Plain Language Study Summary

SRP-9001-102: A Placebo-Controlled Clinical Study to Study the Effects of Delandistrogene Moxeparvovec as a Treatment for Duchenne Muscular Dystrophy

Sarepta would like to thank the study participants and their families for their participation in this study. Their contribution helped researchers learn more about delandistrogene moxeparvovec as a treatment for Duchenne muscular dystrophy.

Sarepta created this summary to share the results of the study with the participants, their family members, and the general public.

This summary only shows the results from this study. Other studies with delandistrogene moxeparvovec could have different results. Researchers evaluate results of many studies to understand which treatments work, how well they work, and how safe they are for patients.

This summary shows the overall results of this study. Results for each participant may have been different and are not part of this summary.

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

Here are the key parts of this summary:

If you are reading this on a computer, you can click on a topic below to skip to that section.

Why was this study done?

Researchers are looking for better ways to treat **Duchenne muscular dystrophy**, or **Duchenne** for short. Duchenne 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.

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 have instructions for how to make a shorter form of dystrophin called **delandistrogene moxeparvovec dystrophin**. Each copy of the gene is packaged in a special carrier called a **vector**. The vector acts like a delivery vehicle that helps get the gene to the right place inside 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.

Not all gene therapies have the same components. The vector (rAAVh74) and the gene (delandistrogene moxeparvovec) in the treatment for this study are different than those used in other gene therapies.

This study was done to see if delandistrogene moxeparvovec could help people with Duchenne.

Who took part?

Researchers asked for the help of males with Duchenne. Everyone in this study was between 4 and 7 years old when they joined. There were 41 participants. This study was done in the United States.

What treatment was studied and what was the dose?

The treatment studied was delandistrogene moxeparvovec. All 41 participants got delandistrogene moxeparvovec, which is a one-time infusion.

In this study, different participants received different doses:

- 6 of 41 participants received a dose of 8.94×10^{13} vg/kg (89.4 trillion vg/kg)
- 6 of 41 participants received a dose of 6.29×10^{13} vg/kg (62.9 trillion vg/kg)
- The remaining 29 participants received a dose of 1.33×10^{14} vg/kg (133 trillion vg/kg)

What does this dose mean?

Another way to write **1.33×10^{14}** is 133 trillion. **vg** is short for vector genome (a vector genome has 1 copy of the gene that helps make delandistrogene moxeparvovec dystrophin). **kg** is short for kilograms of body weight. So, **vg/kg** is short for the number of vector genomes per kilogram of body weight, which means that the total number of vector genomes each participant received depended on how much they weighed in kilograms. 1 kilogram = 2.2 pounds.

What happened during the study?

The study was done in 3 parts – Part 1, Part 2, and Part 3.

In Part 1, about half of the participants got delandistrogene moxeparvovec. The other half got a dose of a **placebo**. The placebo was an infusion that looked like delandistrogene moxeparvovec but did not have any active ingredients. When participants receive a placebo in a clinical study, they follow the same steps and receive the same care as someone who gets the study treatment. The only difference is whether or not they get the study treatment. This helps researchers better understand the actual effects of the study treatment.

After participants got their assigned treatments in Part 1, study doctors kept track of the participants' health outcomes for about 1 year.

