Sarepta - EMBARK

A Phase 3 Multinational, Randomized, Double-Blind, Placebo-Controlled Systemic Gene Delivery Study to Evaluate the Safety and Efficacy of SRP-9001 in Patients With Duchenne Muscular Dystrophy (EMBARK)

Hub Summary

This study will evaluate the safety and efficacy of gene transfer therapy in boys aged between 4 and 7 with DMD. It is a randomized, double-blind, placebo-controlled study. The participants who are randomized to the placebo arm will have an opportunity for treatment with gene transfer therapy at the beginning of the second year.

Study Number: NCT05096221

Description by Sarepta Therapeutics, Inc.

This is a randomized, double-blind, placebo-controlled 2-part study of systemic gene delivery of SRP-9001 in approximately 120 male DMD ambulatory subjects aged between 4 and 7 years of age. All patients will have the opportunity to receive intravenous (IV) SRP-9001 in either Part 1 or Part 2. The study will consist of 4 periods as follows:

• A Baseline Period (pre-infusion) which begins when eligibility is confirmed and ends on the day prior to the Day 1 infusion during which baseline assessments will be completed.

• Approximately 60 subjects will receive IV SRP-9001 and approximately 60 subjects will receive placebo (saline, 0.9% sodium chloride solution) in the Infusion Period in Part 1. In the Infusion Period in Part 2, subjects who received placebo in Part 1 will receive IV SRP-9001, and subjects who received SRP-9001 in Part 1 will receive placebo. All subjects, parents/caregivers, Investigators, and site staff, with the exception of the unblinded site pharmacist, will be blinded to subject treatment (SRP-9001 or placebo).

• A 104-week Follow-up Period (post Part 1infusion) during which safety and efficacy parameters will be evaluated in Part 1 and Part 2. Subjects will be expected to attend both remote and in-person visits to complete required procedures/assessments. Additional, unscheduled visits are allowed per the Investigator's clinical judgement. For subjects who complete the study, the last study visit will occur at Part 2 Week 52. For subjects who prematurely discontinue post-infusion follow-up, an end of study/early termination visit will be required; however, each subject

• Muscle biopsies are only required for those patients that enrol at a recruiting trial site carrying out biopsies (in the UK these location are Newcastle and London - GOSH).

• All patients who enrol at a trial site which is also an MRI site, must also participate in an MRI sub-study (In the UK this will be the following trial sites: Newcastle, Liverpool - Alder Hey, and London - GOSH.

Primary Outcome Measures

1. Part 1: Change From Baseline in NSAA Total Score at Week 52 [Time Frame: Baseline, Week 52]

Secondary Outcome Measures

1. Part 1: Quantity of Micro-Dystrophin Protein Expression at Week 12 as Measured by Western Blot, in a Subset of Participants
   [Time Frame: Week 12]
2. Part 1: Change From Baseline in Time to Rise From the Floor, Time to Complete 100 and 10 meter Walk/Run, and the Timed Stair Ascend 4 Steps Test at Week 52 [Time Frame: Baseline, Week 52]

Trial Status
Trial complete

UK Locations
London - GOSH, Trial complete/terminated, Newcastle, Trial complete /terminated, Oxford, Trial complete/terminated

Trial Sponsor
Sarepta Therapeutics, Inc.

Phase
3

Length Of Participation
108 Weeks

Recruitment Target
120 participants

Ambulatory
Ambulant

Therapeutic Category
Gene Therapy

Age
4 to 7 Years

Mutation Specific
Mutation specific therapies, A pathogenic frameshift mutation or premature stop codon contained between exons 18 and 79 (inclusive), with the exception of mutation fully contained within exon 45.

Muscle Biopsy
Muscle Biopsy Required

MRI
Yes

3. Part 1: Change From Baseline in Stride Velocity 95th Centile (SV95C) Measured by a Wearable Device [Time Frame: Baseline up to Week 52]
4. Part 1: Change from Baseline in Patient-Reported Outcomes Measurement Information (PROMIS) Score per Domain at Week 52 [Time Frame: Baseline, Week 52]

   PROMIS is a family of instruments developed and validated to assess health-related quality of life. Parents will be asked "Taking into account all aspects of your child's observable symptoms, physical ability, ability to perform daily activities and overall health, how would you rate the change in clinical status for your child since the study start? using the following rating scale 1=very much improved, 2=much improved, 3=minimally improved, 4=no change, 5=minimally worse, 6=much worse, and 7=very much worse."

5. Part 1: Number of Skills Gained or Improved at Week 52 as Measured by the NSAA [Time Frame: Baseline up to Week 52]
6. Number of Participants with a Treatment Emergent Adverse Event (TEAE), Serious Adverse Event (SAE), and Adverse Event of Special Interest (AESI) [Time Frame: Baseline up to Week 52]

Can I take part?

Inclusion Criteria

- ✔ Is ambulatory and from 4 to under 8 years of age at time of randomization.
- ✔ Definitive diagnosis of DMD based on documented clinical findings and prior genetic testing.
- ✔ Ability to cooperate with motor assessment testing.
- ✔ Stable daily dose of oral corticosteroids for at least 12 weeks prior to Screening, and the dose is expected to remain constant throughout the study (except for modifications to accommodate changes in weight).
- ✔ rAAVrh74 antibody titers are not elevated as per protocol-specified requirements.
- ✔ A pathogenic frameshift mutation or premature stop codon contained between exons 18 and 79 (inclusive), with the exception of mutation fully contained within exon 45.

Exclusion Criteria

- ✖ Exposure to gene therapy, investigational medication, or any treatment designed to increase dystrophin expression within protocol specified time limits.
- ✖ Abnormality in protocol-specified diagnostic evaluations or laboratory tests.
- ✖ Presence of any other clinically significant illness, medical condition, or requirement for chronic drug treatment that in the opinion of the Investigator creates unnecessary risk for gene transfer.

Other inclusion or exclusion criteria could apply.

For contact details and to find out more, please refer to dmdhub.org.

Duchenne UK