UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 8, 2020

Sarepta Therapeutics, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-14895**	**93-0797222**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

215 First Street
Suite 415
Cambridge, MA 02142
(Address of principal executive offices, including zip code)

Registrant's Telephone Number, Including Area Code: (617) 274-4000

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, Par Value $0.0001 per share	SRPT	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On June 8, 2020, Sarepta Therapeutics, Inc. (the "Company") issued a press release and conducted an investor webcast presenting expression and functional data from the SRP-9003 gene therapy trial to treat limb-girdle muscular dystrophy Type 2E. Copies of the press release and the presentation are being furnished as Exhibits 99.1 and 99.2, respectively.

The information in this report furnished pursuant to Item 7.01, including Exhibits 99.1 and 99.2 attached hereto, shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 of this report.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release dated June 8, 2020: Sarepta Therapeutics Announces Positive Expression and Functional Data From the SRP-9003 Gene Therapy Trial to Treat Limb-Girdle Muscular Dystrophy Type 2E
99.2	Presentation dated June 8, 2020: Clinical Update - SRP-9003 Beta-Sarcoglycanopathy Gene Therapy Program Limb-Girdle Muscular Dystrophy Type 2E
104	The cover page from this Current Report on Form 8-K of Sarepta Therapeutics, Inc., formatted in Inline XBRL and included as Exhibit 101

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Sarepta Therapeutics, Inc.

Date: June 8, 2020

By: /s/ Douglas S. Ingram
Douglas S. Ingram
President and Chief Executive Officer

Sarepta Therapeutics Announces Positive Expression and Functional Data From the SRP-9003 Gene Therapy Trial to Treat Limb-Girdle Muscular Dystrophy Type 2E

-- In post-treatment muscle biopsies, clinical trial participants in the high-dose cohort showed a dose-dependent increase in transduction and expression when compared with the low-dose cohort, with a mean of 72% beta-sarcoglycan (beta-SG) positive fibers, as measured by immunohistochemistry (IHC), substantially exceeding the pre-defined 50% measure for success --
-- A mean signal intensity of 73% in the high-dose group was observed compared to normal control --
-- A mean beta-sarcoglycan expression of 62% as measured by Western blot was observed in the high-dose cohort compared to normal control --
-- An 89% mean reduction of creatine kinase (CK) from baseline was observed in the high-dose cohort --
-- Continued functional improvement was observed in the low-dose cohort at one year --

CAMBRIDGE, Mass., June 8, 2020 (GLOBE NEWSWIRE) – Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today announced positive results from a study of SRP-9003, its investigational gene therapy for limb-girdle muscular dystrophy Type 2E (LGMD2E). Results included safety and expression results from three clinical trial participants in the high-dose cohort measured at 60 days, and one-year functional data from three clinical trial participants in the low-dose cohort. SRP-9003 is in development for the treatment of LGMD2E (also known as beta-sarcoglycanopathy and LGMDR4), a devastating monogenic neuromuscular disease caused by a lack of beta-sarcoglycan (beta-SG) proteins. SRP-9003 is a gene construct that transduces skeletal and cardiac muscle, delivering a gene that codes for the full-length beta-sarcoglycan protein, the absence of which is the sole cause of progressive degeneration and a shortened lifespan characterized by the disease.

“We were very encouraged by the previously reported results from our first cohort of patients treated with a lower dose of SRP-9003, including impressive expression, good tolerability, and positive functional signals, which continue impressively at one year. We are excited to have been able to achieve even more impressive expression and other biomarkers in our higher-dose cohort for SRP-9003, along with good tolerability. The SRP-9003 gene construct, vector and promoter were designed with the goal of robustly

delivering to skeletal and cardiac muscles a gene coding for the missing beta-sarcoglycan protein that causes LGMD2E. These data support the conclusion that the therapy is achieving its intended purpose, driving robust expression in the muscles where it is needed," said Doug Ingram, President and CEO, Sarepta. "SRP-9003 employs the same vector, AAVrh74, and same promoter, MHCK7, as SRP-9001, our therapy in development to treat Duchenne muscular dystrophy. And Cohort 2 received a similar dose as our ongoing SRP-9001 studies for Duchenne. The safety and efficacy results with these two doses of SRP-9003 provide us with additional experience and confidence with the rh74 vector and the MHCK7 promoter as we select the dose for the pivotal trial of SRP-9003 and work to quickly develop this therapy for patients who currently have no treatment options."

The SRP-9003 study has two cohorts, each studying a different dose-per-kilogram based on the weight of the patient. Three participants in the low-dose cohort (Cohort 1) were treated with a one-time infusion of SRP-9003 dosed at $5x10^{13}$ vg/kg and an additional three participants in the high-dose cohort (Cohort 2) received a one-time infusion dosed at $2x10^{14}$ vg/kg. The six participants were between the ages of 4 and 13. Post-treatment biopsies were taken at 60 days. Sarepta previously shared data from Cohort 1 in 2019, including positive and robust expression and biomarker data and positive 9-month functional results.

Preliminary results from Cohort 2 (n=3) are as follows:

- Strong dose-dependent increase in transduction and expression transduction and expression when compared with the low-dose cohort.
- The three participants showed a robust mean expression of 72.3% of transduced beta-SG, properly localized to the muscle sarcolemma, as measured by immunohistochemistry (IHC). These results exceeded the pre-defined measure of success for the study of 50% positive fibers which was previously achieved in Cohort 1.
- Mean fiber intensity, as measured by IHC, was 73.1% compared to normal control.
- All participants showed robust quantification of beta-SG, as measured by Western blot, with mean beta-SG of 62.1% of normal control.
- All participants showed a reduction in serum creatine kinase (CK) levels from pre-treatment baseline measure to last measure at 90 days, with a mean CK reduction of 89.1% from baseline. CK is an enzyme biomarker strongly associated with muscle damage.

- Adverse events in Cohort 2 were generally mild to moderate in severity. One serious adverse event – dehydration resulting from vomiting 3 days after infusion which resolved in 2 days with ondansetron, promethazine and IV fluids – was observed.
- No other clinically significant laboratory findings were observed, including no finding of decreases in platelet counts outside of the normal range or signs of complement activation.
- These results will help inform dosing in future studies.

In Cohort 1 (low dose), at one year all three participants continued to show improvements from baseline across all functional measures, including the North Star Assessment for Limb-Girdle Muscular Dystrophies, time-to-rise, four-stair climb, 100-meter walk test and 10-meter walk test. These results are distinctly different from what an age-matched, natural history group would predict. There have been no new drug-related safety signals observed since the 9-month update, and no decreases in platelet counts outside of the normal range or signs of complement activation were observed.

“LGMD2E is a devastating neuromuscular disease that causes significant disability in the children we see and currently lacks treatment options beyond tailored physical therapy,” said Jerry Mendell, M.D., principal investigator at the Center for Gene Therapy at the Abigail Wexner Research Institute at Nationwide Children’s Hospital and lead investigator for the study. “We are pleased that these data show robust expression, similar to what we observed in the micro-dystrophin program, for the protein that is missing in children with LGMD2E, and remain hopeful that this brings us one step closer to a therapy that can help improve both prognosis and quality of life.”

About SRP-9003 and the study
SRP-9003 uses the AAVrh74 vector, which is designed to be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle, making it an ideal candidate to treat peripheral neuromuscular diseases. AAVrh74 has lower immunogenicity rates than reported with other human AAV vectors. The MHCK7 promoter has been chosen for its ability to robustly express in the heart, which is critically important for patients with limb-girdle muscular dystrophy Type 2E (LGMD2E), also known as beta-sarcoglycanopathy and LGMDR4, many of whom die from pulmonary or cardiac complications.

This first-in-human study is evaluating a single intravenous infusion of SRP-9003 among children with LGMD2E between the ages of four and 15 years with significant symptoms of disease. Sarepta has exclusive rights to the LGMD2E gene therapy program initially developed at the Abigail Wexner Research Institute at Nationwide Children's Hospital.

About Limb-Girdle Muscular Dystrophy
Limb-girdle muscular dystrophies are genetic diseases that cause progressive, debilitating weakness and wasting that begin in muscles around the hips and shoulders before progressing to muscles in the arms and legs.

Patients with limb-girdle muscular dystrophy Type 2E (LGMD2E) begin showing neuromuscular symptoms such as difficulty running, jumping and climbing stairs before age 10. The disease, which is an autosomal recessive subtype of LGMD, progresses to loss of ambulation in the teen years and often leads to early mortality. There is currently no treatment or cure for LGMD2E.

Sarepta has five LGMD gene therapy programs in development, including subtypes for LGMD2E, LGMD2D, LGMD2C, LGMD2B and LGMD2L, and holds an option for a sixth program for LGMD2A.

About Sarepta Therapeutics
At Sarepta, we are leading a revolution in precision genetic medicine and every day is an opportunity to change the lives of people living with rare disease. The Company has built an impressive position in Duchenne muscular dystrophy (DMD) and in gene therapies for limb-girdle muscular dystrophies (LGMDs), mucopolysaccharidosis type IIIA, Charcot-Marie-Tooth (CMT), and other CNS-related disorders, with more than 40 programs in various stages of development. The Company's programs and research focus span several therapeutic modalities, including RNA, gene therapy and gene editing. For more information, please visit **www.sarepta.com** or follow us on **Twitter**, **LinkedIn**, **Instagram** and **Facebook**.

Forward-Looking Statements
This press release contains "forward-looking statements." Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements

include statements regarding the goal of the SRP-9003 gene construct, vector and promoter of robustly delivering to skeletal and cardiac muscles a gene coding for the missing beta-sarcoglycan protein that cause LGMD2E; SRP-9003's potential to improve both prognosis and quality of life; the potential read through of the SRP-9003 trial results to SRP-9001; our plans to select the dose for the pivotal trial of SRP-9003 and work to quickly develop this therapy for patients; and the potential market opportunities with respect to SRP-9003 and SRP-9001.

These forward-looking statements involve risks and uncertainties, many of which are beyond our control. Known risk factors include, among others: success in preclinical trials and early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; the data presented in this release may not be consistent with the final data set and analysis thereof or result in a safe or effective treatment benefit; different methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters may yield different statistical results, and even if we believe the data collected from clinical trials of our product candidates are positive, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities; we may not be able to execute on our business plans and goals, including meeting our expected or planned regulatory milestones and timelines, clinical development plans, and bringing our product candidates to market, due to a variety of reasons, some of which may be outside of our control, including possible limitations of company financial and other resources, manufacturing limitations that may not be anticipated or resolved for in a timely manner, regulatory, court or agency decisions, such as decisions by the United States Patent and Trademark Office with respect to patents that cover our product candidates and the COVID-19 pandemic; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve the expected revenues from the sale of such products; and those risks identified under the heading "Risk Factors" in Sarepta's most recent Annual Report on Form 10-K for the year ended December 31, 2019, and most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) as well as other SEC filings made by the Company which you are encouraged to review.

Any of the foregoing risks could materially and adversely affect the Company's business, results of operations and the trading price of Sarepta's common stock. For a detailed description of risks and uncertainties Sarepta faces, you are encouraged to review the SEC filings made by Sarepta. We caution investors not to place considerable reliance on the forward-looking statements contained in this press release. Sarepta does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

Internet Posting of Information
*We routinely post information that may be important to investors in the 'For Investors' section of our website at **www.sarepta.com**. We encourage investors and potential investors to consult our website regularly for important information about us.*

Source: Sarepta Therapeutics, Inc.

Sarepta Therapeutics, Inc.

Investors:
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Media:
Tracy Sorrentino, 617-301-8566
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Exhibit 99.2

SAREPTA THERAPEUTICS

Clinical Update:

SRP-9003 Beta-Sarcoglycanopathy Gene Therapy Program

Limb-Girdle Muscular Dystrophy Type 2E

Cambridge, MA
June 8, 2020

Forward-Looking Statements

This presentation contains "forward-looking statements." Any statements contained in this presentation that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements regarding the potential benefits of SRP-9003 and potential market opportunities; and our plans to select a final dose for registration by Q3 2020, to engage with global regulatory agencies to discuss pivotal trial designs, and to initiate registrational study in 2021.

These forward-looking statements involve risks and uncertainties, many of which are beyond Sarepta's control. Actual results could materially differ from those stated or implied by these forward-looking statements as a result of such risks and uncertainties. Known risk factors include, among others: success in preclinical trials and early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; the data presented in this release may not be consistent with the final data set and analysis thereof or result in a safe or effective treatment benefit; different methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters may yield different statistical results, and even if we believe the data collected from clinical trials of our product candidates are positive, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities; we may not be able to execute on our business plans and goals, including meeting our expected or planned regulatory milestones and timelines, clinical development plans, and bringing our product candidates to market, due to a variety of reasons, some of which may be outside of our control, including possible limitations of company financial and other resources, manufacturing limitations that may not be anticipated or resolved for in a timely manner, regulatory, court or agency decisions, such as decisions by the United States Patent and Trademark Office with respect to patents that cover our product candidates and the COVID-19 pandemic; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve the expected revenues from the sale of such products; and those risks identified under the heading "Risk Factors" in Sarepta's most recent Annual Report on Form 10-K for the year ended December 31, 2019, and most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) as well as other SEC filings made by the Company which you are encouraged to review.

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Welcome and Introduction

Doug Ingram
President and CEO
Sarepta Therapeutics, Inc.

Clinical Update:

SRP-9003 Beta-Sarcoglycanopathy Gene Therapy Program

Limb-Girdle Muscular Dystrophy Type 2E

Louise Rodino-Klapac, Ph.D.
Senior Vice President, Gene Therapy
Sarepta Therapeutics, Inc.

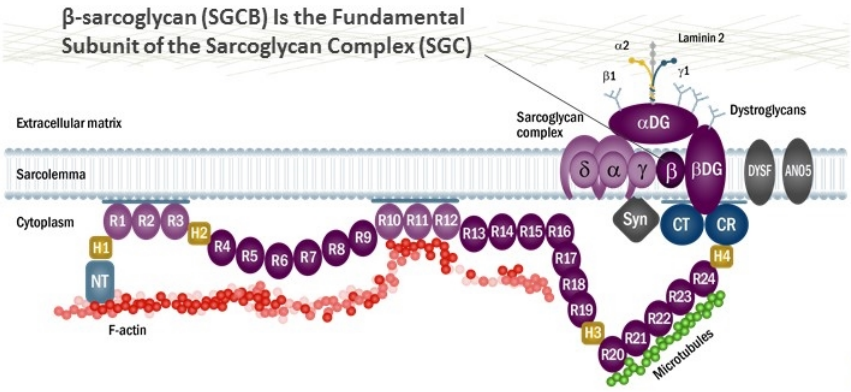
LGMDs Are Devastating Muscular Dystrophies

Monogenic, rare neuromuscular diseases that affect hundreds of thousands globally

- **LGMDs are progressive, debilitating muscle-wasting diseases with no therapies[1,2]**
  - Affect males and females equally
  - Affect skeletal muscle
  - Affect cardiac muscle in some types
  - Elevated creatine kinase (CK) levels
  - Symptoms often develop before age 10
  - Loss of ambulation often in early teens
  - More severe forms mimic DMD
  - Death can result before age 30
  - No approved therapies
- **Consistent disease progression within each LGMD subtype**
- **Each of the ~30 LGMD subtypes is a rare disease**

1. NIH website. www.nih.gov. Accessed June 16, 2018.
2. MDA website. www.mda.org/disease/limb-girdle-muscular-dystrophy/causes-inheritance. Accessed June 16, 2018.

LGMD Portfolio Addresses Monogenic Mutations that Result in the Lack of One of the Proteins Comprising the Dystrophin-associated Protein Complex



- **Sarcoglycans** prevent muscle damage during contraction
  - All 4 functional sarcoglycans must be present to form a functional sarcoglycan complex (SCG)
    - **β-sarcoglycan (SRP-9003)**
    - **α-sarcoglycan (SRP-9004)**
    - **γ-sarcoglycan (SRP-9005)**
  - Sarcoglycan deficiency leads to dystrophin deficiency
- **Dysferlin** and **ANO5** support muscle membrane repair (SRP-6004 and SRP-9006)
  - Failed muscle repair leads to chronic muscle degeneration

ANO5, anoctamin-5; FKRP, fukutin-related protein; POMT, protein-O-mannosyltransferase; TRIM, tripartite motif.

LGMD2E Phase I/II Study

ClinicalTrials.gov Identifier: NCT03652259

LGMD Type 2E Open-label Trial Design

- **6 subjects treated with systemic delivery of AAVrh74.MHCK7.SGCB†**
  - Cohort 1: 3 subjects; **$5x10^{13}$ vg/kg**
  - Cohort 2: 3 subjects; **$2x10^{14}$ vg/kg**
- **Inclusion criteria**
  - Subjects ages 4 through age 15, inclusive
  - Beta-sarcoglycan (SG) DNA gene mutations at both alleles
  - Negative for AAVrh74 antibodies
  - ≥40% of Normal 100 meter walk test*
- **Prednisone 1 day prior to gene transfer, 60 days 1 mg/kg, taper**

†Ongoing study, database is not locked
*Adjusted for predicted for age-, height-, gender-, and weight-matched healthy controls at the screening visit

Endpoints in the LGMD2E Study

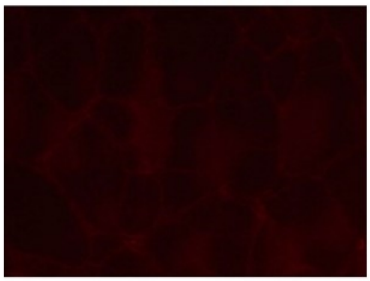
- **Primary endpoint**
  - Safety
- **Secondary endpoints:**
  - β–sarcoglycan expression at week 8*
- **Other endpoints:**
  - Decrease in CK
  - Functional endpoints
    - North Star Assessment for Limb-girdle muscular dystrophies (NSAD)
    - 100-meter walk/run (100MWR)
    - 10-meter walk/run (10MWR)
    - Time to ascend 4 stairs
    - Time to rise from floor

*Based on pre-clinical studies, the goal was to achieve expression levels of ≥20%

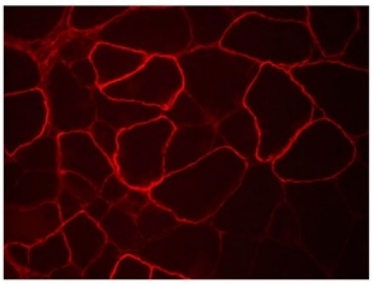
Pre-clinical Models Correlated Expression and Function

≥20 percent expression leads to increased function

Pretreatment

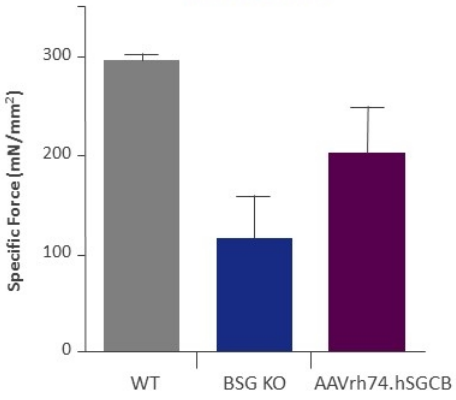


Post Treatment



5x10^{12} vg/kg

Function



LGMD2E Study
Day 60 Expression Results:
Cohort 1 (n=3)

Cohort 1 - LGMD2E Subject Demographics at Baseline[1]

Subject	Age (years)	Mutation	Weight (kg)*	CK Levels at Baseline (U/L)
1	13	Exon 3	57	10,727
2	4	Exon 4	18	12,286
3	13	Exon 3	50	10,985

- Exons 3-6 encode for the extracellular domain of SGCB
- Mutations in these exons lead to complete absence of or severely reduced expression of SGCB, and a severe phenotype that includes cardiomyopathy[2]

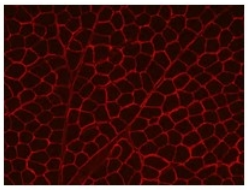
β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

1. Sarepta Therapeutics 2019. Data on file. 2. Semplicini C, et al. *Neurology*. 2015;84(17):1772-1781.

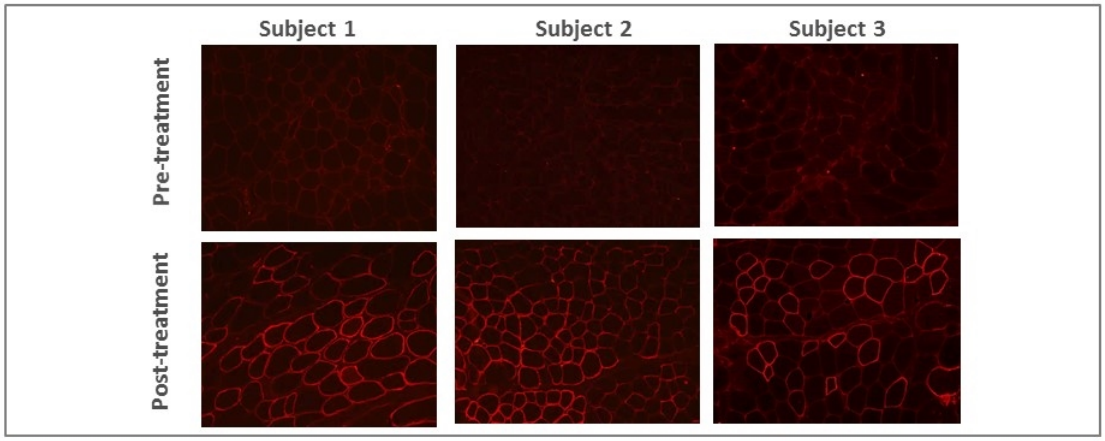
*Values updated following database transfer

Cohort 1 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $5x10^{13}$ vg/kg

Normal Control



Beta-Sarcoglycan Expression (IF)



	Percentage of SGCB-positive Fibers	Intensity
Mean (n=3)*	51%	47%

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

*Values represent average of Tibialis Anterior (TA) and Biceps (BIC) muscles

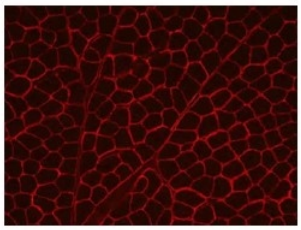
Cohort 1 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $5x10^{13}$ vg/kg

Subject	Percentage of SGCB-Positive Fibers	Mean Intensity
1	63%	47%
2	49%	57%
3	42%	38%
Mean	**51%**	**47%**

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Cohort 1 - SGCB Expression Significantly Upregulated SGC Complex at a Dose of $5x10^{13}$ vg/kg

Normal Control



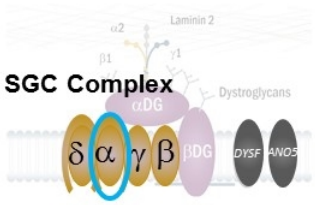
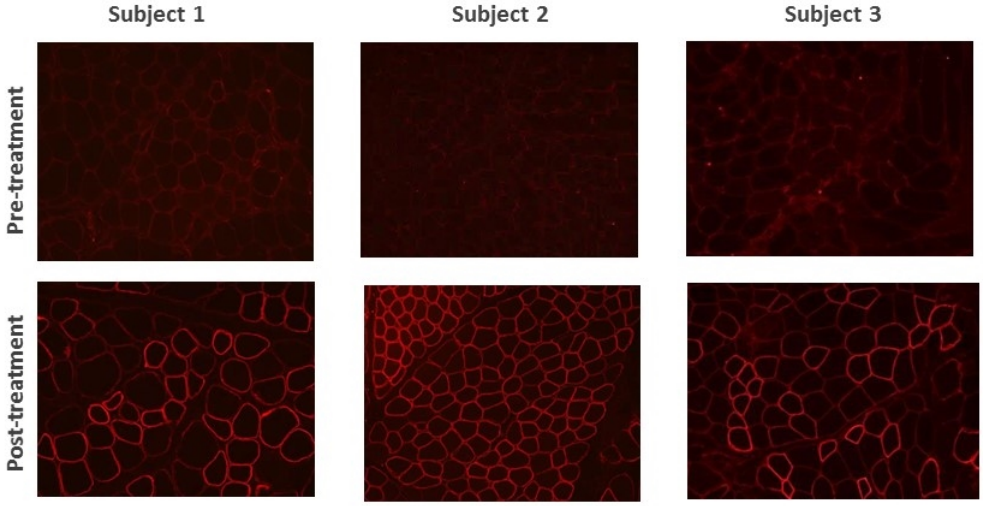


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

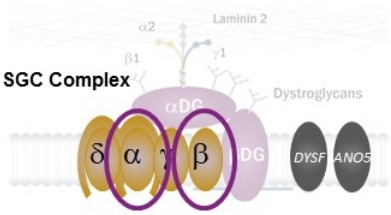
α-Sarcoglycan Expression (IF)



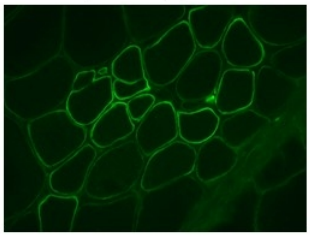
β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Sarepta Therapeutics 2019. Data on file.

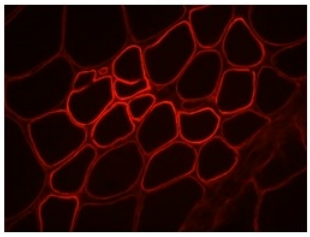
SGCB Expression Significantly Upregulated SGC Complex Protein at a Dose of $5x10^{13}$ vg/kg



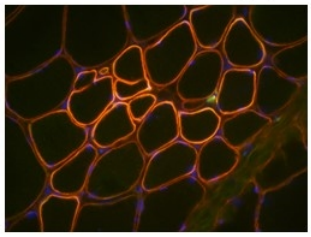
β-sarcoglycan



α-sarcoglycan



Colocalization (Merge)



β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Sarepta Therapeutics 2019. Data on file. Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2012;14(6):373-378.

Cohort 1 - Detection of β-sarcoglycan Expression by Western Blot Post-treatment in All 3 Subjects

Subject	Mean SGCB Expression vs Normal
1	34.7%
2	39.2%
3	34.5%
Mean	36.1%

The gene transfer delivers full-length SGCB

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.
Sarepta Therapeutics 2019. Data on file.

Cohort 1 - β-Sarcoglycan Expression is Supported by Vector Genome Counts

Beta-Sarcoglycan Expression (IF)

	Percentage of Beta-Sarcoglycan-positive Fibers	Intensity
Mean (n=3)	51%	47%

Beta-Sarcoglycan (Western Blot)

	Percent of Normal
Mean (n=3)	36.1%

Vector Genome Number

	Vector Copies/µg DNA	Copies per Nucleus
Mean (n=3)	>E04	0.60

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Cohort 1 - Safety Review (n=3)

- **2 subjects had elevated liver enzymes, 1 of which was designated an SAE, as the subject had associated transient increase in bilirubin**
  - Both events occurred when the subjects were tapered off oral steroids
  - Elevated liver enzymes returned to baseline and symptoms resolved within days following supplemental steroid treatment
- **2 patients had transient mild nausea generally within the first week coincident with increased steroid dosing**
  - Did not correlate with liver enzyme elevations or any other abnormality
- **No other clinically significant laboratory findings**
  - No decreases in platelet counts observed outside of the normal range
  - No signs of complement activation observed

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LGMD2E Study
One Year Functional Results:
Cohort 1 (n=3)

Cohort 1 - Summary of Functional Data at 1-Year

ALL SUBJECTS SHOWED IMPROVEMENT IN ALL FUNCTIONAL MEASURES

Subject	Assessment	NSAD*	Time to Rise (sec)	4 Stairs Up (sec)	100 MWR* (sec)	10 MWR (sec)
1	Baseline	40	5.0	2.4	52.0	5.0
	Day 270	41	4.1	2.3	47.7	4.5
	1-year	44	3.8	2.2	48.4	4.5
	Change from Baseline	**4**	**1.2**	**0.2**	**3.6**	**0.5**
2	Baseline	48	1.5	1.6	35.1	3.4
	Day 270	54	1.2	1.3	30.7	3.2
	1-year	54	1.0	1.1	31.8	2.9
	Change from Baseline	**6**	**0.5**	**0.5**	**3.3**	**0.5**
3	Baseline	41	3.5	2.8	48.8	5.2
	Day 270	47	3.0	1.9	41.5	4.3
	1-year	48	2.9	2.0	39.9	4.3
	Change from Baseline	**7**	**0.6**	**0.8**	**8.9**	**0.9**

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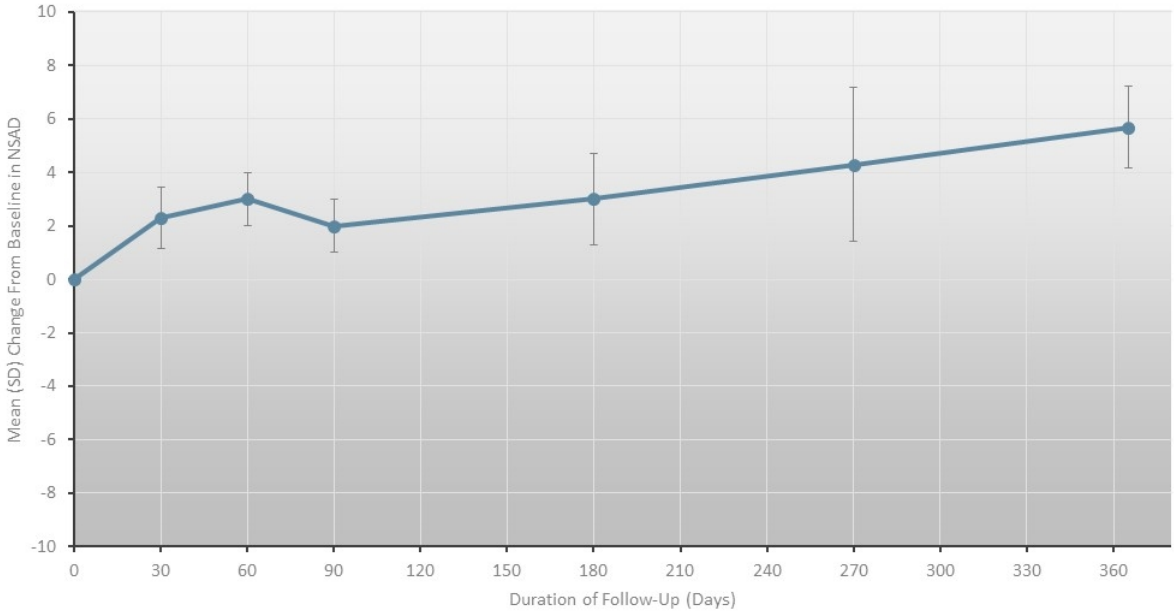
*Values updated following database transfer

Cohort 1 - Mean Change from Baseline in NSAD



β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

LGMD2E Study
Day 60 Expression Results:
Cohort 2 (n=3)

Cohort 2 - LGMD2E Subject Demographics at Baseline[1]

Subject	Age (years)	Mutation	Weight (kg)	CK Levels at Baseline (U/L)
4	11	Exon 4	29.1	6320
5	11	Exon 3	39.5	8938
6	8	Exon 1	26.6	5743

- Exons 3-6 encode for the extracellular domain of SGCB
- Mutations in these exons lead to complete absence of or severely reduced expression of SGCB, and a severe phenotype that includes cardiomyopathy[2]

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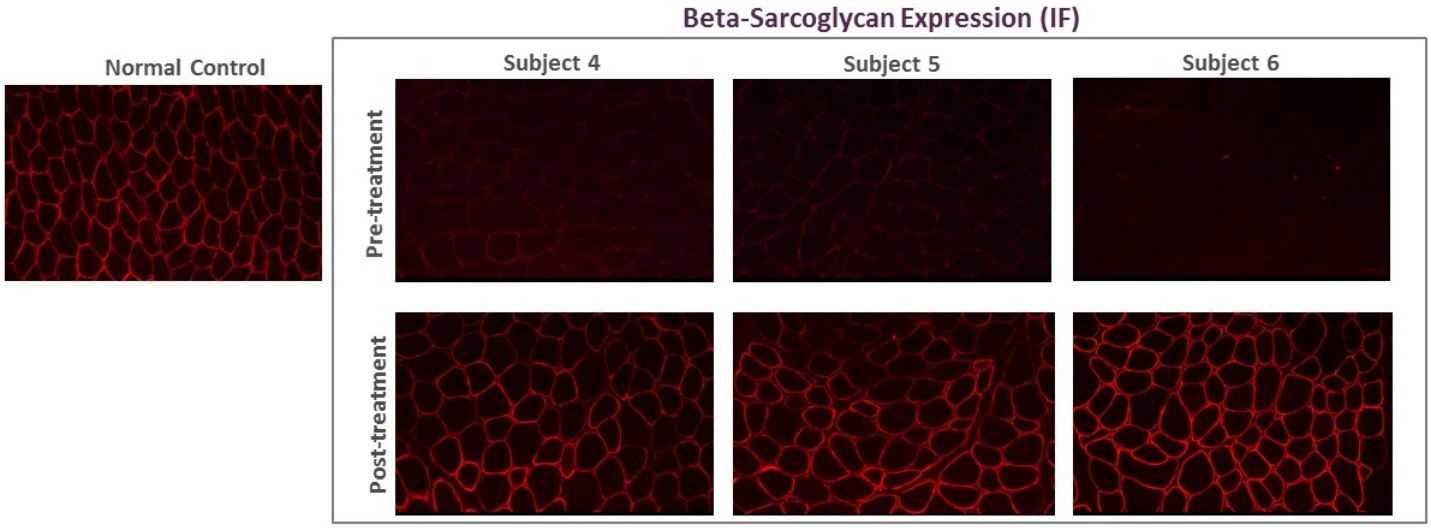
1. Baseline is Baseline/Screening visit measurement.
2. Semplicini C, et al. *Neurology*. 2015;84(17):1772-1781.

Cohort 2 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $2x10^{14}$ vg/kg



	Percentage of SGCB-positive Fibers	Intensity
Mean (n=3)*	72%	73%

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

*Values represent average of TA and BIC muscles

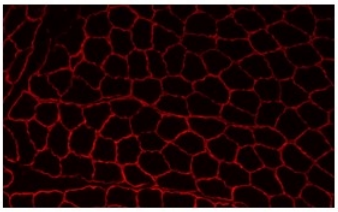
Cohort 2 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $2x10^{14}$ vg/kg

Subject	Percentage of SGCB-Positive Fibers	Mean Intensity
4	65%	55%
5	77%	67%
6	75%	97%
Mean	**72%**	**73%**

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Cohort 2 - Robust α-Sarcoglycan Expression Significantly Upregulated Sarcoglycan Complex at a Dose of $2x10^{14}$ vg/kg

Normal Control



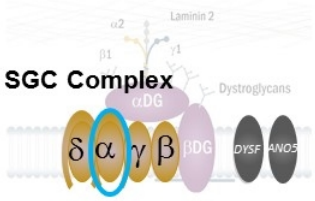
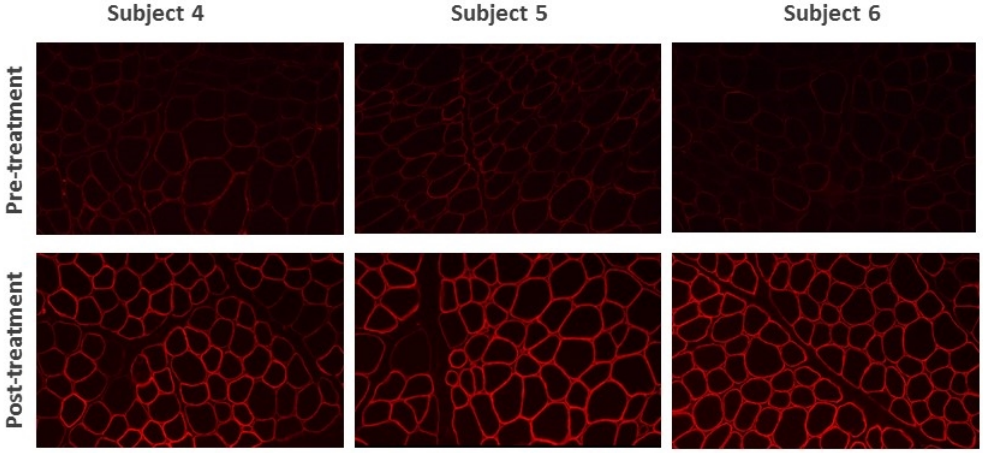


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

α-Sarcoglycan Expression (IF)



β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Sarepta Therapeutics 2020. Data on file.

Cohort 2 - Detection of β-Sarcoglycan Expression by Western Blot Post-treatment in All 3 Subjects at Day 60

Subject	Mean SGCB Expression vs Normal
4	53.0%
5	63.1%
6	70.3%
Mean	62.1%

The gene transfer delivers full-length SGCB

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Sarepta Therapeutics 2020. Data on file.

Cohort 2 - β-Sarcoglycan Expression is Supported by Vector Genome Counts

Beta-Sarcoglycan Expression (IF)

	Percentage of Beta-Sarcoglycan-positive Fibers	Intensity
Mean (n=3)	72.3%	73.1%

Beta-Sarcoglycan (Western Blot)

	Percent of Normal
Mean (n=3)	62.1%

Vector Genome Number

	Vector Copies/µg DNA	Copies per Nucleus
Mean (n=3)	>E05	4.2

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Cohort 2 - 89.1% Mean Reduction of Creatine Kinase (CK) Levels Observed with β-Sarcoglycan Gene Therapy

Subject	Age (years)	CK Levels at Baseline (U/L)	CK Levels at Last Visit (Day 90) (U/L)
4	11	6320	852
5	11	8938	498
6	8	5743	776

89.1% Mean Reduction in CK at Day 90

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Comparison of Expression Results from Cohort 1 and Cohort 2

Cohort	Dose	IF % Positive Fibers (% of NC)	Mean Intensity (% of NC)	Western Blot (% of NC)	qPCR (copies/nucleus)
1 (n=3)	$5x10^{13}$ vg/kg	51%	47%	36.1%	0.60
2 (n=3)	$2x10^{14}$ vg/kg	72%	73%	62.1%	4.2

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Safety Review of Cohort 2 (n=3)

- Majority of patients had AEs mild/moderate in severity, which resolved
- One SAE observed
  - Dehydration resulting from vomiting 3 days after infusion which resolved in 2 days with ondansetron, promethazine and IV fluids
- No stopping/discontinuation rules were triggered by AEs
- No other clinically significant laboratory findings
  - No decreases in platelet counts observed outside of the normal range
  - No signs of complement activation observed

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Summary

Data reflects optimized LGMD2E construct design

- AAVrh74 efficiently transduces all muscle types
- MHCK7 promoter allows for cardiac and skeletal transgene muscle expression
- Low pre-existing immunity for AAVrh74

Preliminary clinical results

- Increased beta-sarcoglycan expression across all patients at a systemic dose of **$2x10^{14}$ vg/kg** compared to dose of **$5x10^{13}$ vg/kg**
- Substantial reduction in CK in both cohorts
- Sustained improvement in all functional measures in all patients in Cohort 1
- Similar safety and tolerability profile observed in Cohorts 1 and 2

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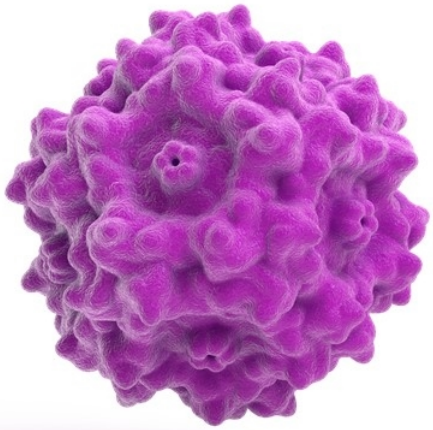
Next Steps for Clinical Development



AAVrh74.MHCK7.SGCB
(SRP-9003)

- Final dose for registration trial will be selected by Q3
- Engagement with global regulatory agencies to discuss pivotal trial designs
- Commenced run on commercial manufacturing process to support further clinical development
- Initiation of registrational study in 2021

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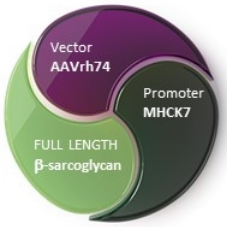
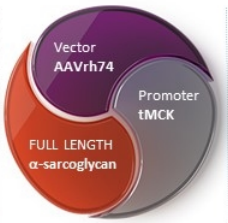
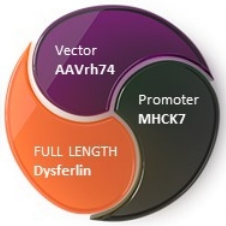
Sarepta Therapeutics 2020. Data on file.

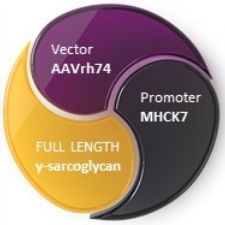
Sarepta's Current Clinical Programs in LGMD

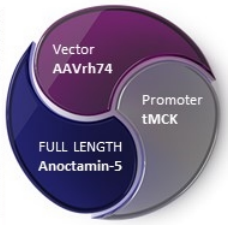
Partnered Program: Calpain (LGMD2A)
NCH: Dr Zarife Sahenk











	LGMD2E	LGMD2D	LGMD2B	LGMD2C	LGMD2L
Program	SRP-9003	SRP-9004	SRP-6004	SRP-9005	SRP-9006
Target Function	Stabilizes DAPC, prevents muscle damage during contraction	Stabilizes DAPC, prevents muscle damage during contraction	Muscle membrane repair	Stabilizes DAPC, prevents muscle damage during contraction	Muscle membrane repair

Programs shown are investigational at Sarepta Therapeutics, Inc. and have not been reviewed or approved by any regulatory authority.

Questions & Answers