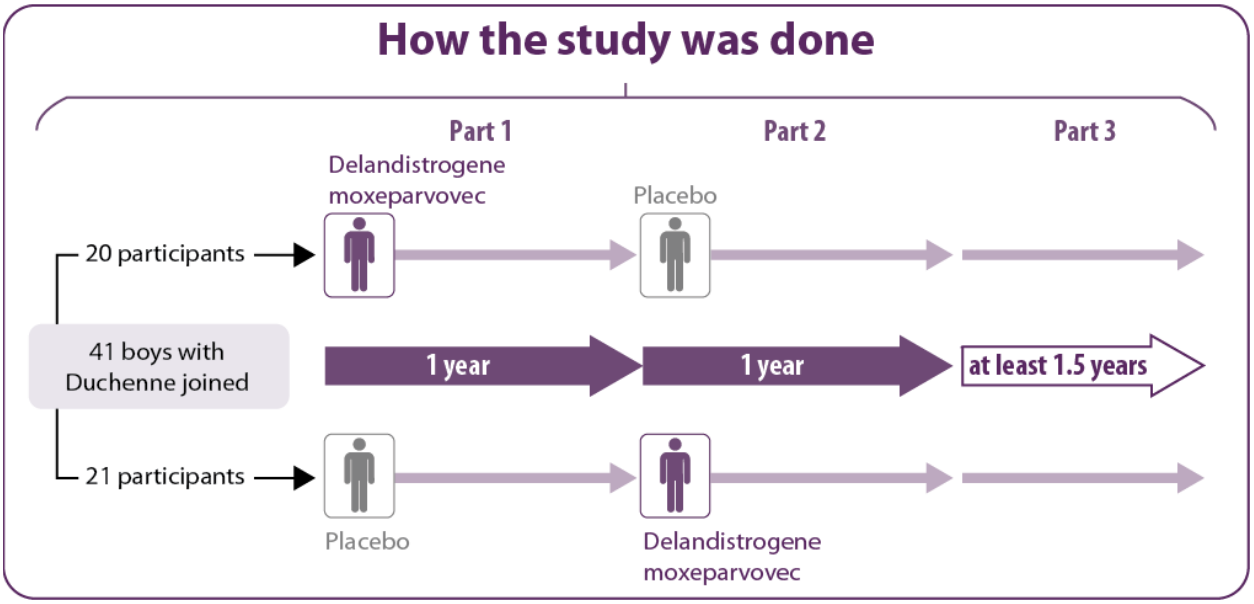
In Part 2, participants who got a dose of the placebo in Part 1 got delandistrogene moxeparvovec in Part 2. Participants who got delandistrogene moxeparvovec in Part 1 got a dose of the placebo in Part 2.

After participants got their assigned treatments in Part 2, study doctors kept track of the participants' health outcomes for about 1 year.

This was a **double-blind** study. This means that no one involved in the study, including participants, study doctors or the study sponsor, knew during the study which treatment each participant got in each part. Some studies are done this way because knowing what treatment a participant is getting can affect the results.

Researchers used a computer program to randomly assign the order in which participants received delandistrogene moxeparvovec and the placebo. This helped make sure the treatment order was assigned without bias to individual participants.

In Part 3, participants stayed in the study for at least another 1.5 years, to bring their total participation to at least 3.5 years. After their final study visit, participants were given the option to participate in a separate long-term follow-up study to keep track of their health outcomes.



Throughout the study, the participants visited a study site (one of the hospitals or research centers where this study was done) regularly.

During the study:

The participants:

- Got a check-up
- Gave blood and urine samples
- Completed different activities, such as walking or running, climbing steps, and getting up from the floor
- Had 3 muscle **biopsies** (one before treatment, one after 12 weeks in Part 1, and one after 12 weeks in Part 2)

What is a biopsy?

A biopsy is a procedure in which doctors collect a small amount of tissue. In this study, doctors collected samples of muscle tissue so they could measure how delandistrogene moxeparvovec dystrophin levels changed after treatment.

The participants and their families told study doctors about:

- How the participant was feeling
- Any new or worsening medical issues the participant might be having
- Any medications the participant was taking

What were the main goals of the study?

