Plain Language Study Summary

SRP-6004-102 (NAVIGENE): A gene transfer study to evaluate the safety, tolerability, and efficacy of SRP-6004 in ambulatory participants with limb girdle muscular dystrophy, Type 2B/R2 (LGMD2B/R2, Dysferlin [DYSF] Related)

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

This study was discontinued earlier than originally planned. 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 and the general public. The goal of this summary is to help explain why and how the study was done so that people understand the important role that the study participants played in helping researchers learn more about a possible treatment for limb girdle muscular dystrophy, Type 2B/R2.

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

What are limb girdle muscular dystrophies?

Limb girdle muscular dystrophies, or **LGMDs** for short, are a group of rare diseases that affect the muscles. LGMDs are caused by **genetic mutations**. These genetic mutations cause errors in the instructions our bodies have for making proteins that are important for muscle health. Without these proteins, people with LGMD have muscle loss and weakness that get worse with time.

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.

One type of LGMD is called **LGMD Type 2B/R2**, or **LGMD2B/R2** for short. People with LGMD2B/R2 have a genetic mutation that prevents them from properly making a protein called dysferlin. **Dysferlin** helps keep muscles healthy by repairing them when they get damaged.

Why was this study done?

This study was done to learn about a possible treatment for LGMD2B/R2 called SRP-6004.

SRP-6004 is an experimental gene therapy that was developed to deliver a genetic "instruction

manual" into muscles cells that would allow a person with LGMD2B/R2 to make a functional version of the dysferlin protein.

SRP-6004 is given as a one-time **intravenous (IV) infusion** (through a needle in the vein). Each infusion contains many copies of the instructions for how to make dysferlin. These instructions are delivered to muscle cells using a special carrier called a **vector**. The vector is called **rAAVrh74**.

Who took part?

This study included adults with LGMD2B/R2 who were between 18 and 50 years old. There were 2 people who joined the study, which took place in the United States.

People could join the study only if they were ambulatory (able to walk without help) and if they did not have elevated levels of antibodies to the rAAVrh74 vector. **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 muscle cells. Because of this, people who had high levels of antibodies to the rAAVrh74 vector were not eligible to take part in this study.

What was the study plan?

Everyone who joined the study received 1 dose of SRP-6004. After treatment, the participants were asked to stay in the study for up to 5 years so that the study team could keep track of their long-term health outcomes.

The participants in the study also agreed to have up to 3 muscle **biopsies**, including one before treatment with SRP-6004, a second about 3 months after treatment, and a third about 15 months after treatment.

What are biopsies?
A biopsy is a procedure in which doctors collect a small amount of tissue. In this study, doctors collected samples of muscle tissue before and after treatment with SRP-6004. This let them measure how dysferlin levels changed in the participants' muscle cells after treatment.

This study started in May 2023. The decision was made to end the study early in July 2025. The last participant visit occurred in June 2025.

What were the main goals of the study?

The main goal of the study was to learn about the safety of SRP-6004 as a possible treatment for LGMD2B/R2. When researchers study the safety of a new treatment, they look at any new or worsening medical events that participants have after they receive the treatment, including possible side effects.

A secondary goal of the study was to look at the biopsy samples that the participants provided to see if their muscles started making the functional dysferlin protein after treatment with SRP-6004.

How has this study helped?

Even though this study ended early, the participants helped doctors, researchers, and health authorities learn more about LGMD2B/R2 and possible ways to treat it. In this Phase 1 NAVIGENE study, researchers found that the gene therapy successfully produced the full dysferlin gene as intended. While the results showed that the approach could work, the amount of dysferlin protein produced did not reach the level we had hoped for. There were no new safety signals seen in this study. This research paves the way for companies to continue to advance studies of potential next-generation therapies in the future.

Where can I learn more about this study?

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

http://www.clinicaltrials.gov → On this website, type **NCT05906251** into one of the search boxes and click "Search".

Full study title: An Open-label, Systemic Gene Transfer Study to Evaluate the Safety, Tolerability, and Efficacy of SRP-6004 Administered by Systemic Infusion in Ambulatory Subjects with Limb Girdle Muscular Dystrophy Type 2B/R2 (LGMD2B/R2, Dysferlin Related)

Protocol number: SRP-6004-102

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.