Clinical trial results:
A 2-Part, Randomized, Double-Blind, Placebo-Controlled, Dose Titration, Safety, Tolerability, and Pharmacokinetics Study (Part 1) Followed by an Open-Label Efficacy and Safety Evaluation (Part 2) of SRP-4053 in Patients with Duchenne Muscular Dystrophy Amenable to Exon 53 Skipping

Summary

EudraCT number	2014-002008-25
Trial protocol	GB IT FR
Global end of trial date	25 March 2019

Results information

Result version number	v1
This version publication date	25 September 2020
First version publication date	25 September 2020

Trial information

Trial identification

Sponsor protocol code	4053-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02310906
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sarepta Therapeutics, Inc.
Sponsor organisation address	215 First Street, Cambridge,MA, United States, 02142
Public contact	Medical Director, Sarepta Therapeutics, Inc., +1 800-690-2003, clinicaltrials@sarepta.com
Scientific contact	Medical Director, Sarepta Therapeutics, Inc., +1 800-690-2003, clinicaltrials@sarepta.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001722-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	25 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

PART 1: To evaluate the safety and tolerability of four escalating doses of golodirsen administered once weekly for at least 2 weeks per dose level compared to placebo.

PART 2:
- To assess ambulation, endurance, and muscle function as measured by change from Baseline at Week 144 on the 6-Minute Walk Test (6MWT) in treated and untreated subjects.
- To assess the biological activity of golodirsen via dystrophin expression at Week 48 compared to pre-treatment.

Protection of trial subjects:

Written informed consent from each subject or subject's parent(s) or legal guardian(s), if applicable, and written assent from each subject, if applicable, were obtained before any study-specific screening or baseline period evaluations were performed. The anonymity of participating subject will be maintained to the extent required by applicable laws and in accordance with current HIPAA standards. This study was designed and monitored in accordance with Sponsor procedures, which complied with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	33 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 16
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	35
Adolescents (12-17 years)	4
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 5 sites in the France, Italy, and United Kingdom from 13 January 2015 to 25 March 2019.

Pre-assignment

Screening details:

Study conducted in 2 parts: Part 1 and Part 2. When Part 1 was completed and cumulative safety data was reviewed by an independent Data Safety Monitoring Board (DSMB), Part 2 was conducted.

Period 1

Period 1 title	Part 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Placebo

Arm description:

Participants received placebo-matched to golodirsen intravenous (IV) infusions, once weekly up to 12 weeks in Part 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received placebo-matched to golodirsen IV infusions, once weekly up to 12 weeks in Part 1.

Arm title	Part 1: Golodirsen

Arm description:

Subjects received golodirsen IV infusions, at four dose levels of 4 milligrams per kilograms (mg/kg) once weekly for 2 weeks, followed by 10 mg/kg once weekly for the next 2 weeks (i.e., up to Week 4), followed by 20 mg/kg once weekly for the next 2 weeks (i.e., up to Week 6), followed by 30 mg/kg once weekly from Week 7 to Week 12 in Part 1.

Arm type	Experimental
Investigational medicinal product name	Golodirsen
Investigational medicinal product code	SRP-4053
Other name	SRP-4053
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received golodirsen IV infusions at dose levels of 4 mg/kg, 10 mg/kg , 20 mg/kg , 30 mg/kg weekly on weeks 1, 3, 5, 7.

Number of subjects in period 1	Part 1: Placebo	Part 1: Golodirsen
Started	4	8
Received 4 mg/kg	0 [1]	8
Received 10 mg/kg	0 [2]	8
Received 20 mg/kg	0 [3]	8
Received 30 mg/kg	0 [4]	8
Completed	4	8

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: There were no separate or defined dose level for Placebo.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: There were no separate or defined dose level for Placebo.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: There were no separate or defined dose level for Placebo.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: There were no separate or defined dose level for Placebo.

Period 2

Period 2 title	Part 2
Is this the baseline period?	Yes[5]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	No
Arm title	Part 2a: Total Golodirsen Group

Arm description:

All subjects from Part 1 (who previously received placebo or golodirsen) and including additional new subjects received Golodirsen 30 milligram (mg)/kilogram (kg) once weekly, for up to 168 weeks. Dosing was interrupted or halted when any specific predefined stopping criteria was met or if warranted at the discretion of the Sponsor or Investigator.

Arm type	Experimental
Investigational medicinal product name	Golodirsen
Investigational medicinal product code	SRP-4053
Other name	SRP-4053
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received golodirsen IV infusions, 30 mg/kg weekly, for up to 168 weeks in Part 2.

Arm title	Part 2b: Untreated Group (Natural History of Non-exon 53)

Arm description:

Untreated subjects intended to evaluate the natural history of the disease with DMD and various genetic

mutations (not amenable to exon 53 skipping) were included in this group and did not received any treatment. Subjects underwent the same study assessments as treated subjects in other reporting groups (except for pharmacokinetic [PK] sampling and muscle biopsies), but at a reduced schedule through Week 144. Thus, the untreated subjects are not considered a control group.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Notes:

[5] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: 12 subjects of part 1 were involved in the part 2 of the study (Total Golodirsen Group). Hence, the part 2 of the study was considered as the baseline period.

Number of subjects in period 2	Part 2a: Total Golodirsen Group	Part 2b: Untreated Group (Natural History of Non-exon 53)
Started	25	14
Completed	23	6
Not completed	2	8
Consent withdrawn by subject	2	4
Personal reasons	-	1
Lost to follow-up	-	1
Due to enrollment in therapeutic study	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Part 2a: Total Golodirsen Group
Reporting group description:	
All subjects from Part 1 (who previously received placebo or golodirsen) and including additional new subjects received Golodirsen 30 milligram (mg)/kilogram (kg) once weekly, for up to 168 weeks. Dosing was interrupted or halted when any specific predefined stopping criteria was met or if warranted at the discretion of the Sponsor or Investigator.	
Reporting group title	Part 2b: Untreated Group (Natural History of Non-exon 53)
Reporting group description:	
Untreated subjects intended to evaluate the natural history of the disease with DMD and various genetic mutations (not amenable to exon 53 skipping) were included in this group and did not received any treatment. Subjects underwent the same study assessments as treated subjects in other reporting groups (except for pharmacokinetic [PK] sampling and muscle biopsies), but at a reduced schedule through Week 144. Thus, the untreated subjects are not considered a control group.	

Reporting group values	Part 2a: Total Golodirsen Group	Part 2b: Untreated Group (Natural History of Non-exon 53)	Total
Number of subjects	25	14	39
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	8.4	8.5	
standard deviation	± 2.18	± 1.91	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	25	14	39
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Black	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	23	11	34
Other	2	2	4
Ethnicity Units: Subjects			
Hispanic or Latino	4	0	4
Not Hispanic or Latino	9	9	18
Unknown or Not Reported	12	5	17

End points

End points reporting groups

Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received placebo-matched to golodirsen intravenous (IV) infusions, once weekly up to 12 weeks in Part 1.	
Reporting group title	Part 1: Golodirsen
Reporting group description:	
Subjects received golodirsen IV infusions, at four dose levels of 4 milligrams per kilograms (mg/kg) once weekly for 2 weeks, followed by 10 mg/kg once weekly for the next 2 weeks (i.e., up to Week 4), followed by 20 mg/kg once weekly for the next 2 weeks (i.e., up to Week 6), followed by 30 mg/kg once weekly from Week 7 to Week 12 in Part 1.	
Reporting group title	Part 2a: Total Golodirsen Group
Reporting group description:	
All subjects from Part 1 (who previously received placebo or golodirsen) and including additional new subjects received Golodirsen 30 milligram (mg)/kilogram (kg) once weekly, for up to 168 weeks. Dosing was interrupted or halted when any specific predefined stopping criteria was met or if warranted at the discretion of the Sponsor or Investigator.	
Reporting group title	Part 2b: Untreated Group (Natural History of Non-exon 53)
Reporting group description:	
Untreated subjects intended to evaluate the natural history of the disease with DMD and various genetic mutations (not amenable to exon 53 skipping) were included in this group and did not received any treatment. Subjects underwent the same study assessments as treated subjects in other reporting groups (except for pharmacokinetic [PK] sampling and muscle biopsies), but at a reduced schedule through Week 144. Thus, the untreated subjects are not considered a control group.	
Subject analysis set title	Part 1: Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received placebo-matched to golodirsen IV infusions, once weekly for up to 12 weeks in Part 1	
Subject analysis set title	Part 1: Golodirsen (4 mg/kg)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received golodirsen IV infusions, at dose level of 4 mg/kg, once weekly for 2 weeks in Part 1.	
Subject analysis set title	Part 1: Golodirsen (10 mg/kg)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received golodirsen IV infusions, at a dose level of 10 mg/kg, once weekly for the next 2 weeks (i.e., up to Week 4) in Part 1.	
Subject analysis set title	Part 1: Golodirsen (20 mg/kg)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received golodirsen IV infusions, at a dose level of 20 mg/kg, once weekly for the next 2 weeks (i.e., up to Week 6) in Part 1.	
Subject analysis set title	Part 1: Golodirsen (30 mg/kg)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received golodirsen IV infusions, at a dose level of 30 mg/kg, once weekly from Week 7 to Week 12 in Part 1.	

Primary: Part 1: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Discontinuation

End point title	Part 1: Number of Subjects with Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Discontinuation[1]

End point description:

Adverse event (AE) was any untoward medical occurrence in a clinical trial subject, which does not necessarily have a causal relationship with the investigational drug. A Serious adverse event (SAE) was an AE resulting in any of the following outcomes: death; Life-threatening event; Required or prolonged inpatient hospitalization; persistent or significant disability/incapacity; congenital anomaly. TEAEs were defined as AEs that were reported or worsened on or after the start of study drug dosing through 12 weeks. TEAEs included both Serious TEAEs and non-serious TEAEs. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

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: No statistical testing was performed for the primary end point.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects				
Subjects with TEAEs	4	5	5	3
Subjects with Serious TEAEs	0	0	0	0
Subjects with TEAEs leading to discontinuation	0	0	0	0

End point values	Part 1: Golodirsen (30 mg/kg)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects				
Subjects with TEAEs	6			
Subjects with Serious TEAEs	0			
Subjects with TEAEs leading to discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Subjects With Potentially Clinically Significant (PCS) Laboratory Abnormalities Reported as TEAEs

End point title	Part 1: Number of Subjects With Potentially Clinically Significant (PCS) Laboratory Abnormalities Reported as TEAEs[2]

End point description:

Laboratory parameters included hematology, serum chemistry (SC), urinalysis and coagulation. Number of subjects with at least one potentially clinically significant abnormal findings were reported as TEAEs. The Investigator determined whether abnormal assessment results were potentially clinically significant or not. Potentially clinical significance was defined as any variation in assessment results that had medical relevance resulting in an alteration in medical care. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary endpoint.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects				
Hepatic Chemistry	0	0	0	0
Renal Chemistry	0	0	0	0
Hematology	2	0	1	0
Coagulation	0	0	0	0
Urinalysis	0	0	0	0

End point values	Part 1: Golodirsen (30 mg/kg)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects				
Hepatic Chemistry	0			
Renal Chemistry	0			
Hematology	0			
Coagulation	0			
Urinalysis	0			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Vital Signs Reported as TEAEs

End point title	Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Vital Signs Reported as TEAEs[3]

End point description:

Vital sign parameters included systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and body temperature. Number of subjects with at least one potentially clinically significant abnormal vital signs findings were reported as TEAEs. The Investigator determined whether abnormal

assessment results were potentially clinically significant or not. Potential clinical significance was defined as any variation in assessment results that had medical relevance resulting in an alteration in medical care. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects	1	3	1	1

End point values	Part 1: Golodirsen (30 mg/kg)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects	4			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Physical Examinations

End point title	Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Physical Examinations[4]

End point description:

Physical examinations were performed by the Investigator, or qualified study staff. A full physical examination included a review of general appearance, head, eyes, ears, nose and throat, heart, lungs, abdomen, extremities, skin, lymph nodes, musculoskeletal, and neurological systems. Number of subjects with potentially clinically significant abnormalities in physical examinations were reported. Potentially clinically significant abnormalities in physical examinations were based on Investigator's discretion. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects	0	0	2	0

End point values	Part 1: Golodirsen (30 mg/kg)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Electrocardiogram (ECG) Reported as TEAEs

End point title	Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Electrocardiogram (ECG) Reported as TEAEs[5]

End point description:

Twelve-lead ECGs were performed at a consistent time of day throughout the study. Electrocardiograms were performed only after the subject was in the supine position, resting, and quiet for a minimum of 15 minutes. The ECG was manually reviewed and interpreted by medically qualified personnel. Number of subjects with potentially clinically significant abnormalities in ECG reported as TEAEs presented here. The Investigator determined whether abnormal assessment results were potentially clinically significant or not. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects	0	1	0	0

End point values	Part 1: Golodirsen (30 mg/kg)			

Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects	0			

Statistical analyses

No statistical analyses for this end point

Primary: Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Echocardiograms (ECHO)

End point title	Part 1: Number of Subjects With Potentially Clinically Significant Abnormalities in Echocardiograms (ECHO)[6]

End point description:

Standard, 2-dimensional ECHOs were performed at a consistent time of day throughout the study. Cardiac function events included cardiomegaly, tachycardia, and dyspnoea. The ECHO was reviewed and interpreted by medically qualified personnel. Number of subjects with potentially clinically significant abnormalities in ECHO were reported. Part 1 safety set included all randomised subjects who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 12

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

End point values	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	4	8	8	8
Units: Subjects	0	0	0	0

End point values	Part 1: Golodirsen (30 mg/kg)			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Subjects	3			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2a: Change From Baseline in the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 144 in Total Golodirsen Group

End point title	Part 2a: Change From Baseline in the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 144 in Total

	Golodirsen Group[7][8]

End point description:

6MWT was performed by standardized procedures for all subjects. Subjects were asked to walk a set course of 25 meters for 6 minutes (timed), and the distance walked (in meters) was recorded. Change from baseline in 6MWT distance at Week 144 in total golodirsen group was reported. Efficacy Set consisted of all randomized subjects who had at least one post-baseline functional assessment. Here "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 144

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen Group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: meters				
arithmetic mean (standard deviation)	-99.0 (± 123.75)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2a: Change from Baseline in Dystrophin Protein Levels Determined by Western Blot at Week 48 in Total Golodirsen Group

End point title	Part 2a: Change from Baseline in Dystrophin Protein Levels Determined by Western Blot at Week 48 in Total Golodirsen Group[9][10]

End point description:

Change from baseline in dystrophin protein levels (in muscle biopsy samples) were determined by Western blot in total golodirsen group. Muscle biopsy set included all subjects who received at least one dose of study drug and who had data from both baseline (pre-treatment) and Part 2 Week 48 (on-treatment) muscle biopsy samples. Data for this endpoint was not planned to be collected and analysed for untreated group (Natural History of Non-exon 53).

End point type	Primary

End point timeframe:

Baseline, Week 48

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent normal dystrophin protein level				
arithmetic mean (standard deviation)	0.924 (± 1.0129)			

Statistical analyses

No statistical analyses for this end point

Primary: Part 2b: Change From Baseline in the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 144 in Untreated Group (Natural History of Non-exon 53)

End point title	Part 2b: Change From Baseline in the Total Distance Walked During 6-Minute Walk Test (6MWT) at Week 144 in Untreated Group (Natural History of Non-exon 53)[11][12]

End point description:

6MWT was performed by standardized procedures for all subjects. Subjects were asked to walk a set course of 25 meters for 6 minutes (timed), and the distance walked (in meters) was recorded. Change from baseline in 6MWT distance at Week 144 in untreated group (Natural History of Non-exon 53) was reported. Efficacy Set consisted of all randomized subjects who had at least one post-baseline functional assessment. Here "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 144

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the primary end point.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Untreated Group (Natural History of Non-exon 53).

End point values	Part 2b: Untreated Group (Natural History of Non-exon 53)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: meters				
arithmetic mean (standard deviation)	-160.8 (± 162.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Maximum Plasma Concentration (Cmax) of Golodirsen

End point title	Part 1: Maximum Plasma Concentration (Cmax) of Golodirsen

End point description:

Maximum Concentration (Cmax) of golodirsen in plasma was evaluated. Pharmacokinetic (PK) set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	8
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	7840 (± 45.7)	17000 (± 40.9)	39700 (± 71.8)	53300 (± 37.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Time to Reach Maximum Plasma Concentration (Tmax) of Golodirsen

End point title	Part 1: Time to Reach Maximum Plasma Concentration (Tmax) of Golodirsen

End point description:

Time to reach maximum plasma concentration (Tmax) of golodirsen was evaluated. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	8	8
Units: hour				
median (full range (min-max))	1.11 (0.77 to 1.67)	1.09 (0.12 to 1.62)	1.12 (0.80 to 1.58)	1.12 (0.68 to 1.50)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Area Under the Concentration-Time Curve From Time Zero Extrapolated to the Infinity (AUCinf) of Golodirsen in Plasma

End point title	Part 1: Area Under the Concentration-Time Curve From Time Zero Extrapolated to the Infinity (AUCinf) of Golodirsen in Plasma

End point description:

Area under the concentration-time curve from time zero extrapolated to the infinity was evaluated. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects" analysed signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	6	8
Units: hr*ng/mL				
geometric mean (geometric coefficient of variation)	11800 (± 35.5)	26400 (± 42.7)	62300 (± 52.6)	90800 (± 33.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Apparent Volume of Distribution at Steady State (Vss) of Golodirsen

End point title	Part 1: Apparent Volume of Distribution at Steady State (Vss) of Golodirsen

End point description:

Volume of distribution was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. Apparent

volume of distribution at steady state of golodirsen was evaluated. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects" analysed signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	6	8
Units: liter per kilogram (L/kg)				
geometric mean (geometric coefficient of variation)	0.670 (± 38.6)	0.767 (± 43.4)	0.576 (± 84.5)	0.668 (± 32.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Elimination Half-life (T1/2) of Golodirsen

End point title	Part 1: Elimination Half-life (T1/2) of Golodirsen

End point description:

T1/2 is the time measured for the plasma concentration of drug to decrease by one half. T1/2 of golodirsen was evaluated. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects" analysed signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	6	8
Units: hour				
arithmetic mean (standard deviation)	2.36 (± 0.581)	3.63 (± 2.04)	3.27 (± 0.897)	3.42 (± 0.628)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Total Clearance (CL) of Golodirsen

End point title	Part 1: Total Clearance (CL) of Golodirsen

End point description:

Drug clearance is a quantitative measure of the rate at which a drug substance was removed from the blood. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects" analysed signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	6	8
Units: liters per hour per kilogram (L/hr/kg)				
arithmetic mean (standard deviation)	0.381 (± 36.0)	0.405 (± 46.2)	0.338 (± 52.2)	0.346 (± 34.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Mean Residence Time (MRT) of Golodirsen

End point title	Part 1: Mean Residence Time (MRT) of Golodirsen

End point description:

MRT= AUMCinf/AUCinf, where AUMCinf is the area under the first moment curve from time 0 extrapolated to infinite time, calculated using the linear/log trapezoidal method. Mean residence time of golodirsen was evaluated. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects" analysed signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

Pre-dose, 5 to 10 minutes, 1, 1.5, 2, 4, 6, 8, 12, 16 and 24 hours post-dose at Weeks 1 (for 4 mg/kg arm), 3 (for 10 mg/kg arm), 5 (for 20 mg/kg arm) and 7 (for 30 mg/kg arm)

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	6	8
Units: hour				
arithmetic mean (standard deviation)	1.79 (± 0.325)	1.92 (± 0.338)	1.77 (± 0.495)	1.95 (± 0.312)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1: Renal Clearance (CLR) of Golodirsen

End point title	Part 1: Renal Clearance (CLR) of Golodirsen

End point description:

Renal clearance was calculated using the partial AUC0-24 from the non-compartmental analysis in plasma and AE0-24. AUC0-24 was defined as area under the plasma concentration-time curve, from time 0 to 24 hours after completion of dosing. AE0-24 was defined as total cumulative amount excreted from 0 to 24 hours. Summarized data of all urine collection intervals were reported. PK set consisted of all randomised subjects from Part 1 who received the planned full dose of study drug and for whom there were adequate PK samples from which to estimate PK parameters. Here, "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for placebo arm.

End point type	Secondary

End point timeframe:

0 to 1440 min after initiation of dosing on Day 1

End point values	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	8	7	8
Units: L/hr/kg				
geometric mean (geometric coefficient of variation)	0.345 (± 31.9)	0.370 (± 50.6)	0.355 (± 42.1)	0.374 (± 26.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2a: Percent Change from Baseline in Forced Vital Capacity Predicted (FVC %p) to Week144 in Total Golodirsen Group

End point title	Part 2a: Percent Change from Baseline in Forced Vital Capacity Predicted (FVC %p) to Week144 in Total Golodirsen Group[13]

End point description:

FVC is the total amount of air exhaled during the forced expiratory volume test that was measured during spirometry; and was the most important measurement of lung function. This test requires subject to breath into a tube connected to a machine that measures the amount of air that can be

moved in and out of the lungs after taking an inhaled bronchodilator medicine, which was used to dilate subjects bronchial (breathing) tubes. Percent of predicted FVC = (observed value)/ (predicted value) * 100%. Efficacy set consisted of all randomised subjects from Part 1 and all Part 2 subjects who had at least 1 post-baseline functional assessment. Here, "number of subjects analysed" signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 144

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percent change				
arithmetic mean (standard deviation)	-8.382 (± 29.4566)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2a: Change from Baseline in Dystrophin Intensity Levels Determined by Immunohistochemistry (IHC) at Week 48 in Total Golodirsen Group

End point title	Part 2a: Change from Baseline in Dystrophin Intensity Levels Determined by Immunohistochemistry (IHC) at Week 48 in Total Golodirsen Group[14]

End point description:

Change from baseline in dystrophin Intensity levels (in muscle biopsy samples) was determined by Immunohistochemistry in total golodirsen group. Muscle biopsy set included all subjects who received at least 1 dose of study drug and who had data from both baseline (pre-treatment) and Part 2 Week 48 (on-treatment) muscle biopsy samples. Data for this endpoint was not planned to be collected and analysed for untreated group (Natural History of Non-exon 53).

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent dystrophin positive fibers				
arithmetic mean (standard deviation)	0.023 (± 0.0243)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2a: Percent Change from Baseline in Exon 53 Skipping Determined by Reverse Transcription Polymerase Chain Reaction (PCR) at Week 48 in Total Golodirsen Group

End point title	Part 2a: Percent Change from Baseline in Exon 53 Skipping Determined by Reverse Transcription Polymerase Chain Reaction (PCR) at Week 48 in Total Golodirsen Group[15]

End point description:

Percent change from baseline in Exon 53 skipping (in muscle biopsy samples) was determined by reverse transcription polymerase chain reaction in total golodirsen group. Muscle biopsy set included all subjects who received at least 1 dose of study drug and who had data from both baseline (pre-treatment) and Part 2 Week 48 (on-treatment) muscle biopsy samples. Data for this endpoint was not planned to be collected and analysed for untreated group (Natural History of Non-exon 53).

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent change				
arithmetic mean (standard deviation)	16.363 (± 10.6223)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2a: Percent Change from Baseline in Dystrophin Positive Fibers Determined by Immunohistochemistry (IHC) at Week 48 in Total Golodirsen Group

End point title	Part 2a: Percent Change from Baseline in Dystrophin Positive Fibers Determined by Immunohistochemistry (IHC) at Week 48 in Total Golodirsen Group[16]

End point description:

Percent change from baseline in dystrophin positive fibers (in muscle biopsy samples) were determined by Immunohistochemistry at Week 48 in total golodirsen group. Muscle biopsy set included all subjects who received at least 1 dose of study drug and who had data from both baseline (pre-treatment) and Part 2 Week 48 (on-treatment) muscle biopsy samples. Data for this endpoint was not planned to be

collected and analysed for untreated group (Natural History of Non-exon 53).

End point type	Secondary

End point timeframe:

Baseline, Week 48

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Total Golodirsen group.

End point values	Part 2a: Total Golodirsen Group			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percent change				
arithmetic mean (standard deviation)	12.508 (± 14.6012)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 2b: Percent Change From Baseline in Forced Vital Capacity Predicted (FVC%p) at Week144 in Untreated Group (Natural History of Non-exon 53)

End point title	Part 2b: Percent Change From Baseline in Forced Vital Capacity Predicted (FVC%p) at Week144 in Untreated Group (Natural History of Non-exon 53)[17]

End point description:

FVC is the total amount of air exhaled during the forced expiratory volume test that is measured during spirometry; and is the most important measurement of lung function. This test required subject to breath into a tube connected to a machine that measures the amount of air that can be moved in and out of the lungs after taking an inhaled bronchodilator medicine which is used to dilate subject's bronchial (breathing) tubes. Percent of predicted FVC = (observed value)/ (predicted value) * 100%. Efficacy set consisted of all randomised subjects from Part 1 and all Part 2 subjects who had at least 1 post-baseline functional assessment. Here, "number of subjects analysed" signifies number of subjects who were evaluable for this end point.

End point type	Secondary

End point timeframe:

Baseline, Week 144

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analysed only for Untreated Group (Natural History of Non-exon 53).

End point values	Part 2b: Untreated Group (Natural History of Non-exon 53)			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: percent change				

arithmetic mean (standard deviation)	-6.739 (± 17.5278)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration up to 189 weeks

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Part 1: Placebo

Reporting group description:

Subjects received placebo-matched to golodirsen IV infusions, once weekly for up to 12 weeks in Part 1.

Reporting group title	Part 1: Golodirsen (4 mg/kg)

Reporting group description:

Subjects received golodirsen IV infusions, at dose level of 4 mg/kg, once weekly for 2 weeks in Part 1.

Reporting group title	Part 1: Golodirsen (10 mg/kg)

Reporting group description:

Subjects received golodirsen IV infusions, at a dose level of 10 mg/kg, once weekly for the next 2 weeks (i.e., up to Week 4) in Part 1.

Reporting group title	Part 1: Golodirsen (20 mg/kg)

Reporting group description:

Subjects received golodirsen IV infusions, at a dose level of 20 mg/kg, once weekly for the next 2 weeks (i.e., up to Week 6) in Part 1.

Reporting group title	Part 1: Golodirsen (30 mg/kg)

Reporting group description:

Subjects received golodirsen IV infusions, at a dose level of 30 mg/kg, once weekly from Week 7 to Week 12 in Part 1.

Reporting group title	Part 2a: Total Golodirsen Group

Reporting group description:

All subjects from Part 1 (who previously received placebo or golodirsen) and including additional new subjects received golodirsen 30 milligram (mg)/kilogram (kg) once weekly, for up to 168 weeks in Part 2. Dosing was interrupted or halted when any specific predefined stopping criteria was met or if warranted at the discretion of the Sponsor or Investigator.

Reporting group title	Part 2b: Untreated Group (Natural History of Non-exon 53)

Reporting group description:

Untreated subjects intended to evaluate the natural history of the disease with DMD and various genetic mutations (not amenable to exon 53 skipping) were included in this group and did not received any treatment. Subjects underwent the same study assessments as treated subjects in other reporting groups (except for pharmacokinetic [PK] sampling and muscle biopsies), but at a reduced schedule through Week 144. Thus, the untreated subjects are not considered a control group.

Serious adverse events	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth development disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)	Part 2a: Total Golodirsen Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth development disorder			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 2b: Untreated Group (Natural History of Non-exon 53)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tooth development disorder			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part 1: Placebo	Part 1: Golodirsen (4 mg/kg)	Part 1: Golodirsen (10 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 8 (62.50%)	5 / 8 (62.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Haemangioma of skin			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 8 (25.00%)	1 / 8 (12.50%)
occurrences (all)	6	2	1
Abasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site bruise			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Infusion site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Choking			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Aggression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Panic attack			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0

Investigations			
Vitamin D decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	2 / 4 (50.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	12	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Back injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Joint injury			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Glossitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Tooth discolouration			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pruritus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Petechiae			
subjects affected / exposed	0 / 4 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	3	1	0
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	3	1	0
Influenza			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hordeolum			

subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchiolitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Scarlet fever			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 4 (25.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1: Golodirsen (20 mg/kg)	Part 1: Golodirsen (30 mg/kg)	Part 2a: Total Golodirsen Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)	6 / 8 (75.00%)	25 / 25 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	6
Haemangioma of skin			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Haematoma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	4 / 8 (50.00%)	13 / 25 (52.00%)
occurrences (all)	1	16	33
Abasia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	4
Catheter site bruise			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	3 / 25 (12.00%)
occurrences (all)	0	2	4
Catheter site pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	1	0	5
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	7
Infusion site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	4
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Peripheral swelling			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Catheter site related reaction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 8 (0.00%)	3 / 8 (37.50%)	16 / 25 (64.00%)
occurrences (all)	0	12	57
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	12 / 25 (48.00%)
occurrences (all)	0	6	43
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	6 / 25 (24.00%)
occurrences (all)	0	2	11
Choking			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	2 / 25 (8.00%)
occurrences (all)	0	4	3
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Pharyngeal erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Productive cough			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Stress			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Aggression			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Investigations			
Vitamin D decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Platelet count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	9 / 25 (36.00%)
occurrences (all)	0	2	13
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	6 / 25 (24.00%)
occurrences (all)	0	0	18
Limb injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	6 / 25 (24.00%)
occurrences (all)	0	0	7
Scratch			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	6 / 25 (24.00%)
occurrences (all)	0	0	9
Arthropod bite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	4 / 25 (16.00%)
occurrences (all)	0	2	5
Back injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	4 / 25 (16.00%)
occurrences (all)	0	2	7
Ligament sprain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	6
Procedural pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	5
Head injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	3 / 25 (12.00%)
occurrences (all)	0	2	4
Joint injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	4
Muscle strain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Spinal compression fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Hand fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Ventricular dysfunction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	3 / 8 (37.50%)	11 / 25 (44.00%)
occurrences (all)	1	12	51
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Dizziness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	3
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	4
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	7 / 25 (28.00%)
occurrences (all)	0	4	21
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	2 / 25 (8.00%)
occurrences (all)	0	2	4
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	1 / 8 (12.50%)	15 / 25 (60.00%)
occurrences (all)	1	2	38
Diarrhoea			

subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	14 / 25 (56.00%)
occurrences (all)	0	2	29
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	9 / 25 (36.00%)
occurrences (all)	0	0	19
Abdominal pain upper			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	9 / 25 (36.00%)
occurrences (all)	1	4	25
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	10
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	6
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Gingival pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Glossitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Tooth discolouration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 8 (0.00%)	6 / 25 (24.00%)
occurrences (all)	1	0	8
Ecchymosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	8
Dry skin			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	4
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Petechiae			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Rash papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	11 / 25 (44.00%)
occurrences (all)	0	4	16

Back pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	10 / 25 (40.00%)
occurrences (all)	0	4	38
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	9 / 25 (36.00%)
occurrences (all)	0	2	26
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	2 / 8 (25.00%)	16 / 25 (64.00%)
occurrences (all)	0	4	31
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	13 / 25 (52.00%)
occurrences (all)	0	2	39
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	8 / 25 (32.00%)
occurrences (all)	0	2	14
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	5 / 25 (20.00%)
occurrences (all)	0	0	7
Ear infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	4
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Gastroenteritis viral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	4
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	4
Oral herpes			

subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Device related infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	3
Viral infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Bronchiolitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Scarlet fever			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Iron deficiency			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2b: Untreated Group (Natural History of Non-exon 53)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 14 (71.43%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Haemangioma of skin			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abasia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Catheter site bruise			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infusion site pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Catheter site related reaction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 14 (21.43%)		
occurrences (all)	3		
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Choking			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pharyngeal erythema			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Stress			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Aggression			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

Investigations			
Vitamin D decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Platelet count increased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Arthropod bite			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Back injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Procedural pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Joint injury			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hand fracture			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ventricular dysfunction			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Anaemia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	 0 / 14 (0.00%) 0		
Eye disorders Eye pain subjects affected / exposed occurrences (all)	 0 / 14 (0.00%) 0		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	 1 / 14 (7.14%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2		
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0		
Rectal haemorrhage			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gingival pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Glossitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Tooth discolouration			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pruritus			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Petechiae			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Influenza			

subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Ear infection				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Gastroenteritis viral				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Otitis media				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	2 / 14 (14.29%)			
occurrences (all)	2			
Tonsillitis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Device related infection				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Hordeolum				

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Bronchiolitis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Scarlet fever			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2014	Amendment 1: Added the occurrence of greater than or equal to (>=) 2 severe AEs to the stopping rules. Added that if interruption of dosing was warranted at the discretion of Sarepta or Investigation, re-initiation of dosing was permitted, if deemed appropriate following safety data review by Sarepta.
19 November 2014	Amendment 2: Changed magnetic resonance imagings (MRIs) to optional at 12 weeks and 24 weeks for the untreated control group in Part 2. Removed the Week 36 leg muscle MRI for both treated and untreated groups in Part 2. Removed the untreated control group Part 2 Week 1 functional assessments for North Star Ambulatory Assessment (NSAA), 6MWT, pulmonary function tests, and the timed 4-step. Removed the assessment of vital signs for the untreated control group from Weeks 5 to 7, 9 to 11, 13 to 15, 17 to 19, 21 to 23, 25 to 35, and 37 to 47. Updated language for the untreated control group functional assessments in Study Assessments. Clarified that subjects in the untreated control group could have been enrolled concurrently in an observational study, unless it interfered with assessments in this study. Corrected the concentration of the human equivalent dose in Rationale for Initial Dose.
07 April 2015	Amendment 3: Changed the stopping rule regarding increases in serum creatinine to take into account the natural variability of serum creatinine levels observed in DMD subjects and to reflect the standard practice of requiring a confirmatory laboratory test for changes in test results. Reduced the frequency of assessments for the untreated control group in Part 2 of the study in order to reduce the burden on subjects and parents in this group. Separated the informed consent from the inclusion/exclusion criteria assessments. Removed the assessment of anti-PMO antibodies from the study.
09 October 2015	Amendment 4: Added an Extension Phase to Part 2, which extended the Part 2 treatment period by 96 weeks and defined the end of study as Week 148 (144 weeks of treatment and a follow-up safety visit 4 weeks after the last on-study dose). This included adding a schedule of assessments for the safety extension phase in Part 2.

20 April 2016	Amendment 5: Part 2 and the Part 2 Extension Phase, which was added in Amendment 4, were combined. In addition, the comparison period between treated subjects and untreated control subjects was extended from Week 48 (original end of Part 2) to Week 144 (end of Extension Phase of Part 2). Clarified that new subjects in Part 2 were treatment-naïve. Added specific information on requirements for muscle biopsies at Week 48. Clarified that modifications to dose based on weight was acceptable, provided the dose was equivalent. Removed RT-PCR as the methodology used to determine exon 53 skipping. Included immunogenicity in safety endpoints. Clarified strategy for interim review of safety and efficacy data by the DSMB. Changed that magnetic resonance scans were to be performed at Baseline and Week 12 of Part 1, not at Week 1. Added the collection of blood samples at Week 1 prior to the first infusion to provide a baseline for biomarkers and immunogenicity. Clarified that control subjects were to undergo all procedures at Screening and Baseline except for skin/muscle biopsies. Added MoviPlate to Screening/Baseline assessments. Added language regarding an interim analysis and specified that safety data were to be reviewed in an ongoing basis by the DSMB.
20 October 2016	Amendment 6: Removed actimetry as an endpoint due to problems with the measurement device (ActiMyo).
21 April 2017	Amendment 7: Added text to distinguish the difference between efficacy and biological (ie, pharmacodynamics) endpoints. Switched the primary biological endpoint (percentage of dystrophin-positive fibers) with a secondary biological endpoint (dystrophin protein levels by Western blot).
08 November 2017	Amendment 8: Extended the treatment period for golodirsen-treated subjects from 144 weeks to 168 weeks, thereby also extending the total study duration for golodirsen-treated subjects from 166 weeks to 190 weeks. Added the option of actimetry assessment at Week 144 (±2 weeks) using a newly available version of the ActiMyo device. Specified that forced vital capacity% was the key respiratory function endpoint. Added an interim analysis to permit muscle biopsy analysis after the last biopsy was collected (i.e, after all golodirsen-treated subjects from Part 1 and Part 2 had completed the Week 48 muscle biopsy in Part 2).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported