description:

Subject received a dose level of SOBI003 3 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	SOBI003
Investigational medicinal product code	
Other name	Modified recombinant human sulphamidase
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subject received SOBI003 3 mg/kg IV infusion once weekly over a period of time of 4 hours using a central access venous port.

Arm title	Experimental: SOBI003 10 mg/kg

Arm description:

Subject received a dose level of SOBI003 10 mg/kg IV infusion once weekly for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	SOBI003
Investigational medicinal product code	
Other name	Modified recombinant human sulphamidase
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subject received SOBI003 10 mg/kg IV infusion once weekly over a period of time of 4 hours using a central access venous port.

Number of subjects in period 1	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg
Started	3	3
Completed	3	3

Baseline characteristics

Reporting groups	
Reporting group title	Experimental: SOBI003 3 mg/kg
Reporting group description:	
Subject received a dose level of SOBI003 3 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly for 24 weeks.	
Reporting group title	Experimental: SOBI003 10 mg/kg
Reporting group description:	
Subject received a dose level of SOBI003 10 mg/kg IV infusion once weekly for 24 weeks.	

Reporting group values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg	Total
Number of subjects	3	3	6
Age categorical Units: Subjects			
Age continuous			
Age at day of first infusion (months).			
Units: months			
arithmetic mean	46.3	29.0	
standard deviation	± 24.2	± 12.2	-
Gender categorical Units: Subjects			
Female	1	1	2
Male	2	2	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	6
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	3	6
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Experimental: SOBI003 3 mg/kg
Reporting group description:	
Subject received a dose level of SOBI003 3 milligrams per kilogram (mg/kg) intravenous (IV) infusion once weekly for 24 weeks.	
Reporting group title	Experimental: SOBI003 10 mg/kg
Reporting group description:	
Subject received a dose level of SOBI003 10 mg/kg IV infusion once weekly for 24 weeks.	

Primary: Safety as Measured by Adverse Events Frequencies (by Type and Severity)

End point title	Safety as Measured by Adverse Events Frequencies (by Type and Severity)[1]
End point description:	
Number of adverse events, by type and severity, from start of infusion up to 24 weeks. Safety analysis set was the primary analysis set and consists of all subjects who received at least 1 dose of IMP.	
End point type	Primary
End point timeframe:	
From start of first infusion up to Week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics were performed; no inferential statistical analyses were performed.

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Number of events				
number (not applicable)				
Any adverse event	53	128		
Any non-treatment emergent serious adverse event	0	1		
Any treatment emergent adverse event (TEAE)	53	124		
Any non-serious TEAE	52	121		
Any serious TEAE	1	3		
Any serious drug-related TEAE	0	0		
Any TEAE leading to study or treatment withdrawal	0	0		
Drug-related TEAE leading to treatment withdrawal	0	0		
Any serious TEAE leading to treatment withdrawal	0	0		
Any TEAE leading to death	0	0		
Any Infusion related Reaction	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: The Observed Serum Concentration Immediately Before the Start of Infusion of SOBI003

End point title	The Observed Serum Concentration Immediately Before the Start of Infusion of SOBI003

End point description:

The observed serum concentration immediately before the start of infusion of SOBI003 (CPre-dose).The table report number of available pharmacokinetic (PK) samples. Here, "n" signifies to subjects who are evaluable at given timepoints and "-99999" was used as a space filler which states that median or minimum or maximum data was not computed as the value was less than lower limit of quantification (LLOQ). PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or Cerebrospinal fluid (CSF) concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 8, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: nanogram per milliliter (ng/mL)				
median (full range (min-max))				
At Week 1 (n=3,3)	-99999 (-99999 to 99999)	-99999 (-99999 to 99999)		
At week 2(n=3,3)	58.4 (33.0 to 62.2)	109.0 (85.7 to 137.0)		
At Week 3 (n=2,2)	68.85 (55.2 to 82.5)	135.5 (114.0 to 157.0)		
At Week 4 (n=3,3)	71.4 (-99999 to 97.7)	49.8 (31.4 to 603.0)		
At Week 8 (n=3,2)	-99999 (-99999 to 27.0)	25.5 (-99999 to 51)		
At Week 12 (n=2,3)	33.75 (26.6 to 40.9)	-99999 (-99999 to 10.3)		
At Week 24 (n=3,3)	-99999 (-99999 to 99999)	16.4 (-99999 to 90.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Observed Serum Concentration at the End of Infusion of SOBI003

End point title	The Observed Serum Concentration at the End of Infusion of SOBI003

End point description:

The observed serum concentration at the end of infusion of SOBI003 (CEnd of inf). The table report number of available PK samples. Here, "n" signifies to subjects who are evaluable at given timepoints. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 8, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng/mL				
arithmetic mean (full range (min-max))				
At Week 1 (n=3,3)	33800 (29500 to 36400)	87500 (75300 to 114000)		
At Week 2 (n=2,2)	34950 (33300 to 36600)	108200 (99400 to 117000)		
At Week 3 (n=2,2)	36750 (31300 to 42200)	82700 (73300 to 92100)		
At Week 4 (n=3,3)	35700 (16200 to 36600)	77400 (71800 to 102000)		
At Week 8 (n=3,3)	20800 (65.5 to 36600)	50900 (33300 to 68600)		
At Week 12 (n=3,3)	30500 (32.5 to 36700)	56900 (56100 to 71000)		
At Week 24 (n=3,3)	17500 (47.5 to 35400)	93500 (69700 to 103000)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Time of the End of the Infusion of SOBI003

End point title	The Time of the End of the Infusion of SOBI003

End point description:

The time of the end of infusion of SOBI003 (tEnd of inf). The table report number of available PK samples. Here, "n" signifies to subjects who are evaluable at given timepoints. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 8, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Hours				
median (full range (min-max))				
At Week 1 (n=3,3)	4.57 (4.27 to 4.62)	4.33 (4.02 to 4.33)		
At Week 2 (n=2,2)	4.565 (4.30 to 4.83)	4.245 (4.07 to 4.42)		
At Week 3 (n=2,2)	4.28 (4.13 to 4.43)	4.1 (3.98 to 4.22)		
At Week 4 (n=3,3)	4.28 (4.05 to 4.50)	4.42 (4.27 to 4.90)		
At Week 8 (n=3,2)	4.85 (4.42 to 6.58)	8.17 (8.17 to 8.17)		
At Week 12 (n=3,3)	4.23 (4.10 to 6.42)	6.83 (5.08 to 7.03)		
At Week 24 (n=3,3)	4.45 (4.08 to 4.53)	4.75 (4.47 to 5.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Maximum Observed Serum Concentration of SOBI003

End point title	The Maximum Observed Serum Concentration of SOBI003

End point description:

The Maximum Observed Serum Concentration of SOBI003 (Cmax). Samples were taken centrally and/or peripherally. The table report number of available PK samples. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

0, 1, 2, 3, 4, 6, 8, 12, 24, 48, 72, 96 hours post-dose on Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng/mL				
median (full range (min-max))				
At Week 1	33800 (29500 to 36400)	87500 (75300 to 114000)		
At Week 4	35700 (16200 to 36600)	77400 (71800 to 102000)		
At Week 12	30500 (32.5 to 36700)	56900 (56100 to 71000)		
At Week 24	17500 (47.5 to 35400)	93500 (69700 to 103000)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Time at Which the Maximum Serum Concentration of SOBI003 is Observed

End point title	The Time at Which the Maximum Serum Concentration of SOBI003 is Observed

End point description:

The time after start of infusion at which the maximum serum concentration is observed (tmax). The table report number of available PK samples. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: hours				
median (full range (min-max))				
At Week 1	4.57 (4.27 to 4.62)	4.33 (4.02 to 4.33)		
At Week 4	4.28 (4.05 to 4.50)	4.42 (4.27 to 4.90)		
At Week 12	4.23 (4.10 to 6.42)	6.83 (5.08 to 7.03)		
At Week 24	4.45 (4.08 to 4.53)	4.75 (4.47 to 5.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Minimum Observed Serum Concentration of SOBI003

End point title	The Minimum Observed Serum Concentration of SOBI003

End point description:

The minimum observed serum concentration of SOBI003 (CTrough). The table report number of available PK samples. Here "-99999 and 999" was used as a space filler which states that median or minimum or maximum data was not computed as the value was less than LLOQ. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003

serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: ng/ml				
median (full range (min-max))				
At Week 1	-99999 (-99999 to 2010)	-99999 (-99999 to 99999)		
At Week 4	28.9 (-99999 to 61.3)	115 (20.8 to 7730)		
At Week 12	26.2 (17.0 to 32.5)	-99999 (-99999 to 29.7)		
At Week 24	44.8 (-99999 to 47.5)	999 (14.6 to 9010)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL)

End point title	Clearance (CL)

End point description:

Clearance of SOBI003. Here,"number of subjects analysed" signifies subjects who were evaluable for this endpoint. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: milliliter per hour perkilogram(mL/h/kg)				
median (full range (min-max))				

