Plain Language Study Summary

SRP-9001-105 (HORIZON): A study to evaluate the safety and efficacy of delandistrogene moxeparvovec (SRP-9001), a gene transfer therapy, following therapeutic plasma exchange (plasmapheresis) in participants with Duchenne muscular dystrophy (DMD) and pre-existing antibodies to AAVrh74

Sarepta would like to thank the study participants and their families for taking part in this study.

This study was ended earlier than originally planned. This decision was not related to safety. Because the study ended early, the data were not able to be fully analyzed in the way that was initially planned.

Sarepta created this summary to share with the participants, their family members, and the general public. The goals of this summary are to help explain why and how the study was done and to share what researchers learned from the study participants. Sarepta hopes this helps people understand the important role that the study participants played in helping researchers find better ways to treat Duchenne.

If you have questions about this summary, please feel free to email Sarepta (advocacy@sarepta.com) or, if you were a participant, talk to your study doctor.

What is Duchenne?

Duchenne muscular dystrophy, or **Duchenne** for short, is a rare disease that affects mostly males. People with Duchenne have a **genetic mutation** that limits their ability to make a protein called **dystrophin**. Dystrophin plays an important role in protecting and strengthening muscles. Without the ability to make dystrophin, people with Duchenne have muscle weakness in many parts of the body that gets worse with time. Duchenne is an irreversible, progressive disease.

What are genetic mutations?
Genes are like tiny instruction manuals contained in the body's cells. Genes tell the cells how to make different kinds of proteins. Proteins play lots of different roles in keeping the body healthy and strong. If someone has a genetic mutation, it means there is a problem with the instructions for making a protein.

Why was this study done?

This study was done to learn whether a treatment for Duchenne called delandistrogene moxeparvovec can be given to people who have elevated levels of antibodies that currently make them ineligible for this treatment.

Delandistrogene moxeparvovec (also known as SRP-9001) is a type of treatment called **gene therapy**. It is given as a one-time **intravenous (IV) infusion** (through a needle in the vein).

Each infusion of delandistrogene moxeparvovec contains many copies of a gene that has instructions for how to make a shorter form of dystrophin called **delandistrogene moxeparvovec dystrophin**. Each copy of the gene is delivered using a special carrier called a **vector**. The vector, which is called **rAAVrh74**, acts like a delivery vehicle that helps get the gene to the right place in the body's cells. Once the new gene is inside the cell, the body can use it as an instruction manual to help make delandistrogene moxeparvovec dystrophin.

Some people have antibodies to vectors like rAAVrh74. **Antibodies** are proteins in the immune system. Their job is to protect the body from foreign substances, such as bacteria and viruses. But if a person has antibodies to a gene therapy vector, these antibodies could block the vector from delivering the gene therapy inside the body's cells.

Because of this, people who have high levels of antibodies to rAAVrh74 are not eligible to receive delandistrogene moxeparvovec.

Antibodies are made in **plasma** (the liquid part of the blood). One way to lower levels of antibodies is with a procedure called **plasmapheresis** (also known as therapeutic plasma exchange).

This study was done to learn whether plasmapheresis could help lower levels of antibodies to the rAAVrh74 vector.

If these antibodies could be removed before treatment with delandistrogene moxeparvovec, it might let

Plasmapheresis involves continuously:

- collecting a person's blood,
- separating the plasma from the other parts of the blood (such as red and white blood cells),
- replacing the removed plasma with a fluid that does not contain the antibodies, and then
- returning the blood to the person receiving treatment.

A single plasmapheresis treatment session typically takes a few hours.

delandistrogene moxeparvovec enter the muscle cells, allowing the muscle cells to make delandistrogene moxeparvovec dystrophin.

Who took part?

This study included males with Duchenne who were between 4 and 8 years old and who had elevated levels of rAAVrh74 antibodies. There were 3 people who joined the study, which took place in the United States.

What was the study plan?

The participants started the study with a plasmapheresis treatment session. Afterward, study doctors measured the levels of rAAVrh74 antibodies in each participant's blood. If a participant's antibody level was low enough after the fourth session, the participant would be eligible to receive delandistrogene moxeparvovec a couple of days later following 1 more session of plasmapheresis. If a participant's antibody level was not low enough, they could try again a couple of days later after another plasmapheresis session.

If a participant's antibody level was not low enough after 5 plasmapheresis sessions, the participant would not be eligible for treatment with delandistrogene moxeparvovec.

How are antibody levels measured?

To measure antibody levels, researchers start with a blood sample. The blood sample is diluted with a solution. When you "dilute" something, you add a liquid to it to make it less concentrated, sort of like adding water to lemonade. The more water you add, the weaker (less concentrated) the lemonade will be.

In an antibody test, a specific amount of solution is added to a blood sample. If the concentration of antibodies in the diluted mixture is low enough, the antibody test will not be able to detect them.

In this study, researchers used a 1:400 dilution. This means that the amount of blood in the blood sample was mixed (diluted) with 400 times that amount of solution.

If the concentration of antibodies in this mixture was low enough that the antibody test could not detect them, this meant that the participant's antibody levels had dropped enough that they could go on to receive delandistrogene moxeparvovec.

If the test could still detect the antibodies, this meant that the participant's antibody levels were still too high, and they would not be eligible to receive delandistrogene moxeparvovec.

After treatment, participants were asked to stay in the study for up to a year so that study doctors could keep track of their long-term health outcomes.

This study started in September 2024 and ended early in August 2025. Even though the study ended early, study doctors continue to monitor the health of the participants who received study treatment.

What were the main goals of the study?

A main goal of this study was to learn whether using plasmapheresis to lower rAAVrh74 antibody levels would allow delandistrogene moxeparvovec to be delivered into the participants' muscle cells so that those muscle cells could make delandistrogene moxeparvovec dystrophin.

To help researchers learn this, the participants provided small amounts of muscle tissue in a procedure called a **biopsy**.

Each biopsy sample provided critical information to the study researchers because it let them measure:

- how many copies of the delandistrogene moxeparvovec dystrophin gene were in the sample of muscle tissue, and
- the amount and location of the delandistrogene moxeparvovec dystrophin protein in the muscle tissue.

Another main goal of the study was to learn about the side effects of the study treatments. These are new or worsening medical events that happened during the study that the study doctors thought might have been related to treatment.

How has this study helped?

Even though this study ended early, the participants helped doctors, researchers, and health authorities learn more about using plasmapheresis to help patients with elevated rAAVrh74 antibodies receive delandistrogene moxeparvovec as a treatment for Duchenne. From the participants in this study, we learned:

- After plasmapheresis, 2 of the 3 participants had antibody levels that were low enough that they could receive delandistrogene moxeparvovec. The third participant, who had the highest antibody levels at the start of the study, did not have antibody levels that were low enough after plasmapheresis. This participant could not receive delandistrogene moxeparvovec.
- The 2 participants who received delandistrogene moxeparvovec then provided muscle tissue through a biopsy procedure. Both participants had increases in delandistrogene moxeparvovec dystrophin expression, with one participant at the lower end and one at the higher end of expression.
- Possible side effects of delandistrogene moxeparvovec in these 2 participants included:
    - Fever (both participants)
    - Vomiting (both participants)
    - Nausea (1 participant)
    - Flushing (1 participant)
    - Eye redness (1 participant)
    - A rapid heart rate (1 participant)

These findings were shared with the medical community at a recent scientific conference.

Where can I learn more about this study?

You can find more information about this study on the website listed below.

ClinicalTrials.gov: http://www.clinicaltrials.gov → On this website, type **NCT06597656** into one of the search boxes and click "Search".

Full study title: An Open-Label, Systemic Gene Delivery Study to Evaluate the Safety, Tolerability and Expression of Delandistrogene Moxeparvovec Following Plasmapheresis in Subjects with Duchenne Muscular Dystrophy and Pre-existing Antibodies to AAVrh74 (HORIZON)

Protocol number: SRP-9001-105

Sponsor: Sarepta Therapeutics, Inc.
Email: advocacy@sarepta.com
Phone: 1-888-SAREPTA (1-888-727-3782), For clinical study information, select option 4

Thank you!

Sarepta is grateful for the participants who helped make this study happen. Clinical study participants help researchers and health authorities find answers to important health questions and discover new treatments for disease.