Clinical trial results:
Systemic Gene Delivery Phase I/IIa Clinical Trial for Duchenne Muscular Dystrophy Using rAAVrh74.MHCK7.micro-dystrophin (microDys-IV-001)

Summary

EudraCT number	2021-000077-83
Trial protocol	Outside EU/EEA
Global end of trial date	25 April 2023

Results information

Result version number	v1 (current)
This version publication date	14 December 2023
First version publication date	14 December 2023

Trial information

Trial identification

Sponsor protocol code	SRP-9001-101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03375164
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., 1 888-727-3782, SareptAlly@sarepta.com
Scientific contact	Medical Director, Sarepta Therapeutics, Inc., 1 888-727-3782, SareptAlly@sarepta.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002677-PIP01-19
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is the assessment of the safety of intravenous (IV) administration of delandistrogene moxeparvovec (SRP-9001/microDys-IV-001) for DMD participants via peripheral limb vein.

Protection of trial subjects:

Written informed consent from each subject or subjects 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	04 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	4
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	4
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In total, 4 participants were screened for the study. There were no screen failures.

Period 1

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

Arms

Arm title	Delandistrogene Moxeparvovec

Arm description:

Participants received a single IV infusion of delandistrogene moxeparvovec on Day 1.

Arm type	Experimental
Investigational medicinal product name	delandistrogene moxeparvovec
Investigational medicinal product code	SRP-9001
Other name	SRP-9001, delandistrogene moxeparvovec-rokl, ELEVIDYS, rAAVrh74.MHCK7.micro-dystrophin, microDys-IV-001
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion

Number of subjects in period 1	Delandistrogene Moxeparvovec
Started	4
Received at Least 1 Dose of Study Drug	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Delandistrogene Moxeparvovec

Reporting group description:

Participants received a single IV infusion of delandistrogene moxeparvovec on Day 1.

Reporting group values	Delandistrogene Moxeparvovec	Total	
Number of subjects	4	4	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	4	4	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	5.14		
standard deviation	± 0.91	-	
Gender Categorical Units: Subjects			
Female	0	0	
Male	4	4	

Subject analysis sets

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

all participants who received study treatment.

Reporting group values	Full Analysis Set		
Number of subjects	4		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	4		
Adolescents (12-17 years)	0		

Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	±		
Gender Categorical			
Units: Subjects			
Female	0		
Male	4		

End points

End points reporting groups

Reporting group title	Delandistrogene Moxeparvovec
Reporting group description: Participants received a single IV infusion of delandistrogene moxeparvovec on Day 1.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description: all participants who received study treatment.	

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[1]
End point description: An AE is any untoward medical occurrence in a clinical study participant that does not necessarily have a causal relationship with the study drug. An AE can, therefore, be any unfavorable and unintended symptom, sign, disease, condition, or test abnormality that occurs during or after administration of a study drug, whether or not considered related to the study drug. A summary of serious and all other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.	
End point type	Primary
End point timeframe: Up to 5 years	

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 pre-specified statistical analysis was carried out for this end point.

End point values	Delandistrogene Moxeparvovec			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: participant	4			

Notes:

[2] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by Western Blot

End point title	Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by Western Blot
End point description: Baseline muscle biopsies with ultrasound guidance were performed pre-treatment and post-treatment (Day 90) on all participants. The change from baseline in delandistrogene moxeparvovec dystrophin protein levels in these muscle biopsy samples was determined by Western blot. An increase in protein expression indicates production of the delandistrogene moxeparvovec dystrophin protein.	
End point type	Secondary
End point timeframe: Baseline, Day 90	

End point values	Delandistrogene Moxeparvovec			
Subject group type	Reporting group			
Number of subjects analysed	4[3]			
Units: percent control				
arithmetic mean (standard deviation)	70.52 (± 76.10)			

Notes:

[3] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Year 5 in the 100 Meter Timed Test

End point title	Change From Baseline at Year 5 in the 100 Meter Timed Test

End point description:

This assessment measures the time needed to move 100 meters and served as the primary motor outcome measure for this study. A decrease in the time needed to move 100 meters indicates increased motor function.

End point type	Secondary

End point timeframe:

Baseline, Year 5

End point values	Delandistrogene Moxeparvovec			
Subject group type	Reporting group			
Number of subjects analysed	4[4]			
Units: second				
arithmetic mean (standard deviation)	-4.02 (± 4.64)			

Notes:

[4] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by IF Percent Dystrophin Positive Fibers (PDPF)

End point title	Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by IF Percent Dystrophin Positive Fibers (PDPF)

End point description:

Baseline muscle biopsies with ultrasound guidance were performed pre-treatment and post-treatment (Day 90) on all participants. The change from baseline in delandistrogene moxeparvovec dystrophin

expression in these muscle biopsy samples was determined by IF PDPF. Automated software was used to quantify the intensity of dystrophin expression post-treatment compared to pre-treatment (Percent Normal). The number of muscle fibers expressing micro-dystrophin was quantified by independent trained evaluators. An increase in IF PDPF indicates increased delandistrogene moxeparvovec dystrophin expression.

End point type	Secondary

End point timeframe:

Baseline, Day 90

End point values	Delandistrogene Moxeparvovec			
Subject group type	Reporting group			
Number of subjects analysed	4[5]			
Units: percent dystrophin positive fibers				
arithmetic mean (standard deviation)	81.18 (± 10.19)			

Notes:

[5] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by Immunofluorescence (IF) Fiber Intensity

End point title	Change From Baseline at Day 90 in Delandistrogene Moxeparvovec Dystrophin Expression as Measured by Immunofluorescence (IF) Fiber Intensity

End point description:

Baseline muscle biopsies with ultrasound guidance were performed pre-treatment and post-treatment (Day 90) on all participants. The change from baseline in delandistrogene moxeparvovec dystrophin expression in these muscle biopsy samples was determined using IF. Automated software was used to quantify the intensity of dystrophin expression post-treatment compared to pre-treatment (Percent Normal). The number of muscle fibers expressing micro-dystrophin was quantified by independent trained evaluators. An increase in IF fiber intensity indicates increased delandistrogene moxeparvovec dystrophin expression.

End point type	Secondary

End point timeframe:

Baseline, Day 90

End point values	Delandistrogene Moxeparvovec			
Subject group type	Reporting group			
Number of subjects analysed	4[6]			
Units: percent fluorescent expression				
arithmetic mean (standard deviation)	93.59 (± 43.86)			

Notes:
[6] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 5 years	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1
Reporting groups	
Reporting group title	Delandistrogene Moxeparvovec
Reporting group description: Participants received a single IV infusion of delandistrogene moxeparvovec on Day 1.	

Serious adverse events	Delandistrogene Moxeparvovec		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Delandistrogene Moxeparvovec		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Fatigue subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Asthma subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 2 1 / 4 (25.00%) 1		
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Investigations Influenza A virus test positive subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 3 / 4 (75.00%) 4		
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all) Clavicle fracture subjects affected / exposed occurrences (all)	 2 / 4 (50.00%) 2 1 / 4 (25.00%) 1		
Cardiac disorders Cardiomyopathy subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 2		
Eye disorders			

Eye irritation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Gastrointestinal disorders Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2		
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Nausea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Anal incontinence subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Abdominal distension subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Vomiting subjects affected / exposed occurrences (all)	4 / 4 (100.00%) 15		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue			

disorders			
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Bone pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Infections and infestations			
Viral infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Subcutaneous abscess			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastroenteritis viral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	4 / 4 (100.00%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2017	Protocol Version 2.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
14 December 2017	Protocol Version 3.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
14 February 2018	Protocol Version 4.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
12 April 2018	Protocol Version 5.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
08 May 2018	Protocol Version 6.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
01 August 2018	Protocol Version 7.0 developed in Nationwide Children's Hospital without summary of changes and redline versions.
26 June 2019	- The protocol was transferred from the Nationwide Children's Hospital template to the Sarepta template. - The protocol was updated to reflect the change in responsibilities from investigator to sponsor.
25 August 2020	Study duration extended to 5 years in order to fulfill regulatory requirements to follow participants in a clinical trial setting for 5 years following therapeutic infusion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32539076

http://www.ncbi.nlm.nih.gov/pubmed/37577753