The main goals were to learn:

- **Whether participants who received delandistrogene moxeparvovec in Part 1 started to make delandistrogene moxeparvovec dystrophin.** Researchers looked at the biopsy samples collected before treatment and again in Part 1. They looked at how delandistrogene moxeparvovec dystrophin levels changed, on average, for participants who got delandistrogene moxeparvovec and compared this result with the change among participants who got a placebo.
- **Whether delandistrogene moxeparvovec helped participants in Part 1 with their physical function.** Study doctors used a scale, called the **North Star Ambulatory Assessment (NSAA)**, to measure each participant's physical function. Researchers looked at how physical function changed for participants from before treatment to the end of Part 1. They compared the results for participants who got delandistrogene moxeparvovec in Part 1 to the results for participants who got a placebo.

What is the NSAA?

The NSAA is a scale that measures a person's ability to perform 17 different activities, such as jumping, standing on one leg, and hopping on one foot. Each activity is scored on a scale from 0 to 2. The highest possible score is 34. Higher NSAA scores mean better physical function.

Another main goal was to learn about side effects of delandistrogene moxeparvovec. These were new or worsening medical events that happened during the study that the study doctors thought might be related to delandistrogene moxeparvovec. Study doctors kept close track of all the participants' health in Part 1, Part 2, and Part 3 to help understand the long-term effects of treatment.

What were the results?

This is a summary of the main results from Part 1 of the study. During Part 1, some participants received delandistrogene moxeparvovec and the other participants received the placebo (they had not yet received delandistrogene moxeparvovec). The researchers compared these results to understand the effects of the treatment.

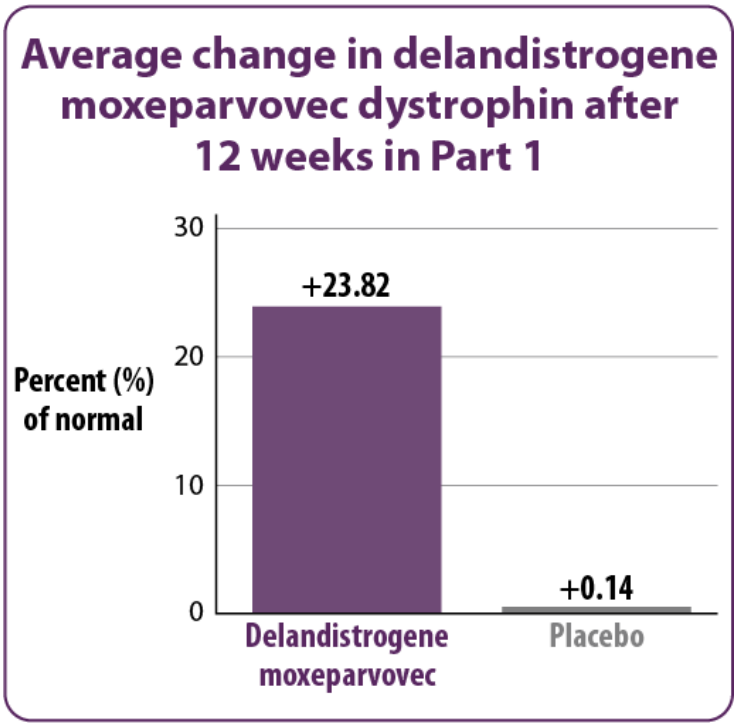
Results for each participant may have been different and are not in this summary.

You can find more information about this study – including additional results from the study – on the websites listed at the end of this summary.

Other studies with delandistrogene moxeparvovec could have different results.

Did participants who received delandistrogene moxeparvovec in Part 1 start to make delandistrogene moxeparvovec dystrophin?

Yes. Researchers compared the amount of delandistrogene moxeparvovec dystrophin present in the muscle biopsies that were collected before treatment and again after 12 weeks in Part 1.



What does this graph mean?

The amount of delandistrogene moxeparvovec dystrophin was measured with a lab test called a **western blot**. The result was shown as a percentage (fraction) of how much dystrophin researchers would expect to see in a muscle tissue sample from someone who does not have Duchenne.

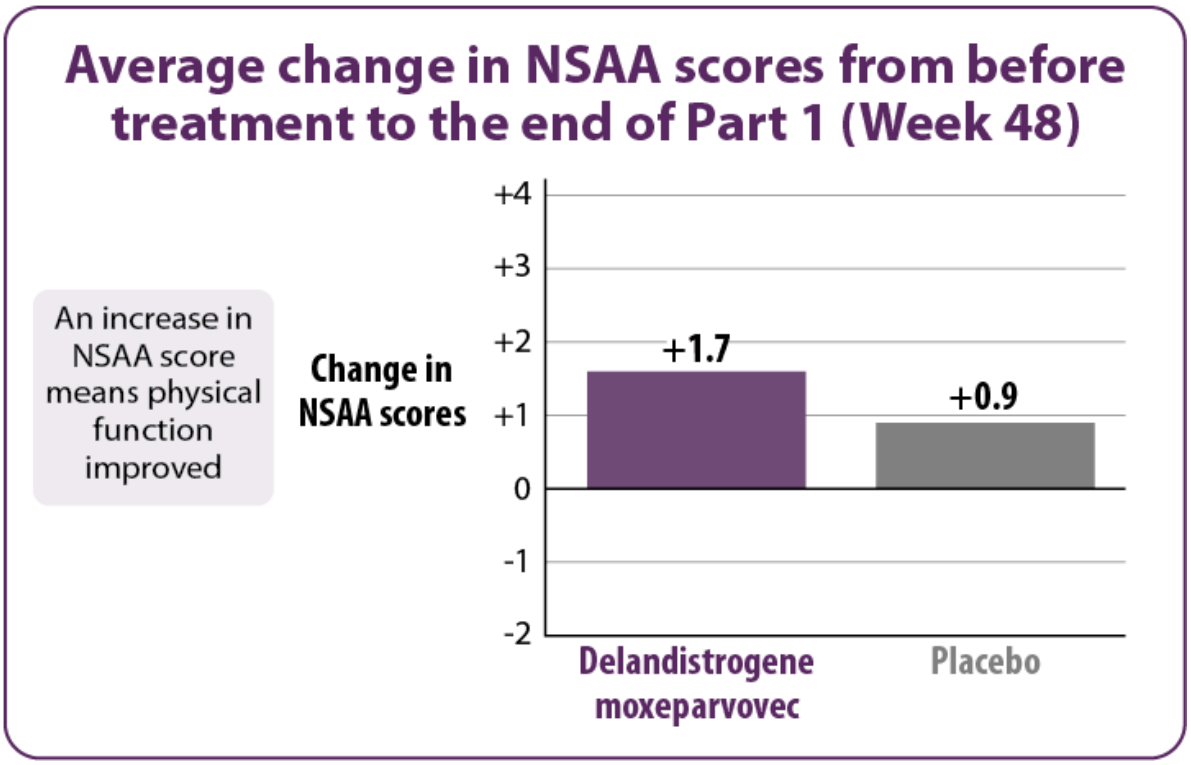
On average, the amount of delandistrogene moxeparvovec dystrophin in the muscle samples increased by 23.82% of normal after treatment with delandistrogene moxeparvovec.

Because there was not a similar change among participants who got a placebo, researchers know this increase happened because participants who got delandistrogene moxeparvovec started making delandistrogene moxeparvovec dystrophin.

Did delandistrogene moxeparvovec help participants in Part 1 with their physical function?

The picture below shows how NSAA scores changed, on average, for participants who got delandistrogene moxeparvovec and for participants who got a placebo in Part 1. The average increase in NSAA score was a bit greater with delandistrogene moxeparvovec than with a placebo. But the difference between these 2 groups was not considered "statistically significant".

In clinical studies, it is important for treatment groups to be as similar as possible at the start of the study. This way, any changes seen in one group that are not seen in the other are likely due to an effect of the treatment received. The researchers found that the average starting NSAA scores were not comparable between some participants who got delandistrogene moxeparvovec and for participants who got a placebo. Therefore, it is more difficult to interpret the effects of delandistrogene moxeparvovec on the NSAA results in this study.


Average change in NSAA scores from before treatment to the end of Part 1 (Week 48)
An increase in NSAA score means physical function improved
Change in NSAA scores
+4
+3
+2
+1
0
-1
-2
+1.7
+0.9
Delandistrogene moxeparvovec
Placebo

What side effects did the participants have?

These results describe the side effects that participants had during the study. These are new or worsening medical events that happened to participants during the study that the study doctors thought might be related to delandistrogene moxeparvovec.

Some side effects are considered "serious". Examples of serious side effects are those that are life threatening, need hospital care for treatment, or cause long-term medical problems or death.

Did the participants have any serious side effects? If so, what were they?

4 participants (10%) had at least 1 serious side effect. These were the serious side effects that happened during the study:

- 3 participants had rhabdomyolysis, which is a breakdown of muscle tissue. Two participants had rhabdomyolysis after getting delandistrogene moxeparvovec. One participant had rhabdomyolysis after getting a placebo in Part 1.
- 1 participant had temporary liver damage.
- 1 participant had high levels of transaminases in their blood. **Transaminases** are **enzymes** (a type of protein). High levels of transaminases are not a medical problem on their own, but they might be a sign of a problem in one of the body's organs, such as the liver.

None of the participants withdrew from the study due to a side effect. There were no deaths during the study.

Did the participants have any non-serious side effects? If so, what were they?

37 participants (90%) had non-serious side effects. The table below shows the most common non-serious side effects that happened during the study. Each of these side effects happened to at least 5% of the participants. There were other side effects, but they happened to fewer participants.

Side Effect	Out of 41 participants
Vomiting	28 (68%)
Decreased appetite	21 (51%)
Nausea	17 (42%)
Upper abdominal pain (pain in or around the stomach between the lower part of the chest and the area around the belly button)	11 (27%)
Increased levels of an enzyme called gamma-glutamyltransferase (increased levels of this enzyme in the blood might be a sign of a problem in the liver or other organs in the body)	11 (27%)
Fever	5 (12%)
Reduced levels of platelets (blood cells that help with clotting)	5 (12%)
Abdominal pain (pain anywhere between the chest and the groin)	4 (10%)
Increased levels of bilirubin (increased levels of bilirubin in the blood might be a sign of a problem in the liver or gallbladder)	4 (10%)
Increased levels of an enzyme called glutamate dehydrogenase (increased levels of this enzyme in the blood might be a sign of a problem in the liver or other organs in the body)	3 (7%)

What were the other results of the study?

The main goals of this study were to:

- Use a western blot test to measure whether treatment with delandistrogene moxeparvovec helped participants make delandistrogene moxeparvovec dystrophin
- Use the NSAA to learn whether changes in the participants' physical function were better after treatment with delandistrogene moxeparvovec than after treatment with a placebo
- Learn about possible side effects of delandistrogene moxeparvovec

In an effort to learn as much as possible about delandistrogene moxeparvovec as a treatment for Duchenne, the researchers also set other (secondary) goals. These included:

- Using other types of tests (in addition to the western blot) to measure delandistrogene moxeparvovec dystrophin in muscle tissue (biopsy samples)
- Looking at changes in the time it took for participants to complete different physical activities, such as the time it took to get off the floor or to climb 4 steps. These timed tests can serve as sensitive measures of disease progression. This is because they can change more quickly than NSAA scores and can be predictive of things like the loss of ability to walk.

This section is a summary of these results from Part 1.

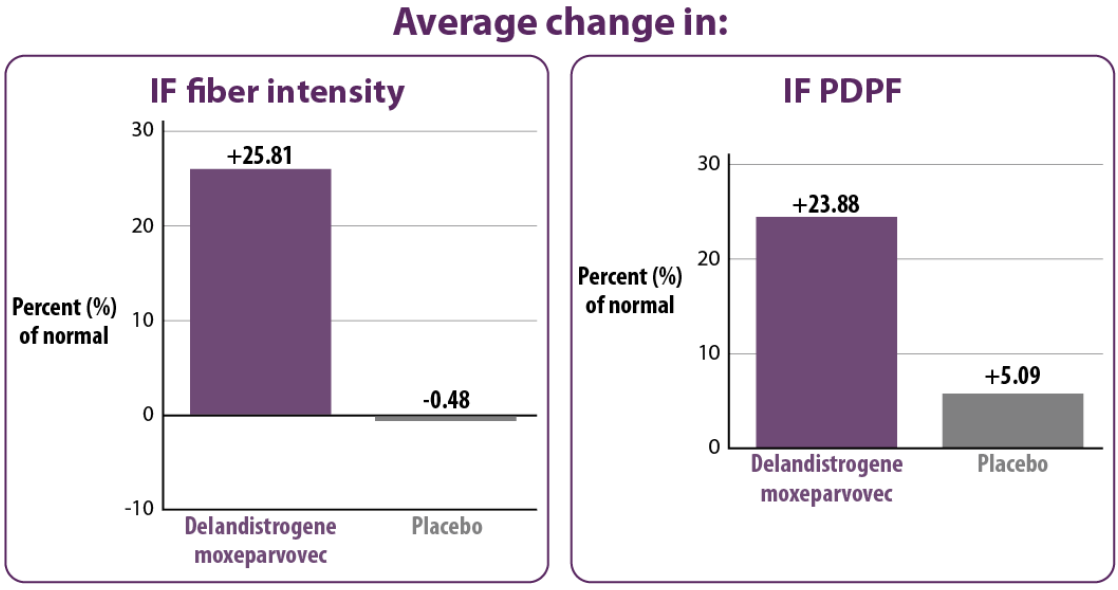
Measuring delandistrogene moxeparvovec dystrophin in muscle tissue using other types of tests

Using the same biopsy samples that were collected from participants for the western blot, researchers used a technique called **immunofluorescence (IF)** to measure changes in delandistrogene moxeparvovec dystrophin levels before and after treatment. IF involves tagging a specific protein (in this study, the protein was delandistrogene moxeparvovec dystrophin) with a fluorescent dye. This lets researchers look at the biopsy samples under a microscope and see muscle fibers that contain the protein.

This allowed researchers to measure 2 things:

- **IF fiber intensity**: IF fiber intensity tells researchers how much of the protein is present and if it is where it is supposed to be. Like the western blot test, the result is shown as the percentage (fraction) of how much dystrophin researchers would expect to see in a muscle tissue sample from someone who does not have Duchenne.
- **IF percent dystrophin-positive muscle fibers (PDPF)**: **IF PDPF** tells researchers how the protein is distributed throughout the muscle cells. The results are shown as a percentage (the percentage of muscle fibers that test positive for delandistrogene moxeparvovec dystrophin).

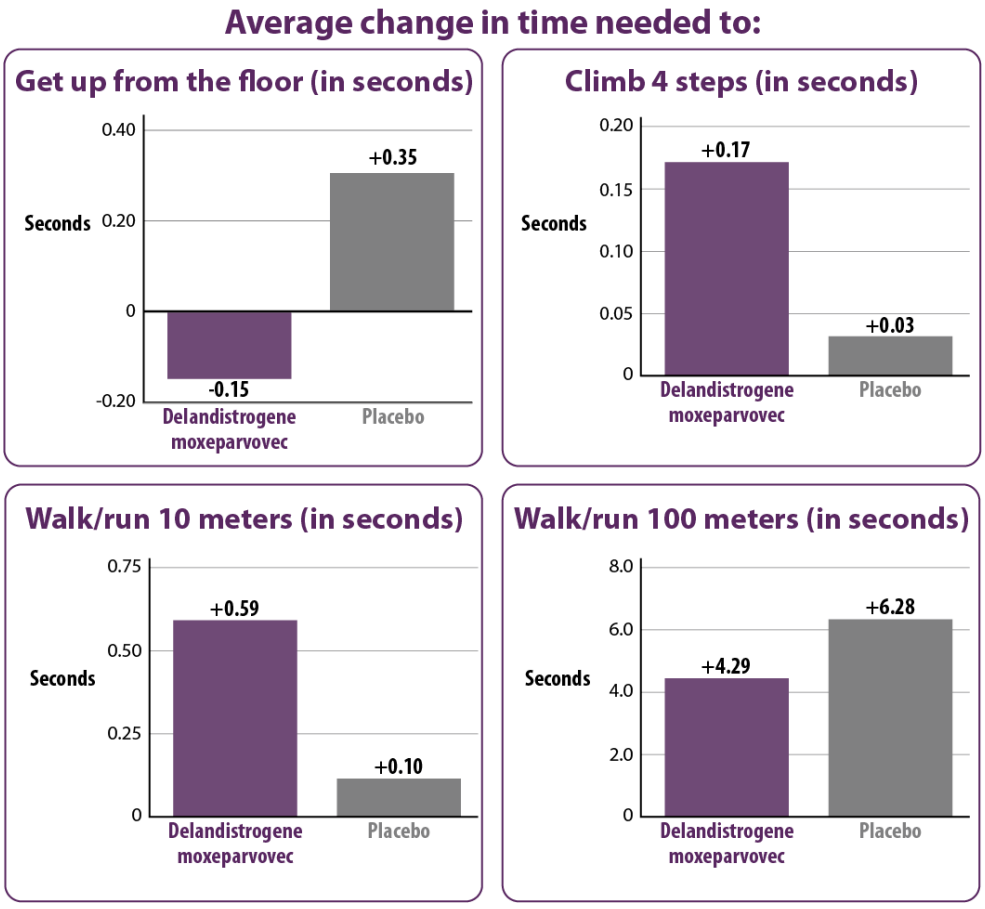
When researchers looked at biopsy samples collected before treatment and again after 12 weeks in Part 1, the results showed that both IF fiber intensity and IF PDPF increased more, on average, for participants who received delandistrogene moxeparvovec than for participants who received a placebo.



Looking at changes in how much time it took for participants to complete different physical activities

Study doctors recorded how long (in seconds) it took for participants to get up from the floor, to climb 4 steps, to walk or run 10 meters (about 33 feet), and to walk or run 100 meters (about 330 feet).

The doctors looked at how each of these times changed, on average, from before treatment to the end of Part 1. A reduction in the time (fewer seconds) to accomplish these tasks indicates an improvement in the skill. They compared the results for participants who got delandistrogene moxeparvovec with the results for participants who got a placebo.



What has happened since the study ended?

The study took about 4 years and 8 months to finish. It started in December 2018 and ended in August 2023. At the end of this study, the participants were invited to join a long-term follow up study.

When the study ended, Sarepta reviewed the data and created a report of the results. This is a summary of that report.

How has this study helped?

The results of this study helped doctors, researchers, and health authorities learn more about delandistrogene moxeparvovec as a possible treatment for Duchenne. The results also helped inform the designs of future studies. Clinical studies like this are important to help researchers understand which treatments work and how well they work.

At this time, additional clinical studies with delandistrogene moxeparvovec are ongoing, including long-term follow-up studies.

Where can I learn more about this study?

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

http://www.clinicaltrials.gov → On this website, type **NCT03769116** into one of the search boxes and click "Search".

http://www.clinicaltrialsregister.eu → On this website, click "Home and Search". Then type **2021-000078-27** in the search box and click "Search".

Full study title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial for Duchenne Muscular Dystrophy Using SRP-9001

Protocol number: SRP-9001-102

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.