At Week 1	10.4 (9.7 to 11.1)	12.8 (12.0 to 13.6)		
At Week 4	8.1 (8.0 to 8.2)	12.75 (12.4 to 13.1)		
At Week 12	9.5 (7.8 to 11.2)	13.45 (12.1 to 14.8)		
At Week 24	19.5 (10.2 to 28.8)	10.4 (9.9 to 10.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-time Curve From Time 0 to 168 Hours

End point title	Area Under the Serum Concentration-time Curve From Time 0 to 168 Hours

End point description:

Area under the serum concentration-time curve from time 0 to 168 hours (AUC 0-168h).The table report number of available PK samples. Here, "n" signifies to subjects who were evaluable for this endpoint. PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

0,1, 2, 3, 4, 6, 8, 12, 24, 48, 72, 96, 120, 144, 168 hours post-dose on Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Hour*nanogram per milliliter (h*ng/mL)				
median (full range (min-max))				
At Week 1 (n=2,3)	290044.5 (275152 to 304937)	834411 (737687 to 2492658)		
At Week 4 (n=2,2)	369915.5 (365435 to 374396)	789106.5 (761760 to 816453)		
At Week 12 (n=2,2)	324999.5 (267722 to 382277)	749864 (674188 to 828540)		
At Week 24 (n=2,2)	198973 (104009 to 293937)	961516.5 (915941 to 1007092)		

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life

End point title	Half-life

End point description:

The half-life of SOBI003 in serum (T1/2). The table report number of available PK samples. Here, "number of subjects analysed" signifies subjects who were evaluable for this endpoint. PK analysis set consists of all participants where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Hours				
median (full range (min-max))				
At Week 1	19.8 (5.4 to 34.2)	22.75 (5.8 to 39.7)		
At Week 4	34.3 (29.7 to 38.9)	7.65 (6.3 to 9.0)		
At Week 12	40.95 (34.4 to 47.5)	10.75 (8.8 to 12.7)		
At Week 24	20.85 (9.3 to 32.4)	15.95 (6.0 to 25.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: SOBI003 Concentration in Cerebrospinal Fluid

End point title	SOBI003 Concentration in Cerebrospinal Fluid

End point description:

SOBI003 concentration in cerebrospinal fluid. Here, "n" signifies to subjects who are evaluable at given timepoints and "-99999" was used as a space filler which states that median or minimum or maximum data was not computed as the value was less than LLOQ. PK analysis set consists of all participants where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Milligram per liter (mg/L)				
median (full range (min-max))				
At Week 12 (n=3,1)	-99999 (-99999 to 99999)	17.8 (17.8 to 17.8)		
At Week 24 (n=3,3)	-99999 (-99999 to 99999)	47.2 (12.2 to 64.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Having Anti-drug Antibodies in Serum

End point title	Number of Subjects Having Anti-drug Antibodies in Serum

End point description:

Number of subjects in each dose group having anti-drug antibodies in serum. Immunogenicity set consists of those subjects in the safety analysis set who had sufficient blood samples taken for ADA testing at Baseline and at least 1 post-dose time point.

End point type	Secondary

End point timeframe:

Weeks 2, 4, 8, 12 and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Subjects				
At Week 2	1	1		
At Week 4	2	3		
At Week 8	3	3		
At Week 12	3	3		
At Week 24	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Having Anti-drug Antibodies in Cerebrospinal Fluid

End point title	Percentage of Subjects Having Anti-drug Antibodies in

	Cerebrospinal Fluid

End point description:

Percentage of subjects having anti-drug antibodies in cerebrospinal fluid. Immunogenicity set consists of those subjects in the safety analysis set who had sufficient blood samples taken for ADA testing at Baseline and at least 1 post-dose time point.

End point type	Secondary

End point timeframe:

Weeks 12 and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Percentage of Subjects				
number (not applicable)				
At Week 12	33.3	66.7		
At Week 24	66.7	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heparan Sulfate Levels in Cerebrospinal Fluid

End point title	Change From Baseline in Heparan Sulfate Levels in Cerebrospinal Fluid

End point description:

Change from baseline, in percent, of Heparan Sulfate levels in cerebrospinal fluid. Safety analysis set was the primary analysis set and consists of all subjects who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: percent change				
median (full range (min-max))				
At Week 12	-5.4 (-33.0 to 7.7)	-52.8 (-64.6 to -28.4)		
At Week 24	-17.5 (-26.5 to 14.7)	-50.9 (-59.4 to 21.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heparan Sulfate Levels in Serum

End point title	Change From Baseline in Heparan Sulfate Levels in Serum

End point description:

Change from baseline in Heparan sulfate levels in serum. Safety analysis set was the primary analysis set and consists of all subjects who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Weeks 2, 3, 4, 8, 12 and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: mg/L				
median (full range (min-max))				
At Week 2	-1.8070 (-1.891 to -0.660)	-1.7460 (-3.409 to -1.705)		
At Week 3	-1.22 (-2.006 to -0.220)	-1.9190 (-3.576 to -1.856)		
At Week 4	-1.9040 (-2.083 to -1.850)	-1.9229 (-3.770 to -1.268)		
At Week 8	-2.1030 (-2.210 to -1.615)	-1.8290 (-3.730 to -1.772)		
At Week 12	-1.8170 (-2.131 to -1.597)	-1.8340 (-3.729 to -1.722)		
At Week 24	-1.7480 (-2.207 to -1.657)	-1.8310 (-3.722 to -1.818)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Heparan Sulfate Levels in Urine

End point title	Change From Baseline in Heparan Sulfate Levels in Urine

End point description:

Change from baseline in Heparan sulfate levels in urine. Safety analysis set was the primary analysis set and consists of all subjects who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Weeks 2, 3, 4, 8, 12 and 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: g/mol				
median (full range (min-max))				
At Week 2	-421.98 (-557.33 to -258.1)	-695.9 (-698.03 to -348.05)		
At Week 3	-494.67 (-592.1 to -390.0)	-597.4 (-618.8 to -309.3)		
At Week 4	-498.53 (-575.8 to -422.79)	-503.465 (-672.17 to -334.76)		
At Week 8	-474.7 (-542.22 to -460.95)	-666.81 (-672.42 to -341.70)		
At Week 12	-534.1 (-540.71 to -442.33)	-640.2 (-668.83 to -326.13)		
At Week 24	-421.98 (-557.33 to -258.1)	-695.9 (-698.03 to -348.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Neurocognitive Development Quotient

End point title	Change From Baseline in Neurocognitive Development Quotient

End point description:

Quotient between age equivalent score and age, 0 - 100, where high values are desirable. The age equivalent score represents the age of the typical and normal individual who would achieve the same result as the one who was tested.

The age equivalent scores are assessed by the Bayley Scales of Infant and Toddler Development®, third edition cognitive subtest or the Kaufman Assessment Battery for Children, Second edition.

The Bayley Scales of Infant and Toddler Development-Third Edition is an individually administered test designed to assess developmental functioning of infants and toddlers. The Bayley-III assesses development in five areas: cognitive, language, motor, social-emotional, and adaptive behavior.

The Kaufman Assessment Battery for Children (K-ABC) is a clinical instrument for assessing cognitive development.

Full analysis set consists of all subjects who had a baseline assessment and at least 1 post-baseline assessment of any secondary or exploratory assessment.

End point type	Secondary

End point timeframe:

Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Unitless				
median (full range (min-max))				
At Week 24	-8.7 (-11.2 to -4.9)	-15.68 (-53.3 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Age-equivalence Score

End point title	Change From Baseline in Age-equivalence Score

End point description:

The age equivalent score represents the age in months of the typical and normal individual who would achieve the same result as the one who was tested.

The age equivalent scores are assessed by the Bayley Scales of Infant and Toddler Development®, third edition cognitive subtest or the Kaufman Assessment Battery for Children, Second edition.

The Bayley Scales of Infant and Toddler Development-Third Edition is an individually administered test designed to assess developmental functioning of infants and toddlers. The Bayley-III assesses development in five areas: cognitive, language, motor, social-emotional, and adaptive behavior.

The Kaufman Assessment Battery for Children (K-ABC) is a clinical instrument for assessing cognitive development.

PK analysis set consists of all subjects where at least 1 SOBI003 dose had been administered correctly and where SOBI003 serum or CSF concentration data was available without any protocol deviation interfering with these results.

End point type	Secondary

End point timeframe:

Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Months				
median (full range (min-max))				
At Week 24	-1.0 (-4 to 1)	-3.0 (-6 to 6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Age-equivalence Score as Assessed by VABS-II

End point title	Change From Baseline in Age-equivalence Score as Assessed by VABS-II

End point description:

The age equivalent score represents the age in months of the typical and normal individual who would achieve the same result as the one who was tested.

The age equivalent scores are assessed by Vineland™ Adaptive Behavior Scales, Expanded Interview Form, Second edition (VABS-II). The Vineland is designed to measure adaptive behavior of individuals from birth to age 90.

The Vineland-II contains 5 domains each with 2-3 subdomains. The main domains are Communication, Daily Living Skills, Socialization, Motor Skills, and Maladaptive Behavior. Full analysis set consists of all subjects who had a baseline assessment and at least 1 post-baseline assessment of any secondary or exploratory assessment.

End point type	Secondary

End point timeframe:

Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: Months				
median (full range (min-max))				
At week 24	1.0 (-9 to 2)	0.0 (-3 to 24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Gray Matter Volume

End point title	Change From Baseline in Gray Matter Volume

End point description:

Grey matter contains most of the brain's neuronal cell bodies. The grey matter includes regions of the brain involved in muscle control, and sensory perception such as seeing and hearing, memory, emotions, speech, decision making, and self-control. The gray matter volume will be measured by volumetric magnetic resonance imaging (MRI). Full analysis set consists of all subjects who had a baseline assessment and at least 1 post-baseline assessment of any secondary or exploratory assessment.

End point type	Secondary

End point timeframe:

Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	3		
Units: milliliter (mL)				
median (full range (min-max))				
At Week 24	10.858 (-6.22 to 42.27)	39.129 (-33.28 to 111.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pediatric Quality of Life Inventory (PedsQL™) Total Score

End point title	Change From Baseline in Pediatric Quality of Life Inventory (PedsQL™) Total Score

End point description:

Pediatric Quality of Life Inventory (PedsQL™) is a modular approach to measuring health-related quality of life (HRQOL) in healthy children and adolescents and those with acute and chronic health conditions. Lower scores indicate better functioning. Min score = 0, and max score = 144. Here,"number of subjects analysed" signifies subjects who were evaluable for this endpoint.Full analysis set consists of all subjects who had a baseline assessment and at least 1 post-baseline assessment of any secondary or exploratory assessment.

End point type	Secondary

End point timeframe:

Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Units on a scale				
arithmetic mean (standard deviation)				
At week 24	-9.3 (± 15.52)	-7.3 (± 14.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PedsQL™ Family Impact Module Total Score

End point title	Change From Baseline in PedsQL™ Family Impact Module Total Score

End point description:

Pediatric Quality of Life Inventory (PedsQL™) is a modular approach to measuring health-related quality of life in healthy children and adolescents and those with acute and chronic health conditions. The measure includes a scale, from where the categorical score "4", "3", "2", "1", and "0" was reversed and linearly transformed to a 0-100 scale to 4=0, 3=25, 2=50, 1=75 and 0=100, where 100 = minimum and 0 = maximum. The Total Score is the sum of all 36 items in the test divided by the number of items answered. Higher scores indicate better functioning. Here,"number of subjects analysed" signifies subjects who were evaluable for this endpoint. Full analysis set consists of all subjects who had a baseline assessment and at least 1 post-baseline assessment of any secondary or exploratory assessment.

End point type	Secondary

End point timeframe:

At Week 24

End point values	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: Units on a scale				
arithmetic mean (standard deviation)				
At Week 24	-9.77 (± 19.05)	1.3 (± 3.11)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period for recording adverse events, including Serious Adverse Events (SAEs), began upon receiving the first dose of SOBI003 and ended at completion of the week 24 visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Experimental: SOBI003 3 mg/kg

Reporting group description:

Subject received a dose level of SOBI003 3 mg/kg IV infusion once weekly for 24 weeks.

Reporting group title	Experimental: SOBI003 10 mg/kg

Reporting group description:

Subject received a dose level of SOBI003 10 mg/kg IV infusion once weekly for 24 weeks.

Serious adverse events	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infestations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Experimental: SOBI003 3 mg/kg	Experimental: SOBI003 10 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	
Vascular disorders			
Hyperaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Medical device site haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Application site irritation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 3 (100.00%)	
occurrences (all)	0	5	
Social circumstances			
Vascular device user			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Restlessness			

subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	
occurrences (all)	0	3	
Product issues			
Device damage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Device malfunction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Device dislocation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	3	
Blood fibrinogen increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Blood pressure diastolic increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood pressure systolic increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
CSF glucose decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
CSF protein increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Eosinophil count increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Haemoglobin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Monocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Neutrophil count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Oxygen saturation decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	5	
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Red blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Vascular access site occlusion			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	
occurrences (all)	4	5	
Arthropod bite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Contusion			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Lip injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Skin abrasion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vascular access complication			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	
occurrences (all)	13	15	
Aortic valve thickening			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	
occurrences (all)	1	4	
Clonus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	
occurrences (all)	2	10	
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Abnormal faeces			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	6	
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	
occurrences (all)	4	13	
Dermatitis diaper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	3	
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	4	
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Rash erythematous			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	
occurrences (all)	7	3	
Viral infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Otitis media acute			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported