Clinical trial results:
A Phase I/II Safety, Tolerability, Ascending Dose and Dose Frequency Study of Recombinant Human Heparan-N-sulfatase (rhHNS) Intrathecal Administration via an Intrathecal Drug Delivery Device in Patients with Sanfilippo Syndrome Type A (MPS IIIA)

Summary

EudraCT number	2009-015984-15
Trial protocol	GB
Global end of trial date	10 September 2012

Results information

Result version number	v1 (current)
This version publication date	13 July 2018
First version publication date	13 July 2018

Trial information

Trial identification

Sponsor protocol code	HGT-SAN-055

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01155778
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire Human Genetic Therapies, Inc.
Sponsor organisation address	300 Shire Way, Lexington, Massachusetts, United States, 02421
Public contact	Olivia Maurel, Shire Human Genetic Therapies AB, 41 224194150, omaurel@shire.com
Scientific contact	Olivia Maurel, Shire Human Genetic Therapies AB, 41 224194150, omaurel@shire.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001634-PIP01-14
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	10 September 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of recombinant human heparan-N-sulfatase (rhHNS) (HGT-1410) via ascending doses administered via a surgically implanted intrathecal drug delivery device (IDDD) once monthly for 6 months, in subjects with Mucopolysaccharidosis IIIA or Sanfilippo Syndrome Type A (MPS IIIA).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that had their origin in the Declaration of Helsinki and that were consistent with Good Clinical Practice (GCP) and applicable regulatory requirements. Known instances of non-conformance were documented and were not considered to have had an impact on the overall conclusions of this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	0
Children (2-11 years)	7
Adolescents (12-17 years)	3
Adults (18-64 years)	2

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Study enrolled 12 subjects and 4 subjects were included in each of the 3 dose groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	HGT-1410 10 mg

Arm description:

HGT-1410/rhHNS 10 milligram (mg) monthly via an intrathecal drug delivery device (IDDD) (every 28 [±7 days]) for a total of 6 months.

Arm type	Experimental
Investigational medicinal product name	Recombinant human heparan N-sulfatase
Investigational medicinal product code	HGT-1410
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

HGT-1410/rhHNS 10 mg monthly via an IDDD (every 28 [±7 days]) for a total of 6 months.

Arm title	HGT-1410 90 mg

Arm description:

HGT-1410/rhHNS 45 mg dose every 14 [±2 days] for a monthly total dose of 90 mg via an IDDD for 6 months.

Arm type	Experimental
Investigational medicinal product name	Recombinant human heparan N-sulfatase
Investigational medicinal product code	HGT-1410
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

HGT-1410/rhHNS 45 mg dose every 14 [±2 days] for a monthly total dose of 90 mg via an IDDD for 6 months.

Arm title	HGT-1410 45 mg

Arm description:

HGT-1410/rhHNS 45 mg monthly via an IDDD (every 28 [±7 days]) for a total of 6 months.

Arm type	Experimental
Investigational medicinal product name	Recombinant human heparan N-sulfatase
Investigational medicinal product code	HGT-1410
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:
HGT-1410/rhHNS 45 mg monthly via an IDDD (every 28 [±7 days]) for a total of 6 months.

Number of subjects in period 1	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg
Started	4	4	4
Completed	4	4	4

Baseline characteristics

Reporting groups	
Reporting group title	HGT-1410 10 mg
Reporting group description:	
HGT-1410/rhHNS 10 milligram (mg) monthly via an intrathecal drug delivery device (IDDD) (every 28 [±7 days]) for a total of 6 months.	
Reporting group title	HGT-1410 90 mg
Reporting group description:	
HGT-1410/rhHNS 45 mg dose every 14 [±2 days] for a monthly total dose of 90 mg via an IDDD for 6 months.	
Reporting group title	HGT-1410 45 mg
Reporting group description:	
HGT-1410/rhHNS 45 mg monthly via an IDDD (every 28 [±7 days]) for a total of 6 months.	

Reporting group values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg
Number of subjects	4	4	4
Age categorical Units: Subjects			
Less than equal to (<=) 18 years	3	3	4
Between 18 and 65 years	1	1	0
Age continuous Units: years			
arithmetic mean	9.15	10.64	9.07
standard deviation	± 4.7	± 8.7	± 9.8
Gender, Male/Female Units: 0x			
Female	1	1	2
Male	3	3	2

Reporting group values	Total		
Number of subjects	12		
Age categorical Units: Subjects			
Less than equal to (<=) 18 years	10		
Between 18 and 65 years	2		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: 0x			
Female	4		
Male	8		

End points

End points reporting groups

Reporting group title	HGT-1410 10 mg
Reporting group description:	
HGT-1410/rhHNS 10 milligram (mg) monthly via an intrathecal drug delivery device (IDDD) (every 28 [±7 days]) for a total of 6 months.	
Reporting group title	HGT-1410 90 mg
Reporting group description:	
HGT-1410/rhHNS 45 mg dose every 14 [±2 days] for a monthly total dose of 90 mg via an IDDD for 6 months.	
Reporting group title	HGT-1410 45 mg
Reporting group description:	
HGT-1410/rhHNS 45 mg monthly via an IDDD (every 28 [±7 days]) for a total of 6 months.	

Primary: Number of Treatment Emergent Serious Adverse Events (SAE)

End point title	Number of Treatment Emergent Serious Adverse Events

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation subject administered as a pharmaceutical product that did not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in-patient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs (TEAEs) were defined as all adverse events (AEs) from the time of the surgery for IDDD implantation to the last follow up contact, 30 (±7) days after the end of study (EOS) procedures. Safety population was defined as all enrolled subjects who received at least 1 dose (full or partial) of study drug.

End point type	Primary

End point timeframe:

Baseline to week 30 (follow-up)

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 done, no inferential statistical analyses were performed.

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: events				
number (not applicable)	5	2	3	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Treatment Emergent Adverse Events (TEAE)

End point title	Number of Treatment Emergent Adverse Events (TEAE)[2]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation subject administered as a pharmaceutical product that did not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged in-patient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs (TEAEs) were defined as all adverse events (AEs) from the time of the surgery for IDDD implantation to the last follow up contact, 30 (±7) days after the end of study (EOS) procedures. Safety population.

End point type	Primary

End point timeframe:

Baseline to week 30 (follow-up)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: events				
number (not applicable)	71	55	42	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Anti-rhHNS Antibody Status in Cerebrospinal Fluid (CSF) by Recombinant Human Heparan N-Sulfatase (rhHNS) Dose Group

End point title	Summary of Anti-rhHNS Antibody Status in Cerebrospinal Fluid (CSF) by Recombinant Human Heparan N-Sulfatase (rhHNS) Dose Group[3]

End point description:

Subjects with positive, negative and missing status were reported. Intent to treat (ITT) population was defined as all enrolled subjects who received at least 1 dose (full or partial) of study drug.

End point type	Primary

End point timeframe:

Baseline, Week 26

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: subjects				
number (not applicable)				
Negative (Baseline)	4	4	4	
Positive (Baseline)	0	0	0	
Missing (Baseline)	0	0	0	
Negative (Week 26)	1	2	1	

Positive (Week 26)	0	0	0	
Missing (Week 26)	3	2	3	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Anti-rhHNS Antibody Status in serum by Recombinant Human Heparan N-Sulfatase (rhHNS) Dose Group

End point title	Summary of Anti-rhHNS Antibody Status in serum by Recombinant Human Heparan N-Sulfatase (rhHNS) Dose Group[4]

End point description:

Subjects with positive, negative and missing status were reported. ITT population

End point type	Primary

End point timeframe:

Baseline, Week 26

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: subjects				
number (not applicable)				
Negative (Baseline)	4	3	3	
Positive (Baseline)	0	1	1	
Missing (Baseline)	0	0	0	
Negative (Week 26)	1	2	2	
Positive (Week 26)	2	0	0	
Missing (Week 26)	1	2	2	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of Intrathecal Drug Delivery Device (IDDD) Failures

End point title	Summary of Intrathecal Drug Delivery Device (IDDD)

End point description:

Subjects with IDDD failures were reported. ITT population.

End point type	Primary

End point timeframe:

Baseline, Week 26

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: subjects				
number (not applicable)	3	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Developmental Quotient (DQ) using Bayley Scales of Infant Development Third Edition (BSID III) and Kaufman Assessment Battery for Children Second Edition (KABC II) at Week 22

End point title	Change from Baseline in Developmental Quotient (DQ) using Bayley Scales of Infant Development Third Edition (BSID III) and Kaufman Assessment Battery for Children Second Edition (KABC II) at Week 22

End point description:

BSID-III was used to assess the cognitive development, language (receptive and expressive), and motor development (fine and gross), of infants and toddlers, ages 0-42 months. KABC-II was an individually administered measure of the processing and reasoning abilities of children and adolescents between the ages of 3 and 18 years and is an alternative to BSID-III. BSID-III DQ score is based on the Cognitive domain. The DQ score was calculated from the data obtained from either BSID-III/KABC-II mental age equivalent of the child in months divided by the calendar age in months (multiplied by 100 to give percentage points). Here, n = subjects evaluable for specified category for each arm, respectively. ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 2, 4, 4)	51.91 (± 27.292)	51.87 (± 36.095)	43.24 (± 23.112)	
Change at Week 22 (n= 2, 4, 4)	-13.6 (± 8.886)	-4.91 (± 7.769)	-0.89 (± 4.341)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Four Point Scoring System/Total Disability Score (FPSS/TDS) at Week 22 and Week 26 (EOS)

End point title	Change from Baseline in Four Point Scoring System/Total Disability Score (FPSS/TDS) at Week 22 and Week 26 (EOS)

End point description:

FPSS a questionnaire specific to Sanfilippo-specific disabilities, which assesses: motor function, expressive/speech language, and cognitive function by a parent questionnaire. Total disability score (TDS) is the average of the motor skills (MS), speech abilities (SA), and cognitive function (CF) scores and the lower scores indicate developmental regression. Here, n = subjects evaluable for specified category for each arm, respectively. ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 22, Week 26

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
MS: Baseline (n= 4, 3, 4)	2.5 (± 0.58)	3 (± 0)	3 (± 0)	
MS: Change at Week 22 (n= 4, 3, 4)	0.3 (± 0.5)	0 (± 0)	0 (± 0)	
MS: Change at Week 26/EOS (n= 2, 2, 3)	0 (± 0)	0 (± 0)	0 (± 0)	
SA: Baseline (n= 4, 3, 4)	2 (± 0.82)	2 (± 0.82)	2 (± 0)	
SA: Change at Week 22 (n= 4, 3, 4)	-0.5 (± 0.58)	0.3 (± 0.5)	0.3 (± 0.58)	
SA: Change at Week 26/EOS (n= 2, 2, 3)	-0.5 (± 0.71)	0.3 (± 0.58)	0 (± 0)	
CF: Baseline (n= 4, 3, 4)	2.3 (± 0.5)	2.8 (± 0.5)	2.3 (± 0.58)	
CF: Change at Week 22 (n= 4, 3, 4)	0 (± 0)	0 (± 0)	0 (± 0)	
CF: Change at Week 26/EOS (n= 2, 2, 3)	0 (± 0)	0 (± 0)	0 (± 0)	
TDS: Baseline (n= 4, 3, 4)	2.25 (± 0.569)	2.58 (± 0.319)	2.44 (± 0.192)	
TDS: Change at Week 22 (n= 4, 3, 4)	-0.08 (± 0.319)	0.08 (± 0.167)	0.11 (± 0.192)	
TDS: Change at Week 26/EOS (n= 2, 2, 3)	-0.17 (± 0.236)	0.11 (± 0.192)	0 (± 0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Sanfilippo Behavioral Rating Scale (SBRS) at Week 22 and Week 26 (EOS)

End point title	Change from Baseline in Sanfilippo Behavioral Rating Scale (SBRS) at Week 22 and Week 26 (EOS)

End point description:

Sanfilippo Behavior Rating Scale a parent-scored behavioral inventory measuring: comprehensive

language skills, expressive language skills, tantrums, mood and emotions, and other behaviors not otherwise classified. Summary of each scores are the sum of the responses within a given domain for a given subject. Higher values of summary scores indicate undesirable behavior. Here, n = subjects evaluable for specified category for each arm, respectively. 99999 signifies standard deviation not reported as there was only 1 evaluable subject and data was not available for the specific measure. ITT population.
Abbreviations: Current Communication (CC), Past Communication (PC), Body Movements (BM), Interaction With Objects (IWO), Activity And Routines (AAR), Emotional Function (EF), Safety-consciousness (SC), Social Interaction (SI), Eye Contact (EC), Comfort Seeking (CS), Self-control/Compliance (SCC), Mood, Anger/Aggression (MAA), Self-gratification (SG)

End point type	Secondary

End point timeframe:

Baseline, Week 22, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
CC: Baseline (n= 4, 4, 2)	8 (± 5.48)	10 (± 5.66)	6.3 (± 6.85)	
CC: Change at Week 22 (n= 4, 4, 2)	5 (± 13.44)	1.5 (± 2.12)	-0.3 (± 1.26)	
CC: Change at Week 26/EOS (n= 3, 2, 2)	1.3 (± 12.5)	1.5 (± 2.12)	-1 (± 1.41)	
PC: Baseline (n= 3, 2, 4)	7.3 (± 6.03)	11 (± 11.37)	8.5 (± 12.02)	
PC: Change at Week 22 (n= 1, 0, 1)	-8 (± 99999)	0 (± 99999)	99999 (± 99999)	
PC: Change at Week 26/EOS (n= 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Orality: Baseline (n= 2, 3, 3)	7 (± 9.9)	17.3 (± 10.26)	10.3 (± 2.08)	
Orality: Change at Week 22 (n= 2, 3, 1)	2 (± 2.83)	4 (± 99999)	6 (± 5.29)	
Orality: Change at Week 26/EOS (n= 1, 1, 1)	0 (± 99999)	4 (± 99999)	5 (± 99999)	
BM: Baseline (n= 4, 4, 2)	5 (± 4.55)	12 (± 2.83)	2.5 (± 2.08)	
BM: Change at Week 22 (n= 3, 4, 2)	2.3 (± 3.51)	-2 (± 2.83)	2 (± 2.45)	
BM: Change at Week 26/EOS (n= 3, 2, 2)	0.3 (± 1.53)	-2 (± 2.83)	0 (± 0)	
IWO: Baseline (n= 4, 3, 4)	4.5 (± 3.11)	8.5 (± 7.9)	10.3 (± 2.08)	
IWO: Change at Week 22 (n= 4, 3, 3)	3.3 (± 4.27)	-2 (± 3.46)	-2 (± 4.58)	
IWO: Change at Week 26/EOS (n= 2, 1, 3)	1 (± 1.41)	-2 (± 3.46)	-1 (± 99999)	
AAR: Baseline (n= 1, 3, 4)	6 (± 99999)	12.3 (± 9.46)	14.3 (± 3.06)	
AAR: Change at Week 22 (n= 1, 3, 4)	8 (± 99999)	-1.3 (± 6.08)	0.7 (± 0.58)	
AAR: Change at Week 26/EOS (n= 0, 1, 3)	99999 (± 99999)	1.7 (± 2.08)	0 (± 99999)	
EF: Baseline (n= 3, 4, 4)	2 (± 3.46)	7.5 (± 5)	2.5 (± 3.11)	
EF: Change at Week 22 (n= 3, 4, 4)	5.3 (± 1.15)	-2.3 (± 3.5)	0 (± 1.41)	
EF: Change at Week 26/EOS (n= 2, 2, 3)	5 (± 1.41)	-1.31 (± 3.06)	0.5 (± 0.71)	
SC: Baseline (n= 4, 4, 4)	7.8 (± 5.44)	11.5 (± 7.9)	9.5 (± 1.91)	
SC: Change at Week 22 (n= 4, 4, 4)	0.5 (± 1)	-0.8 (± 2.5)	1.8 (± 5.74)	
SC: Change at Week 26/EOS (n= 3, 2, 3)	-1 (± 2.65)	-1 (± 3)	-3 (± 2.83)	
Fearfulness: Baseline (n= 3, 3, 3)	7 (± 7.81)	11 (± 6.08)	10.3 (± 8.74)	

Fearfulness: Change at Week 22 (n= 3, 3, 3)	2.7 (± 1.15)	2 (± 1.73)	-1 (± 5.2)	
Fearfulness: Change at Week 26/EOS (n= 2, 1, 3)	2.5 (± 2.12)	2.3 (± 1.53)	-5 (± 99999)	
SI: Baseline (n= 4, 4, 4)	11 (± 3.37)	14.5 (± 6.76)	12.5 (± 2.38)	
SI: Change at Week 22 (n= 4, 3, 4)	3 (± 4.76)	-0.5 (± 3.7)	0.3 (± 4.04)	
SI: Change at Week 26/EOS (n= 3, 2, 3)	0 (± 8)	-0.7 (± 4.62)	-3.5 (± 4.95)	
EC: Baseline (n= 4, 4, 3)	2.8 (± 3.59)	6.7 (± 5.77)	5.5 (± 3.7)	
EC: Change at Week 22 (n= 4, 4, 3)	1.5 (± 1.73)	-1 (± 2.65)	0 (± 3.27)	
EC: Change at Week 26/EOS (n= 3, 2, 3)	0.3 (± 0.58)	-0.7 (± 3.06)	-2 (± 2.83)	
EE: Baseline (n= 2, 4, 4)	8.5 (± 4.95)	8.3 (± 3.3)	7.3 (± 1.71)	
EE: Change at Week 22 (n= 1, 4, 4)	2 (± 99999)	-0.8 (± 2.87)	-0.5 (± 1.29)	
EE: Change at Week 26/EOS (n= 0, 2, 3)	99999 (± 99999)	0.7 (± 1.15)	-1 (± 1.41)	
CS: Baseline (n= 4, 3, 4)	10.3 (± 5.32)	16.5 (± 6.56)	10.3 (± 3.06)	
CS: Change at Week 22 (n= 3, 3, 3)	1.7 (± 4.73)	-2.3 (± 3.21)	-1.7 (± 3.06)	
CS: Change at Week 26/EOS (n= 2, 1, 3)	0 (± 1.41)	-2.3 (± 3.21)	-1 (± 99999)	
Attention: Baseline (n= 4, 4, 4)	8.3 (± 4.65)	10.5 (± 7.72)	8.8 (± 1.26)	
Attention: Change at Week 22 (n= 4, 4, 4)	1 (± 3.16)	2.3 (± 1.71)	2.5 (± 2.38)	
Attention: Change at Week 26/EOS (n= 2, 2, 3)	1.5 (± 2.12)	3.3 (± 1.15)	0.5 (± 0.71)	
SCC: Baseline (n= 4, 4, 4)	8 (± 4.97)	10 (± 7.3)	7.3 (± 2.22)	
SCC: Change at Week 22 (n= 3, 4, 4)	0.3 (± 4.51)	2 (± 1.83)	3.3 (± 3.2)	
SCC: Change at Week 26/EOS (n= 3, 2, 3)	0.7 (± 4.04)	2.7 (± 1.53)	0.5 (± 0.71)	
MAA: Baseline (n= 4, 3, 4)	5.3 (± 4.11)	17.3 (± 15.65)	9.7 (± 3.51)	
MAA: Change at Week 22 (n= 2, 3, 4)	5.5 (± 7.78)	-0.3 (± 2.5)	3.3 (± 5.13)	
MAA: Change at Week 26/EOS (n= 3, 1, 3)	1.7 (± 3.06)	-0.7 (± 2.89)	4 (± 99999)	
SG: Baseline (n= 4, 3, 4)	0.5 (± 1)	4.5 (± 5.26)	0.3 (± 0.58)	
SG: Change at Week 22 (n= 3, 3, 4)	-0.7 (± 1.15)	-1 (± 4.08)	2 (± 1)	
SG: Change at Week 26/EOS (n= 3, 1, 3)	0.3 (± 0.58)	1 (± 1)	1 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Developmental Quotient (DQ) using Vineland Adaptive Behavioral Scales Second Edition (VABS-II) at Week 22

End point title	Change from Baseline in Developmental Quotient (DQ) using Vineland Adaptive Behavioral Scales Second Edition (VABS-II) at Week 22

End point description:

VABS-II measures adaptive behaviors, including the ability to cope with environmental changes, to learn new everyday skills, and to demonstrate independence. This test measures 5 key domains: communication, daily living skills, socialization, motor skills, and the adaptive behavior composite (a composite of the other four domains). The Overall DQ score was calculated from the mean age-equivalent score obtained by averaging out the age equivalent scores for all the sub-domains except for Gross and Fine motor skills. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 4, 4, 4)	44.78 (± 24.747)	47.71 (± 33.687)	47.24 (± 26.612)	
Change at Week 22 (n= 2, 2, 2)	-11.38 (± 12.478)	-10.18 (± 13.333)	-23.96 (± 10.014)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Movement Assessment Battery for Children Second Edition (MABC-2) at Week 26 (EOS)

End point title	Change from Baseline in Movement Assessment Battery for Children Second Edition (MABC-2) at Week 26 (EOS)

End point description:

Movement Assessment Battery for Children, Second Edition (MABC-II) was to be used to identify, describe and guide the treatment of motor impairment in children from 3.0 to 16:11 years of age. Data was not reported as individual subject listings was only reported.

End point type	Secondary

End point timeframe:

Baseline, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[6]	0[7]	0[8]	
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[6] - Data was not reported as individual subject listings was only reported.

[7] - Data was not reported as individual subject listings was only reported.

[8] - Data was not reported as individual subject listings was only reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of life (QoL) using Child Health Questionnaire™ Parent Form 50 (CHQ 50) Questions at Week 22 and Week 26 (EOS)

End point title	Change from Baseline in Quality of life (QoL) using Child Health Questionnaire™ Parent Form 50 (CHQ 50) Questions at Week 22 and Week 26 (EOS)

End point description:

CHQ-PF50 which was designed to measure the physical and psychosocial well-being of children 5 years to 18 years of age, consists of 13 health concepts including 11 multi-item and 2 single item scales: Physical Function (PF), Role/Social-Emotional/Behavioral (REB), Role/Social-Physical (RP), bodily pain (BP), General Behavior (BE), Mental Health (MH), Self Esteem (SE), General Health Perceptions (GH), Change in Health (CH), Parental Impact-Emotional (PE), Parental Impact-Time (PT), Family Activities (FA), and Family Cohesion (FC). Transformed scores for all subscales range from 0 to 100, with a higher score indicating better health. Physical and Psychosocial Summary measures (SM) were scored with the use of norm-based methods that standardize the scores to a mean (± Standard Deviation) of 50 ± 10 on the basis of an assessment of the general United States population. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively. 99999= SD not available.

End point type	Secondary

End point timeframe:

Baseline, Week 22, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
PF: Baseline (n= 2, 4, 2)	66.67 (± 47.14)	66.67 (± 23.57)	80.28 (± 35.141)	
PF: Change at Week 22 (n= 2, 4, 2)	-8.33 (± 51.069)	5.56 (± 15.713)	-16.39 (± 23.047)	
PF: Change at Week 26/EOS (n= 1, 2, 1)	33.33 (± 99999)	-11.11 (± 99999)	-24.44 (± 34.57)	
RP: Baseline (n= 2, 4, 2)	66.67 (± 47.14)	66.67 (± 47.14)	50 (± 57.735)	
RP: Change at Week 22 (n= 2, 4, 2)	8.33 (± 11.785)	0 (± 0)	8.33 (± 16.667)	
RP: Change at Week 26/EOS (n= 1, 2, 1)	33.33 (± 99999)	0 (± 99999)	0 (± 0)	
BP: Baseline (n= 2, 4, 2)	90 (± 14.14)	30 (± 0)	67.5 (± 29.86)	
BP: Change at Week 22 (n= 2, 4, 2)	-20 (± 56.57)	45 (± 7.07)	7.5 (± 15)	
BP: Change at Week 26/EOS (n= 1, 2, 1)	20 (± 99999)	50 (± 99999)	0 (± 0)	
GH: Baseline (n= 2, 4, 2)	45.42 (± 2.946)	33.33 (± 23.57)	27.92 (± 21.457)	
GH: Change at Week 22 (n= 2, 4, 2)	-7.75 (± 38.537)	11.25 (± 15.91)	-5.21 (± 10.417)	
GH: Change at Week 26/EOS(n= 1, 2, 1)	17.5 (± 99999)	0 (± 99999)	0 (± 0)	
REB: Baseline (n= 2, 4, 2)	66.67 (± 47.14)	50 (± 70.711)	41.67 (± 50)	
REB: Change at Week 22 (n= 2, 4, 2)	-38.89 (± 86.424)	0 (± 0)	11.11 (± 64.788)	
REB: Change at Week 26/EOS (n= 1, 2, 1)	22.22 (± 99999)	0 (± 99999)	0 (± 0)	
BE: Baseline (n= 2, 4, 2)	62.5 (± 17.678)	45.83 (± 11.785)	61.04 (± 15.296)	

BE: Change at Week 22 (n= 2, 4, 2)	12.08 (± 8.839)	-2.08 (± 2.946)	-2.92 (± 15.716)	
BE: Change at Week 26/EOS (n= 1, 2, 1)	30.83 (± 99999)	-8.33 (± 99999)	-14.37 (± 14.437)	
MH: Baseline (n= 2, 4, 2)	75 (± 7.07)	10 (± 14.14)	68.8 (± 10.31)	
MH: Change at Week 22 (n= 2, 4, 2)	0 (± 21.21)	17.5 (± 17.68)	-2.5 (± 16.58)	
MH: Change at Week 26/EOS (n= 1, 2, 1)	15 (± 99999)	5 (± 99999)	-5 (± 7.07)	
SE: Baseline (n= 2, 4, 2)	62.5 (± 5.893)	47.92 (± 14.731)	61.46 (± 18.122)	
SE: Change at Week 22 (n= 2, 4, 2)	0 (± 11.785)	-4.17 (± 5.893)	-3.13 (± 7.116)	
SE: Change at Week 26/EOS (n= 1, 2, 1)	16.67 (± 99999)	-8.33 (± 99999)	8.33 (± 11.785)	
PE: Baseline (n= 2, 4, 2)	66.67 (± 47.14)	20.83 (± 17.678)	27.08 (± 22.948)	
PE: Change at Week 22 (n= 2, 4, 2)	-8.33 (± 82.496)	4.17 (± 5.893)	-2.08 (± 14.232)	
PE: Change at Week 26/EOS (n= 1, 2, 1)	16.67 (± 99999)	0 (± 99999)	-4.17 (± 5.893)	
PT: Baseline (n= 2, 4, 2)	50 (± 70.711)	5.56 (± 7.857)	33.33 (± 28.689)	
PT: Change at Week 22 (n= 2, 4, 2)	11.11 (± 62.854)	16.67 (± 23.57)	-5.56 (± 26.45)	
PT: Change at Week 26/EOS (n= 1, 2, 1)	44.44 (± 99999)	0 (± 99999)	-5.56 (± 23.57)	
FA: Baseline (n= 2, 4, 2)	56.25 (± 61.872)	10.42 (± 14.731)	42.71 (± 13.767)	
FA: Change at Week 22 (n= 2, 4, 2)	0 (± 58.926)	0 (± 0)	-7.29 (± 13.767)	
FA: Change at Week 26/EOS (n= 1, 2, 1)	16.67 (± 99999)	0 (± 99999)	-6.25 (± 2.946)	
FC: Baseline (n= 2, 4, 2)	57.5 (± 38.89)	15 (± 21.21)	72.5 (± 14.43)	
FC: Change at Week 22 (n= 2, 4, 2)	27.5 (± 38.89)	15 (± 21.21)	-6.3 (± 12.5)	
FC: Change at Week 26/EOS (n= 1, 2, 1)	55 (± 99999)	30 (± 99999)	0 (± 0)	
SM Physical: Baseline (n= 2, 4, 2)	38.44 (± 23.545)	31.27 (± 18.193)	31.62 (± 23.071)	
SM Physical: Change at Week 22 (n= 2, 4, 2)	-4.63 (± 29.276)	9.21 (± 5.095)	-1.82 (± 6.112)	
SM Physical: Change at Week 26/EOS (n= 1, 2, 1)	17.25 (± 99999)	4.96 (± 99999)	-4.99 (± 8.195)	
SM Psychosocial: Baseline (n= 2, 4, 2)	42.16 (± 14.06)	17.57 (± 2.418)	33.8 (± 10.879)	
SM Psychosocial: Change at Week 22 (n= 2, 4, 2)	-1.18 (± 23.341)	2.27 (± 4.972)	-0.26 (± 14.004)	
SM Psychosocial:Change at Week 26/EOS (n= 1, 2, 1)	13.64 (± 99999)	-2.29 (± 99999)	-1.58 (± 2.584)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quality of Life (QoL) Using Infant Toddler Quality of Life Questionnaire™ (ITQOL) at Week 22 and Week 26 (EOS)

End point title	Change From Baseline in Quality of Life (QoL) Using Infant Toddler Quality of Life Questionnaire™ (ITQOL) at Week 22 and

	Week 26 (EOS)

End point description:

ITQOL was developed for children at least 2 months of age up to 5 years and assesses the physical, mental, and social well being of the child and assesses the quality of the parent/guardian's life. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively. 99999 signifies standard deviation not reported as there was only 1 evaluable subject and data was not available for the specific measure.
Abbreviation: Overall Health (OH), Physical Abilities (PA), Growth And Development (GAD), Bodily Pain (BP), Temperament And Moods (TAM), General Behavior (GEB), Global Behavior (GLB), Getting Along (GA), General Health Perceptions (GHP), PI-Emotion (PIE), PI-Time (PIT), Family Cohesion (FC).

End point type	Secondary

End point timeframe:

Baseline, Week 22, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
OH: Baseline (n= 2, 3, 2)	80 (± 28.28)	65 (± 49.5)	56.7 (± 49.07)	
OH: Change at Week 22 (n= 2, 2, 2)	0 (± 0)	15 (± 21.21)	-12.5 (± 17.68)	
OH: Change at Week 26/EOS (n= 1, 0, 0)	0 (± 99999)	99999 (± 99999)	99999 (± 99999)	
PA: Baseline (n= 2, 3, 2)	83.35 (± 9.405)	93.35 (± 4.738)	75.57 (± 39.496)	
PA: Change at Week 22 (n= 2, 2, 2)	5 (± 11.738)	-1.7 (± 2.404)	1.65 (± 11.809)	
PA: Change at Week 26/EOS (n= 1, 0, 0)	-3.3 (± 99999)	99999 (± 99999)	99999 (± 99999)	
GAD: Baseline (n= 2, 3, 2)	57.2 (± 18.102)	56.8 (± 6.081)	60.83 (± 25.658)	
GAD: Change at Week 22 (n= 2, 2, 2)	-14.7 (± 28.709)	18.2 (± 0.99)	-22.5 (± 7.071)	
GAD: Change at Week 26/EOS (n= 1, 0, 0)	3.1 (± 99999)	99999 (± 99999)	99999 (± 99999)	
BP: Baseline (n= 2, 3, 2)	95.85 (± 5.869)	62.5 (± 29.416)	58.33 (± 36.294)	
BP: Change at Week 22 (n= 2, 2, 2)	-29.2 (± 17.678)	12.5 (± 41.154)	25 (± 11.738)	
BP: Change at Week 26/EOS (n= 1, 0, 0)	-16.7 (± 99999)	99999 (± 99999)	99999 (± 99999)	
TAM: Baseline (n= 2, 3, 2)	72.2 (± 17.678)	52.8 (± 15.698)	68.97 (± 21.731)	
TAM: Change at Week 22 (n= 2, 2, 2)	-23.6 (± 21.637)	-5.6 (± 19.658)	-2.75 (± 33.446)	
TAM: Change at Week 26/EOS (n= 1, 0, 0)	-12.8 (± 99999)	99999 (± 99999)	99999 (± 99999)	
GEB: Baseline (n= 2, 3, 2)	58.35 (± 32.456)	12.5 (± 5.94)	34.73 (± 17.465)	
GEB: Change at Week 22 (n= 2, 2, 2)	-12.5 (± 8.91)	18.75 (± 0.071)	7.25 (± 25.102)	
GEB: Change at Week 26/EOS (n= 1, 0, 0)	-8.3 (± 99999)	99999 (± 99999)	99999 (± 99999)	
GLB: Baseline (n= 2, 3, 2)	57.5 (± 38.89)	0 (± 0)	40 (± 34.64)	
GLB: Change at Week 22 (n= 2, 2, 2)	-15 (± 21.21)	0 (± 0)	0 (± 42.43)	

GLB: Change at Week 26/EOS (n= 1, 0, 0)	0 (± 99999)	99999 (± 99999)	99999 (± 99999)	
GA: Baseline (n= 2, 3, 2)	62.5 (± 17.678)	35.85 (± 1.202)	55 (± 15)	
GA: Change at Week 22 (n= 2, 2, 2)	-22.5 (± 10.607)	-1.65 (± 16.476)	-2.5 (± 22.345)	
GA: Change at Week 26/EOS (n= 1, 0, 0)	-16.7 (± 99999)	99999 (± 99999)	99999 (± 99999)	
GHP: Baseline (n= 2, 3, 2)	48.9 (± 4.808)	57.95 (± 36.982)	31.8 (± 20.178)	
GHP: Change at Week 22 (n= 2, 2, 2)	-18.2 (± 22.486)	-3.8 (± 11.879)	-5.7 (± 1.556)	
GHP: Change at Week 26/EOS (n= 1, 0, 0)	0 (± 99999)	99999 (± 99999)	99999 (± 99999)	
PIE: Baseline (n= 2, 3, 2)	78.55 (± 30.335)	41.65 (± 23.547)	48.83 (± 33.024)	
PIE: Change at Week 22 (n= 2, 2, 2)	-35.7 (± 25.314)	4.75 (± 3.323)	-3.6 (± 25.314)	
PIE: Change at Week 26/EOS (n= 1, 0, 0)	-17.8 (± 99999)	99999 (± 99999)	99999 (± 99999)	
PIT: Baseline (n= 2, 3, 2)	73.8 (± 37.052)	45.25 (± 63.993)	49.2 (± 26.264)	
PIT: Change at Week 22 (n= 2, 2, 2)	-33.35 (± 6.718)	23.8 (± 20.223)	7.2 (± 23.617)	
PIT: Change at Week 26/EOS (n= 1, 0, 0)	-28.6 (± 99999)	99999 (± 99999)	99999 (± 99999)	
FC: Baseline (n= 2, 3, 2)	85 (± 0)	42.5 (± 60.1)	76.7 (± 14.43)	
FC: Change at Week 22 (n= 2, 2, 2)	-12.5 (± 17.68)	-27.5 (± 99999)	-12.5 (± 17.68)	
FC: Change at Week 26/EOS (n= 1, 0, 0)	-25 (± 99999)	99999 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of life (QoL) using Child Health Questionnaire™ Child Form 87 (CHQ 87) at Week 26 (EOS)

End point title	Change from Baseline in Quality of life (QoL) using Child Health Questionnaire™ Child Form 87 (CHQ 87) at Week 26 (EOS)

End point description:

CHQ-CF87 form was designed to be a self-report for subjects 10 years and older. It consists of 87 questions and contains the same scales as the PF-50, (with the omission of the parental impact scales and there are no psychosocial and physical summary scores derived). ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[9]	0[10]	0[11]	
Units: units on a scale				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[9] - Individual subject listings was only reported

[10] - Individual subject listings was only reported

[11] - Individual subject listings was only reported

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of life (QoL) using Children's Sleep Habits Rating Scale at Week 22 and Week 26 (EOS)

End point title	Change from Baseline in Quality of life (QoL) using Children's Sleep Habits Rating Scale at Week 22 and Week 26 (EOS)

End point description:

Children's sleep habits rating scale consisting of 35 items that yield a Total Sleep Disturbance score (TSDS), as well as eight subscale scores (Bedtime Resistance (BR), Sleep Duration (SD), Parasomnias (P), Sleep Disordered Breathing (SDB), Night Waking (NW), Daytime Sleepiness (DS), Sleep Anxiety (SA), and Sleep Onset Delay (SOD)). The questionnaire was designed for children aged 4 through 12 years. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively. 99999 signifies standard deviation not reported as there was only 1 evaluable subject.

End point type	Secondary

End point timeframe:

Baseline, Week 22, Week 26/EOS

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: units on a scale				
arithmetic mean (standard deviation)				
BR: Baseline (n= 4, 4, 4)	8.8 (± 1.89)	11.5 (± 4.65)	7.3 (± 2.5)	
BR: Change at Week 22 (n= 4, 4, 4)	-1.3 (± 1.89)	-0.8 (± 0.96)	1.3 (± 0.96)	
BR: Change at Week 26/EOS (n= 3, 2, 2)	-1 (± 1)	0 (± 0)	1 (± 1.41)	
SOD: Baseline (n= 4, 4, 4)	1.5 (± 1)	2.3 (± 0.96)	1.8 (± 0.96)	
SOD: Change at Week 22 (n= 4, 4, 4)	0 (± 0.82)	0 (± 0.82)	0 (± 0.82)	
SOD: Change at Week 26/EOS (n= 3, 2, 2)	-0.3 (± 0.58)	0 (± 1.41)	-0.5 (± 0.71)	
SD: Baseline (n= 4, 4, 4)	5.3 (± 2.22)	6 (± 2.16)	6.5 (± 2.65)	
SD: Change at Week 22 (n= 4, 4, 4)	-0.8 (± 2.99)	1.3 (± 1.5)	-0.5 (± 1.29)	
SD: Change at Week 26/EOS (n= 3, 2, 2)	-1.7 (± 2.89)	1 (± 1.41)	-1 (± 1.41)	
SA: Baseline (n= 4, 4, 4)	7 (± 1.15)	8.3 (± 3.3)	6 (± 1.41)	
SA: Change at Week 22 (n= 4, 4, 3)	-1.5 (± 1.91)	-0.3 (± 0.58)	0.8 (± 1.71)	
SA: Change at Week 26/EOS (n= 3, 2, 2)	-0.7 (± 1.15)	-0.5 (± 0.71)	0 (± 1.41)	
NW: Baseline (n= 4, 4, 4)	4.3 (± 1.5)	5.8 (± 2.5)	5.5 (± 1.91)	

NW: Change at Week 22 (n= 4, 4, 4)	-0.3 (± 2.06)	-0.5 (± 0.58)	0 (± 1.63)	
NW: Change at Week 26/EOS (n= 3, 2, 2)	-1 (± 1.73)	0 (± 0)	-0.5 (± 0.71)	
P: Baseline (n= 2, 4, 4)	8.5 (± 0.71)	12 (± 2.94)	10 (± 2.31)	
P: Change at Week 22 (n= 2, 4, 4)	-1 (± 0)	-0.3 (± 2.87)	0.3 (± 3.4)	
P: Change at Week 26/EOS (n= 1, 2, 2)	-1 (± 99999)	-0.5 (± 0.71)	-1 (± 0)	
SDB: Baseline (n= 4, 4, 4)	3.3 (± 0.5)	5.8 (± 3.2)	4.3 (± 0.5)	
SDB: Change at Week 22 (n= 4, 4, 3)	0.8 (± 0.96)	-1.7 (± 2.89)	0.5 (± 1.73)	
SDB: Change at Week 26/EOS(n= 3, 2, 2)	0.7 (± 1.15)	0 (± 0)	-0.5 (± 0.71)	
DS: Baseline (n= 4, 4, 4)	9.5 (± 1.29)	11.3 (± 3.4)	11.5 (± 3.87)	
DS: Change at Week 22 (n= 4, 4, 4)	-0.3 (± 0.5)	0.5 (± 2.65)	0.5 (± 0.58)	
DS: Change at Week 26/EOS (n= 3, 2, 2)	0.7 (± 1.15)	1 (± 1.41)	1 (± 0)	
TSDS: Baseline (n= 2, 4, 4)	42.5 (± 2.12)	58.8 (± 16.82)	50.3 (± 12.28)	
TSDS: Change at Week 22 (n= 2, 4, 2)	1.5 (± 4.95)	2 (± 5.66)	2 (± 5.83)	
TSDS: Change at Week 26/EOS (n= 1, 2, 2)	-2 (± 99999)	1 (± 2.83)	-2 (± 4.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Concentration of Recombinant Human Heparan N-Sulfatase (rhHNS) in Cerebrospinal Fluid (CSF) at Week 22

End point title	Change from Baseline in Concentration of Recombinant Human Heparan N-Sulfatase (rhHNS) in Cerebrospinal Fluid (CSF) at Week 22

End point description:

Cerebrospinal fluid samples were collected from subjects through an implanted IDDD or via lumbar puncture (LP) immediately prior to each administration of HGT-1410. There was no evidence of accumulation of HGT-1410 in the CSF over the duration of the study. ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: ng/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[12] - There was no evidence of accumulation of HGT-1410 in the CSF over the duration of the study.

[13] - There was no evidence of accumulation of HGT-1410 in the CSF over the duration of the study.

[14] - There was no evidence of accumulation of HGT-1410 in the CSF over the duration of the study.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Concentration of Heparan Sulfate and Heparan Sulfate derivatives in Cerebrospinal Fluid (CSF) at Week 6, 10, 14, 18, 22 and 26(EOS)

End point title	Change from Baseline in Concentration of Heparan Sulfate and Heparan Sulfate derivatives in Cerebrospinal Fluid (CSF) at Week 6, 10, 14, 18, 22 and 26(EOS)

End point description:

Levels of heparan sulfate and its derivatives were evaluated using the proprietary Sensi-Pro (SP) high-performance liquid chromatography (HPLC) based assay. Here, n = subjects evaluable for specified category for each arm, respectively. ITT population.
Abbreviation: SP Total Heparan Sulfate (SPTHS), SP Non-Reducing End Assay (SPNREA)

End point type	Secondary

End point timeframe:

Baseline, Week 6, 10, 14, 18, 22 and 26(EOS)

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: picomole per milliliter (pmol/mL)				
arithmetic mean (standard deviation)				
SPTHS: Baseline (n= 4, 4, 4)	90570.5 (± 38088.67)	83287 (± 26012.16)	69049.7 (± 42659.28)	
SPTHS: Change at Week 6 (n= 4, 2, 2)	-34167.7 (± 20439.34)	-65862.6 (± 23010.52)	-41331.4 (± 38967.66)	
SPTHS: Week 10 (n= 4, 4, 3)	-41825.4 (± 13482.5)	-54343.7 (± 25891.78)	-39441.8 (± 29771.14)	
SPTHS: Change at Week 14 (n= 4, 3, 3)	-40309 (± 15107.94)	-64763.9 (± 25285.97)	-32249.2 (± 21862.89)	
SPTHS: Change at Week 22 (n= 4, 4, 4)	-35469.5 (± 20922.54)	-60931.7 (± 20699.36)	-44669.5 (± 38360.07)	
SPNREA: Baseline (n= 4, 4, 4)	1255.93 (± 471.403)	1487.67 (± 329.79)	1198.34 (± 627.436)	
SPNREA: Change at Week 6 (n= 4, 2, 2)	-213.25 (± 330.836)	-1022.53 (± 163.905)	-677.79 (± 393.281)	
SPNREA: Change at Week 10 (n= 4, 4, 3)	-411.77 (± 268.961)	-788.65 (± 390.761)	-533.38 (± 476.259)	
SPNREA: Change at Week 14 (n= 4, 3, 3)	-359.15 (± 272.695)	-1033.58 (± 371.566)	-491.24 (± 177.701)	
SPNREA: Change at Week 22 (n= 4, 4, 4)	254.07 (± 333.649)	-877.84 (± 435.044)	-686.13 (± 517.558)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Brain Magnetic Resonance Imaging (MRI) at Week 22

End point title	Change from Baseline in Brain Magnetic Resonance Imaging (MRI) at Week 22

End point description:

Brain MRI was measured for grey matter volume (GMV), white matter volume (WMV) and intracranial cerebro spinal fluid (CSF) Volume [ICSFV] (Ventricles + Additional CSF Space). ITT population.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: milliliter (mL)				
arithmetic mean (standard deviation)				
GMV: Baseline	550.5 (± 111.043)	600.28 (± 67.884)	534.25 (± 117.291)	
GMV: Change at Week 22	-42.84 (± 36.793)	-32.87 (± 36.862)	-33.7 (± 24.161)	
WMV: Baseline	403.72 (± 105.575)	442.45 (± 79.814)	348.28 (± 76.854)	
WMV: Change at Week 22	-2.86 (± 13.997)	-0.44 (± 9.793)	3.33 (± 11.419)	
ICSFV: Baseline	26.152 (± 9.2975)	20.925 (± 15.9681)	22.904 (± 20.8459)	
ICSFV: Change at Week 22	4.739 (± 4.6455)	7.375 (± 6.6573)	2.886 (± 3.9153)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Mean Auditory Brainstem Response (ABR) at Week 22

End point title	Change from Baseline in Mean Auditory Brainstem Response (ABR) at Week 22

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Mean ABR air and bone conduction threshold were assessed. Mean ABR bone conduction threshold was not possible to be reported as there was insufficient data to be analysed. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively. 99999 signifies standard deviation not reported as there was only 1 evaluable subject.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: Decibel Above Normal Adult Hearing Level				
arithmetic mean (standard deviation)				
Right Ear: Baseline (n= 1, 2, 3)	62.5 (± 99999)	49.17 (± 14.216)	56.25 (± 8.839)	
Right Ear: Change at Week 22 (n= 1, 2, 3)	-10 (± 99999)	-0.83 (± 22.407)	-3.75 (± 15.91)	
Left Ear: Baseline (n= 2, 2, 4)	52.5 (± 10.607)	44.38 (± 24.696)	55 (± 7.071)	
Left Ear: Change at Week 22 (n= 2, 2, 4)	5 (± 7.071)	3.13 (± 10.68)	-5 (± 14.142)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Latencies

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Latencies

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. The Inter-peak Latencies (IPL) were calculated by subtracting the absolute latencies (AL). The Inter-aural Latencies (IAL) were calculated by subtracting the absolute wave V latencies of the right and left ear. IAL, IPL and AL were reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

Abbreviation: Right Ear (RE), Left Ear (LE), Wave (W)

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: millisecond (ms)				
arithmetic mean (standard deviation)				
RE,IPL I-III: Baseline (n= 3, 3, 3)	2.29 (± 0.257)	2.33 (± 0.193)	2.53 (± 0.153)	
RE,IPL I-III: Change at Week 22 (n= 3, 3, 2)	-0.09 (± 0.147)	0.07 (± 0.014)	-0.11 (± 0.183)	
RE,IPL III-V: Baseline (n= 3, 3, 3)	2.04 (± 0.24)	1.96 (± 0.119)	2.17 (± 0.261)	
RE,IPL III-V: Change at Week 22 (n= 3, 3, 2)	-0.08 (± 0.185)	0.06 (± 0.085)	-0.06 (± 0.304)	
RE,IPL I-V: Baseline (n= 3, 3, 3)	4.34 (± 0.047)	4.29 (± 0.238)	4.71 (± 0.352)	
RE,IPL I-V: Change at Week 22 (n= 3, 3, 3)	-0.17 (± 0.269)	0.2 (± 0.131)	-0.17 (± 0.187)	
LE,IPL I-III: Baseline (n= 3, 3, 4)	2.32 (± 0.206)	2.4 (± 0.303)	2.53 (± 0.153)	

LE,IPL I-III: Change at Week 22 (n= 3, 3, 3)	-0.01 (± 0.129)	0.11 (± 0.219)	-0.24 (± 0.065)	
LE,IPL III-V: Baseline (n= 3, 3, 4)	2.06 (± 0.255)	2.09 (± 0.311)	2.15 (± 0.225)	
LE,IPL III-V: Change at Week 22 (n= 3, 3, 3)	-0.02 (± 0.075)	0.06 (± 0.04)	0.09 (± 0.091)	
LE,IPL I-V: Baseline (n= 3, 3, 4)	4.39 (± 0.264)	4.48 (± 0.394)	4.68 (± 0.33)	
LE,IPL I-V: Week 22 (n= 3, 3, 3)	-0.03 (± 0.185)	0.17 (± 0.191)	-0.15 (± 0.07)	
IAL: Baseline (n= 3, 3, 3)	-0.05 (± 0.061)	0.07 (± 0.081)	-0.07 (± 0.058)	
IAL: Change at Week 22 (n= 3, 3, 3)	0.04 (± 0.301)	0.46 (± 0.849)	0.28 (± 0.312)	
AL-RE,WI: Baseline (n= 3, 3, 3)	1.73 (± 0.237)	1.76 (± 0.012)	1.59 (± 0.156)	
AL-RE,WI: Change at Week 22 (n= 3, 3, 3)	0 (± 0.466)	0.47 (± 0.987)	0.46 (± 0.54)	
AL-RE,WIII: Baseline (n= 3, 3, 3)	4.02 (± 0.45)	4.09 (± 0.181)	4.12 (± 0.197)	
AL-RE,WIII: Change at Week 22 (n= 3, 3, 2)	-0.09 (± 0.355)	-0.03 (± 0.042)	0.35 (± 0.687)	
AL-RE,WV: Baseline (n= 3, 3, 3)	6.06 (± 0.283)	6.06 (± 0.227)	6.3 (± 0.454)	
AL-RE,WV: Change at Week 22 (n= 3, 3, 3)	-0.17 (± 0.478)	0.67 (± 1.109)	0.29 (± 0.633)	
AL-LE,WI: Baseline (n= 3, 3, 4)	1.73 (± 0.13)	1.78 (± 0.233)	1.68 (± 0.144)	
AL-LE,WI: Change at Week 22 (n= 3, 3, 3)	-0.18 (± 0.111)	0.04 (± 0.16)	0.16 (± 0.33)	
AL-LE,WIII: Baseline (n= 3, 3, 4)	4.05 (± 0.323)	4.18 (± 0.504)	4.22 (± 0.189)	
AL-LE,WIII: Change at Week 22 (n= 3, 3, 3)	-0.19 (± 0.165)	0.15 (± 0.306)	-0.08 (± 0.266)	
AL-LE,WV: Baseline (n= 3, 3, 4)	6.12 (± 0.278)	6.26 (± 0.612)	6.36 (± 0.412)	
AL-LE,WV: Change at Week 22 (n= 3, 3, 4)	-0.21 (± 0.178)	0.24 (± 0.227)	0.01 (± 0.324)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Amplitudes

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Amplitudes

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR amplitudes by left ear (LE) and right ear (RE) were reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: microvolt (mcV)				
arithmetic mean (standard deviation)				
RE, Wave I: Baseline (n= 2, 3, 3)	0.49 (± 0.042)	0.26 (± 0.097)	0.42 (± 0.118)	
RE, Wave I: Change at Week 22 (n= 2, 3, 3)	-0.23 (± 0.042)	-0.03 (± 0.216)	-0.17 (± 0.147)	
RE, Wave III: Baseline (n= 2, 3, 3)	0.33 (± 0.156)	0.24 (± 0.113)	0.35 (± 0.195)	
RE, Wave III: Change at Week 22 (n= 2, 3, 2)	-0.05 (± 0.099)	-0.16 (± 0.156)	-0.12 (± 0.117)	
RE, Wave V: Baseline (n= 2, 3, 3)	0.64 (± 0.403)	0.32 (± 0.101)	0.47 (± 0.144)	
RE, Wave V: Change at Week 22 (n= 2, 3, 3)	-0.28 (± 0.354)	-0.14 (± 0.201)	-0.09 (± 0.145)	
LE, Wave I: Baseline (n= 2, 3, 4)	0.4 (± 0.028)	0.26 (± 0.133)	0.44 (± 0.199)	
LE, Wave I: Change at Week 22 (n= 2, 3, 3)	-0.1 (± 0.17)	-0.01 (± 0.135)	0.02 (± 0.221)	
LE, Wave III: Baseline (n= 2, 3, 4)	0.22 (± 0.106)	0.21 (± 0.102)	0.38 (± 0.194)	
LE, Wave III: Change at Week 22 (n= 2, 3, 3)	0.05 (± 0.057)	0.02 (± 0.047)	-0.09 (± 0.188)	
LE, Wave V: Baseline (n= 2, 3, 4)	0.52 (± 0.269)	0.29 (± 0.17)	0.48 (± 0.123)	
LE, Wave V: Change at Week 22 (n= 2, 3, 4)	-0.13 (± 0.24)	-0.01 (± 0.085)	-0.02 (± 0.134)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Amplitude Ratio

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Amplitude Ratio

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR amplitudes(A), log-transformed amplitudes (LTA), square-root transformed amplitudes (STA) by left ear (LE) and right ear (RE) wave V/I in ratio was reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively. 99999 signifies standard deviation not reported as there was only 1 evaluable subject and data was not available for the specific measure.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: ratio				
arithmetic mean (standard deviation)				
A-RE, Wave V/I: Baseline (n= 2, 2, 2)	1.34 (± 0.94)	1.83 (± 0.403)	1.09 (± 0.057)	

A-RE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.14 (± 0.269)	-1.48 (± 99999)	0.42 (± 99999)	
A-LE, Wave V/I: Baseline (n= 2, 2, 2)	1.33 (± 0.764)	2.43 (± 2.341)	1.26 (± 0.014)	
A-LE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.37 (± 0.453)	-0.15 (± 99999)	0.28 (± 99999)	
LTA-RE, Wave V/I: Baseline (n= 2, 2, 2)	0.146 (± 0.7733)	0.589 (± 0.2227)	0.086 (± 0.0519)	
LTA-RE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.188 (± 0.3011)	-3.245 (± 99999)	0.336 (± 99999)	
LTA-LE, Wave V/I: Baseline (n= 2, 2, 2)	0.195 (± 0.6093)	0.572 (± 1.1791)	0.231 (± 0.0112)	
LTA-LE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.188 (± 0.1787)	-0.217 (± 99999)	0.202 (± 99999)	
STA-RE, Wave V/I: Baseline (n= 2, 2, 2)	1.116 (± 0.4212)	1.347 (± 0.1496)	1.044 (± 0.0271)	
STA-RE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.082 (± 0.1409)	-0.996 (± 99999)	0.188 (± 99999)	
STA-LE, Wave V/I: Baseline (n= 2, 2, 2)	1.128 (± 0.3385)	1.449 (± 0.8078)	1.122 (± 0.0063)	
STA-LE, Wave V/I: Change at Week 22 (n= 2, 1, 1)	0.13 (± 0.1448)	-0.09 (± 99999)	0.119 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Log Tranformed Latencies

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Log Tranformed Latencies

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR log-transformed latencies (LTL) by left and right ear were reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: log tranformed (latency [ms])				
arithmetic mean (standard deviation)				
LTL-RE, Wave I: Baseline (n= 3, 3, 3)	0.54 (± 0.1326)	0.567 (± 0.0066)	0.461 (± 0.0956)	
LTL-RE, Wave I: Change at Week 22 (n= 3, 3, 3)	-0.006 (± 0.2585)	0.179 (± 0.4104)	0.242 (± 0.2791)	
LTL-RE, Wave III: Baseline (n= 3, 3, 3)	1.387 (± 0.1121)	1.409 (± 0.0439)	1.416 (± 0.0483)	
LTL-RE, Wave III: Change at Week 22 (n= 3, 3, 2)	-0.019 (± 0.0882)	-0.008 (± 0.0108)	0.074 (± 0.148)	

LTL-RE, Wave V: Baseline (n= 3, 3, 3)	1.802 (± 0.0461)	1.801 (± 0.0374)	1.838 (± 0.0731)	
LTL-RE, Wave V: Change at Week 22 (n= 3, 3, 3)	-0.028 (± 0.0794)	0.093 (± 0.1529)	0.044 (± 0.0963)	
LTL-LE, Wave I: Baseline (n= 3, 3, 4)	0.546 (± 0.0769)	0.57 (± 0.1268)	0.518 (± 0.0838)	
LTL-LE, Wave I: Change at Week 22 (n= 3, 3, 3)	-0.106 (± 0.0653)	0.019 (± 0.0927)	0.088 (± 0.1812)	
LTL-LE, Wave III: Baseline (n= 3, 3, 4)	1.397 (± 0.0804)	1.424 (± 0.1213)	1.438 (± 0.0455)	
LTL-LE, Wave III: Change at Week 22 (n= 3, 3, 3)	-0.046 (± 0.0394)	0.032 (± 0.0657)	-0.02 (± 0.0624)	
LTL-LE, Wave V: Baseline (n= 3, 3, 4)	1.81 (± 0.045)	1.831 (± 0.0955)	1.849 (± 0.0658)	
LTL-LE, Wave V: Change at Week 22 (n= 3, 3, 4)	-0.034 (± 0.0281)	0.036 (± 0.0338)	0.002 (± 0.0494)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Log Tranformed Amplitude

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Log Tranformed Amplitude

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR log-transformed amplitudes (LTA) by left and right ear were reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: log transformed (amplitude [mcV])				
arithmetic mean (standard deviation)				
LTA-RE, Wave I: Baseline (n= 2, 3, 3)	-0.715 (± 0.0867)	-1.379 (± 0.3627)	-0.893 (± 0.2741)	
LTA-RE, Wave I: Change at Week 22 (n= 2, 3, 3)	-0.659 (± 0.2456)	-0.24 (± 1.018)	-0.76 (± 0.8475)	
LTA-RE, Wave III: Baseline (n= 2, 3, 3)	-1.168 (± 0.4901)	-1.527 (± 0.589)	-1.17 (± 0.6224)	
LTA-RE, Wave III: Change at Week 22 (n= 2, 3, 2)	-0.116 (± 0.2867)	-1.239 (± 1.5038)	-0.549 (± 0.4627)	
LTA-RE, Wave V: Baseline (n= 2, 3, 3)	-0.567 (± 0.6834)	-1.19 (± 0.3631)	-0.792 (± 0.2929)	
LTA-RE, Wave V: Change at Week 22 (n= 2, 3, 3)	-0.474 (± 0.5435)	-1.237 (± 1.5458)	-0.214 (± 0.3107)	

LTA-LE, Wave I: Baseline (n= 2, 3, 4)	-0.918 (± 0.0708)	-1.445 (± 0.5468)	-0.875 (± 0.4212)	
LTA-LE, Wave I: Change at Week 22 (n= 2, 3, 3)	-0.409 (± 0.6445)	0.078 (± 0.5695)	-0.268 (± 0.8163)	
LTA-LE, Wave III: Baseline (n= 2, 3, 4)	-1.602 (± 0.5149)	-1.643 (± 0.5086)	-1.057 (± 0.4761)	
LTA-LE, Wave III: Change at Week 22 (n= 2, 3, 3)	0.265 (± 0.3271)	0.053 (± 0.151)	-0.374 (± 0.7773)	
LTA-LE, Wave V: Baseline (n= 2, 3, 4)	-0.726 (± 0.5418)	-1.372 (± 0.5377)	-0.748 (± 0.2486)	
LTA-LE, Wave V: Change at Week 22 (n= 2, 3, 4)	-0.217 (± 0.4692)	0.006 (± 0.3379)	-0.066 (± 0.2771)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Square-root Tranformed Latencies

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Square-root Tranformed Latencies

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR square-root log-transformed latency (STL) by left and right ear were reported. ITT population.Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: square-root transformed (latency [ms])				
arithmetic mean (standard deviation)				
STL-RE, Wave I: Baseline (n= 3, 3, 3)	1.312 (± 0.0886)	1.328 (± 0.0044)	1.26 (± 0.061)	
STL-RE, Wave I: Change at Week 22 (n= 3, 3, 3)	-0.002 (± 0.1734)	0.145 (± 0.3167)	0.166 (± 0.1935)	
STL-RE, Wave III: Baseline (n= 3, 3, 3)	2.003 (± 0.1123)	2.023 (± 0.0446)	2.03 (± 0.0487)	
STL-RE, Wave III:Change at Week 22 (n= 3, 3, 2)	-0.021 (± 0.0884)	-0.008 (± 0.0107)	0.08 (± 0.1593)	
STL-RE, Wave V: Baseline (n= 3, 3, 3)	2.462 (± 0.0571)	2.461 (± 0.0461)	2.508 (± 0.091)	
STL-RE, Wave V: Change at Week 22 (n= 3, 3, 3)	-0.035 (± 0.0974)	0.125 (± 0.2057)	0.056 (± 0.1233)	
STL-LE, Wave I: Baseline (n= 3, 3, 4)	1.315 (± 0.05)	1.332 (± 0.0858)	1.297 (± 0.055)	
STL-LE, Wave I: Change at Week 22 (n= 3, 3, 3)	-0.068 (± 0.0425)	0.014 (± 0.0608)	0.059 (± 0.1223)	

STL-LE, Wave III: Baseline (n= 3, 3, 4)	2.012 (± 0.0805)	2.04 (± 0.1236)	2.053 (± 0.0464)	
STL-LE, Wave III: Change at Week 22 (n= 3, 3, 3)	-0.047 (± 0.0403)	0.035 (± 0.0709)	-0.019 (± 0.0644)	
STL-LE, Wave V: Baseline (n= 3, 3, 4)	2.473 (± 0.0559)	2.5 (± 0.1208)	2.522 (± 0.0824)	
STL-LE, Wave V: Change at Week 22 (n= 3, 3, 4)	-0.042 (± 0.0354)	0.047 (± 0.0438)	0.002 (± 0.0633)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Square-root Tranformed Amplitude

End point title	Change from Baseline in Auditory Brainstem Response (ABR) at Week 22: Square-root Tranformed Amplitude

End point description:

ABR assessments were to be conducted under anesthesia and measured the electrical response evoked by acoustic stimuli as sound is processed along the auditory pathway. Data for change from baseline in ABR square-root transformed amplitude (STA) by left and right ear were reported. ITT population. Here, n = subjects evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline, Week 22

End point values	HGT-1410 10 mg	HGT-1410 90 mg	HGT-1410 45 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	4	4	
Units: square-root transformed(amplitude [mcV])				
arithmetic mean (standard deviation)				
STA-RE, Wave I: Baseline (n= 2, 3, 3)	0.7 (± 0.0303)	0.507 (± 0.0933)	0.644 (± 0.0896)	
STA-RE, Wave I: Change at Week 22 (n= 2, 3, 3)	-0.193 (± 0.0535)	-0.044 (± 0.2298)	-0.172 (± 0.1615)	
STA-RE, Wave III: Baseline (n= 2, 3, 3)	0.566 (± 0.1374)	0.479 (± 0.1274)	0.575 (± 0.171)	
STA-RE, Wave III: Change at Week 22 (n= 2, 3, 2)	-0.038 (± 0.0838)	-0.211 (± 0.2317)	-0.122 (± 0.0927)	
STA-RE, Wave V: Baseline (n= 2, 3, 3)	0.775 (± 0.2599)	0.557 (± 0.0954)	0.678 (± 0.1022)	
STA-RE, Wave V: Change at Week 22 (n= 2, 3, 3)	-0.18 (± 0.2183)	-0.197 (± 0.2547)	-0.069 (± 0.1049)	
STA-LE, Wave I: Baseline (n= 2, 3, 4)	0.632 (± 0.0224)	0.499 (± 0.133)	0.655 (± 0.1437)	
STA-LE, Wave I: Change at Week 22 (n= 2, 3, 3)	0.101 (± 0.1638)	0.006 (± 0.1365)	-0.028 (± 0.1961)	
STA-LE, Wave III: Baseline (n= 2, 3, 4)	0.456 (± 0.1162)	0.45 (± 0.1131)	0.601 (± 0.1508)	
STA-LE, Wave III: Change at Week 22 (n= 2, 3, 3)	0.057 (± 0.068)	0.015 (± 0.0422)	-0.085 (± 0.1798)	

STA-LE, Wave V: Baseline (n= 2, 3, 4)	0.709 (± 0.1896)	0.518 (± 0.1488)	0.692 (± 0.0873)	
STA-LE, Wave V: Change at Week 22 (n= 2, 3, 4)	-0.084 (± 0.167)	-0.004 (± 0.0832)	-0.019 (± 0.0956)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline to Week 30 (follow-up)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups	
Reporting group title	10 mg rhHNS
Reporting group description:	
10 mg monthly via an IDDD (every 28 [+/-7 days]) for a total of 6 months Recombinant human heparan N-sulfatase (rhHNS)	
Reporting group title	90 mg rhHNS
Reporting group description:	
90 mg monthly via an IDDD (every 28 [+/-7 days]) for a total of 6 months Recombinant human heparan N-sulfatase (rhHNS)	
Reporting group title	45 mg rhHNS
Reporting group description:	
45 mg monthly via an IDDD (every 28 [+/-7 days]) for a total of 6 months Recombinant human heparan N-sulfatase (rhHNS)	

Serious adverse events	10 mg rhHNS	90 mg rhHNS	45 mg rhHNS
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	1 / 4 (25.00%)	3 / 4 (75.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Surgical and medical procedures			
Medical device change			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Device breakage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device component issue			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Postoperative wound infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	10 mg rhHNS	90 mg rhHNS	45 mg rhHNS
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	4 / 4 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Infection prophylaxis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Administration site pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Device breakage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Device failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Catheter site erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Implant site swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Medical device complication			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 4 (25.00%)	2 / 4 (50.00%)
occurrences (all)	5	2	7
Immune system disorders			
Seasonal allergy			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Penile adhesion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Labia enlarged			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Investigations			
Csf white blood cell count increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Csf protein increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Lymphocyte count increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Norovirus test positive			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Serum ferritin decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Open wound			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Post procedural discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Procedural site reaction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Procedural vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	6	0
Crying			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cognitive disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Drooling			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	4	10	0
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Motor dysfunction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Memory impairment			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Tympanic membrane disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abnormal faeces			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	2 / 4 (50.00%)
occurrences (all)	5	0	3
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Regurgitation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	1 / 4 (25.00%)
occurrences (all)	6	2	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	6	0
Urinary incontinence			

subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Trigger finger			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Candida nappy rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Post procedural infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Proteus infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rhinitis			

subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	2 / 4 (50.00%)
occurrences (all)	3	2	4
Postoperative wound infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	1 / 4 (25.00%)
occurrences (all)	2	2	1
Viral rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2010	Clarified that the study's primary investigation is focused on the safety and tolerability of the investigation drug, HGT-1410. This clarification was achieved through the modification of the primary objective and primary endpoint with the removal of language stating the safety, tolerability, and patency of the IDDD will be an objective and endpoint of the study. In addition, the need to draw a blood sample of PK analysis on Day 1 of the IT dosing week. As PK blood samples are drawn only prior to or following HGT-1410 IT injection.
25 February 2010	Clarified the Shire HGT safety review and communication process before the enrollment and implantation of an IDDD in a new subject.
14 May 2010	Clarified the IDDD replacement timeframe (if the failure of device is confirmed [defined as two successive months of non-operation); to update safety information on IT drug delivery via lumbar puncture; to shorten both the required time a subject must stay after study drug treatment and the PK sampling time points to 3 days (formerly 7 days) to be less onerous on the subject and family. In addition, the inclusion criterion requiring confirmation of MPS IIIA allowed the subject to have a documented mutations for MPS IIIA were added as alternative criterion for the diagnosis of MPS IIIA in screened subjects, since this type of testing has been found to be fairly common in subjects with MPS IIIA.
13 December 2010	Incorporated: a change in Medical Monitor, a reduction in the amount of time a subject would be required to remain at a study center, a harmonization and clarification of the study stopping rules as they relate to study drug dose escalation and data monitoring committee (DMC) review, and the addition of a requirement of pregnancy testing for female subjects who have reached menarche.
14 July 2011	Changed Cohort 3's dose and dosing schedule. Additionally, the protocol was amended to align the protocol study processes with the processes followed at the study site, in particular: subjects may miss the Day 1 visit if a subject meets specific criteria, and ABR and MRI may be performed under the same anesthesia as that of the IDDD implantation. In addition, the text regarding the management of IDDD-related issues was simplified in the protocol, with the management details specified in a new protocol Appendix 5.
28 September 2011	Stipulated the total number of times that a subject may have an IDDD revision (partial or complete replacement) during the course of the trial was 2, and the total number of times a subject may have an X-ray was limited to 6. It was also specified that in the event that the IDDD failed again after the 2 permissible revisions that HGT-1410 may have been administered and CSF collected by lumbar puncture for the remainder of the subject's participation in the study. Additionally, the ABR language was modified for clarity and it was specifically stated that all subjects were to undergo ABR testing.

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.

Comparison to values obtained in a longitudinal, 12 month, natural history study of untreated subjects with MPS IIIA was not reported as it was to be compared with another study protocol HGT-SAN-053

Notes: