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.

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.

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.

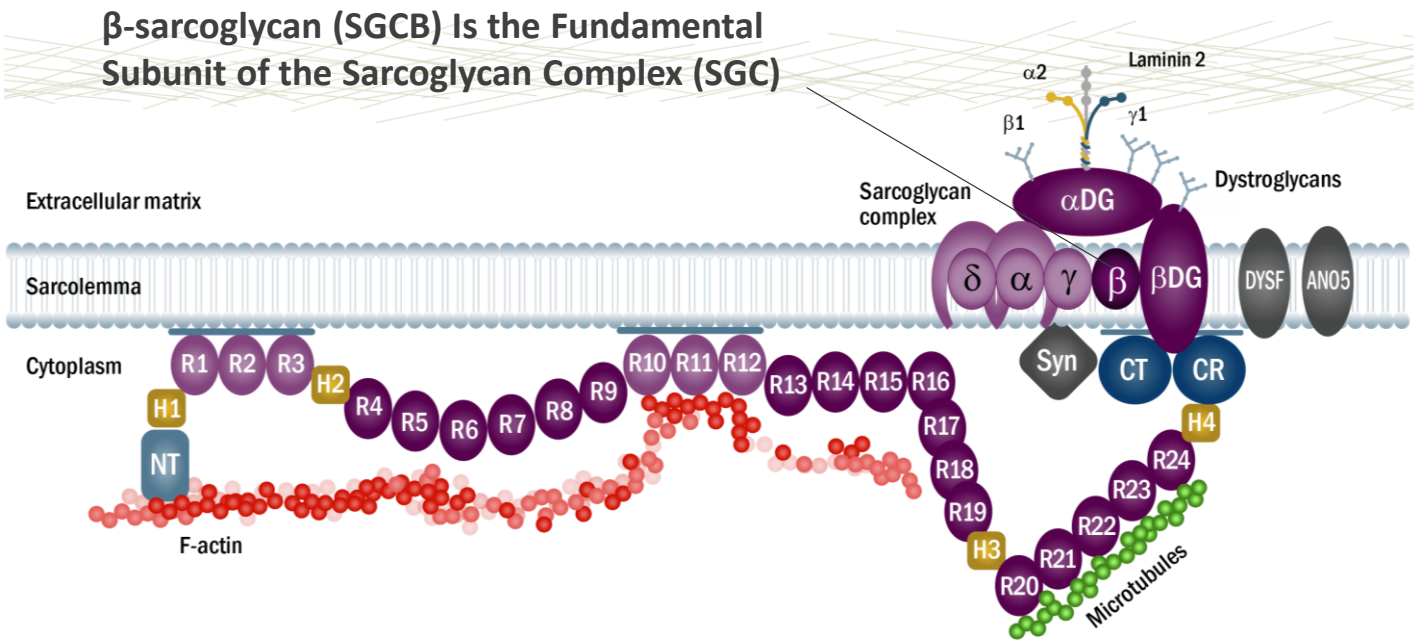
LGMDs Are Devastating Muscular Dystrophies

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

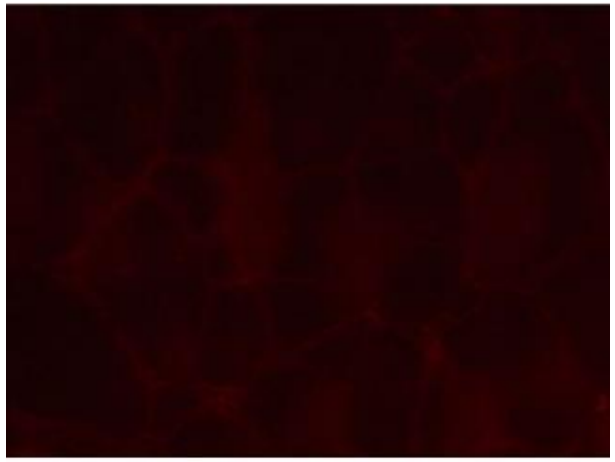
- **Primary endpoint**
  - Safety
- **Secondary endpoints:**
  - β–sarcoglycan expression at week 8*
- **Other endpoints:**
  - Decrease in CK
  - Functional endpoints
    - North Star Assessment for Limb-girdle muscular dystrophies (NSAD)
    - 100-meter walk/run (100MWR)
    - 10-meter walk/run (10MWR)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

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

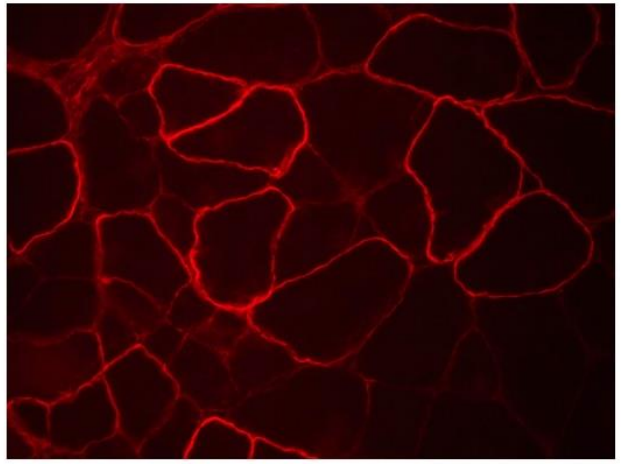
Pre-clinical Models Correlated Expression and Function

≥20 percent expression leads to increased function

Pretreatment

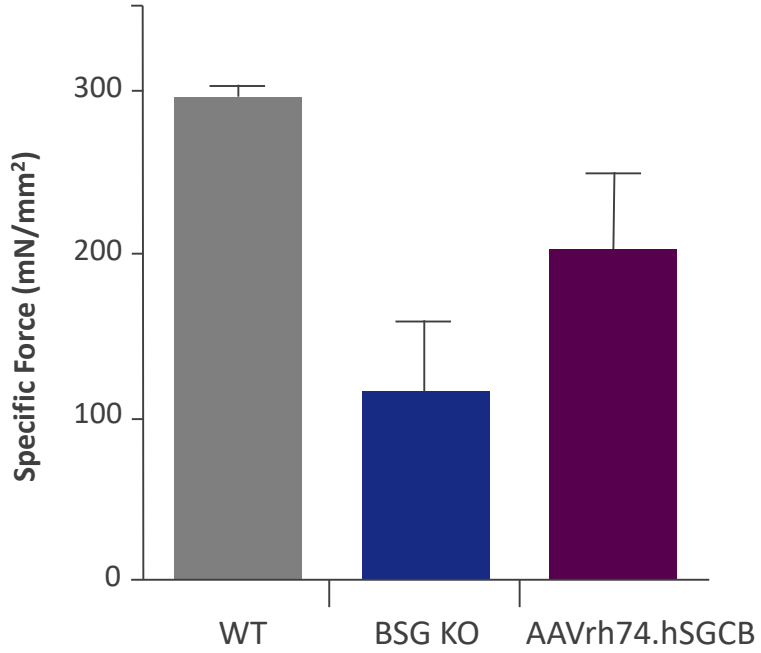


Post Treatment



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]

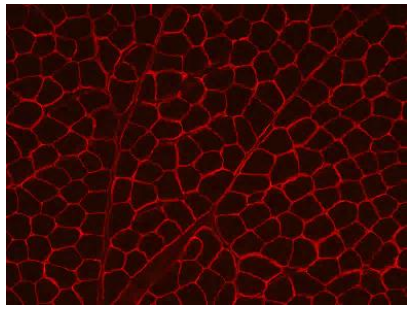
β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

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

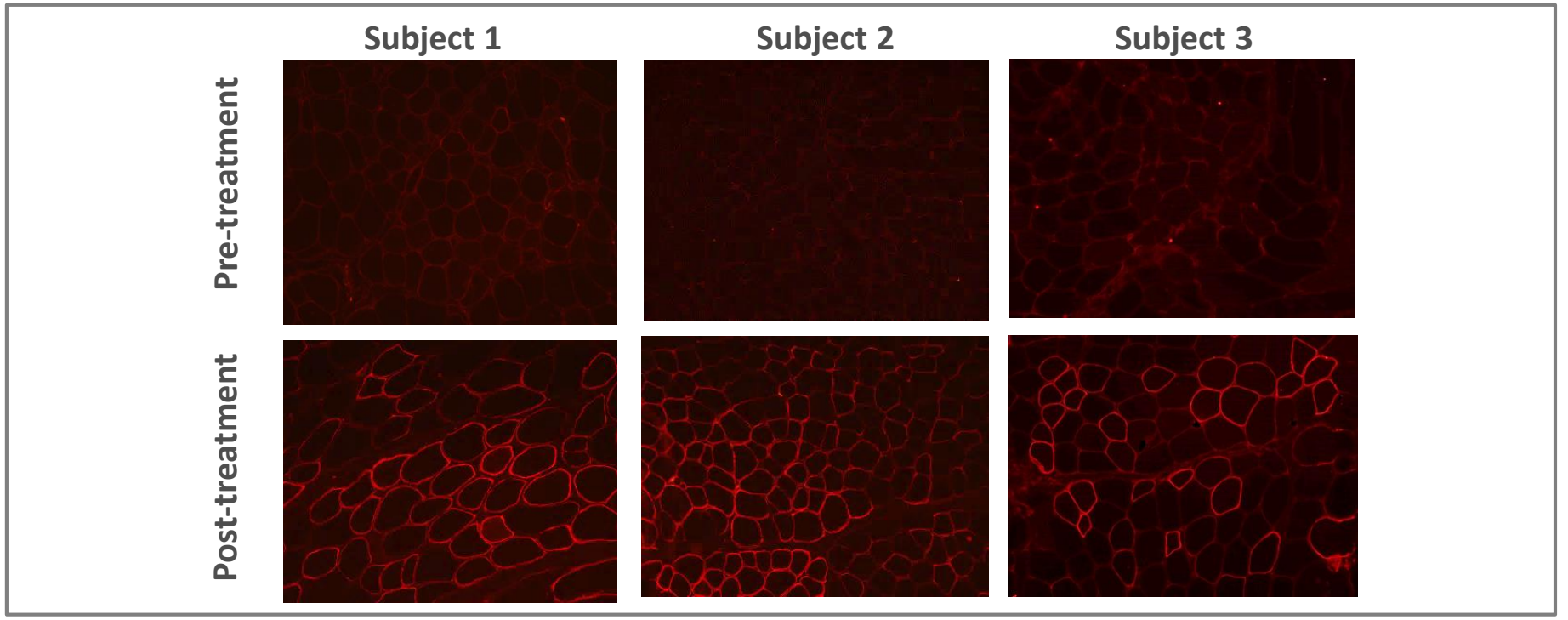
*Values updated following database transfer

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%

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

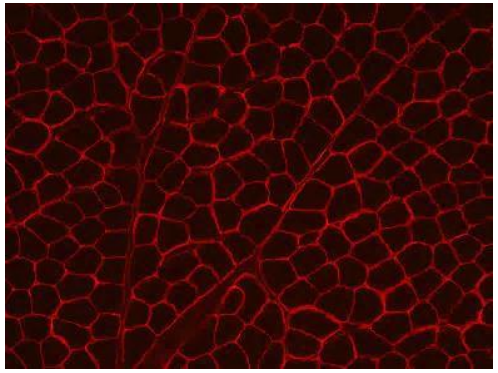
Cohort 1 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $5x10^{13}$ vg/kg

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



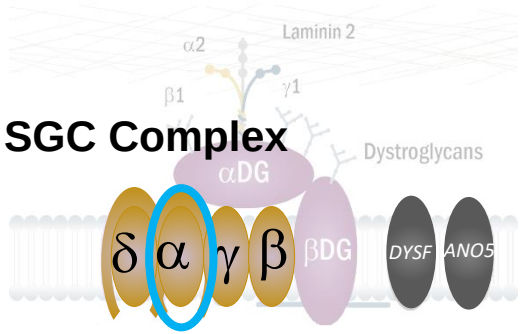
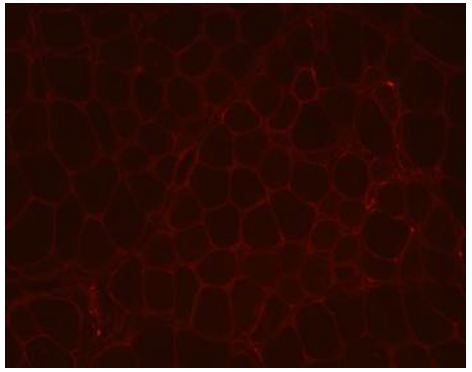
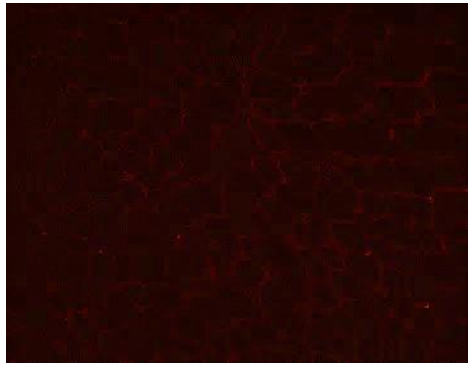
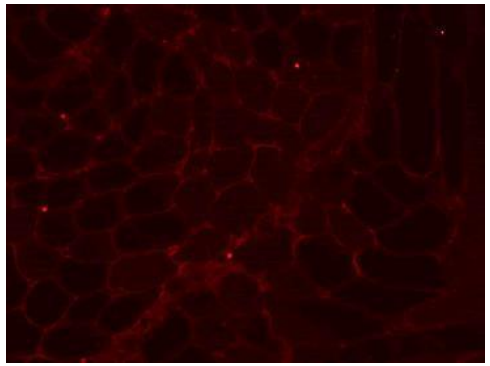
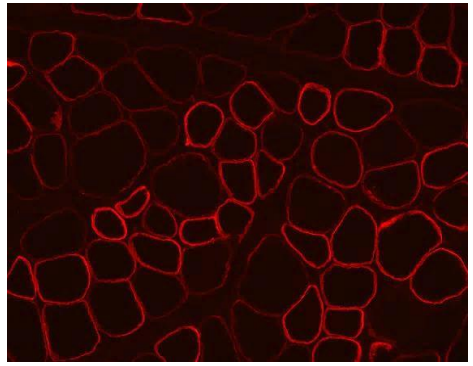
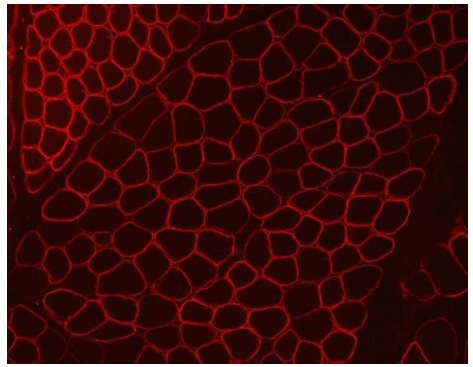
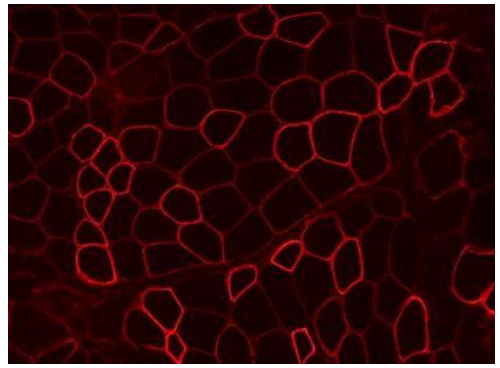


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

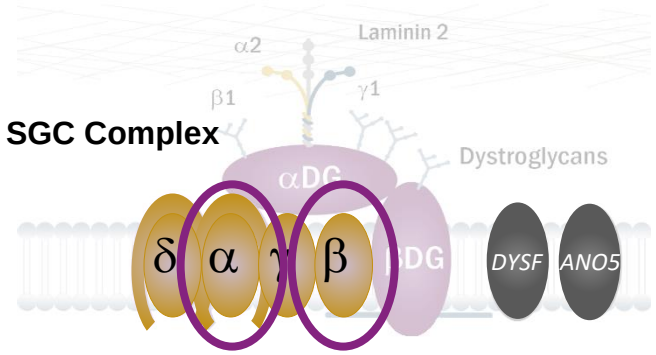
α-Sarcoglycan Expression (IF)

	Subject 1	Subject 2	Subject 3
Pre-treatment			
Post-treatment			

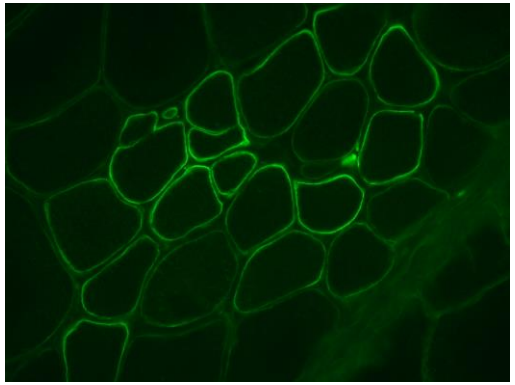
β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. ClinicalTrials.gov Identifier: NCT03652259.

Sarepta Therapeutics 2019. Data on file.

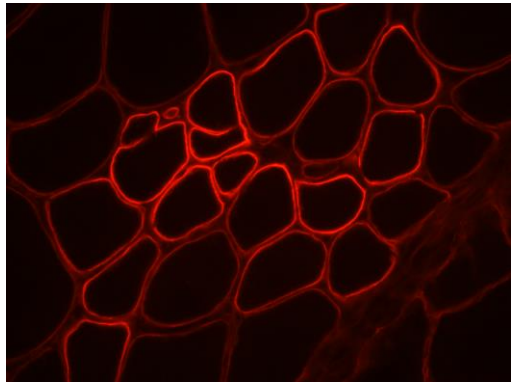
SGCB Expression Significantly Upregulated SGC Complex Protein at a Dose of $5x10^{13}$ vg/kg



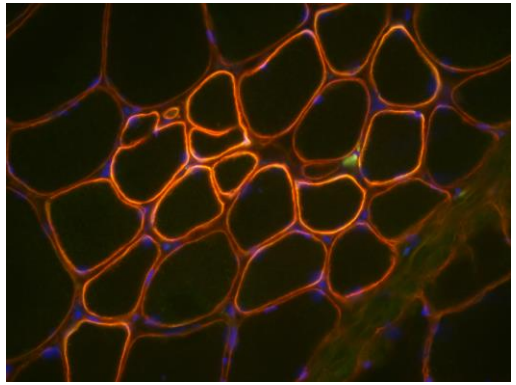
β-sarcoglycan



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

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

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

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

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

Cohort 1 - Summary of Functional Data at 1-Year

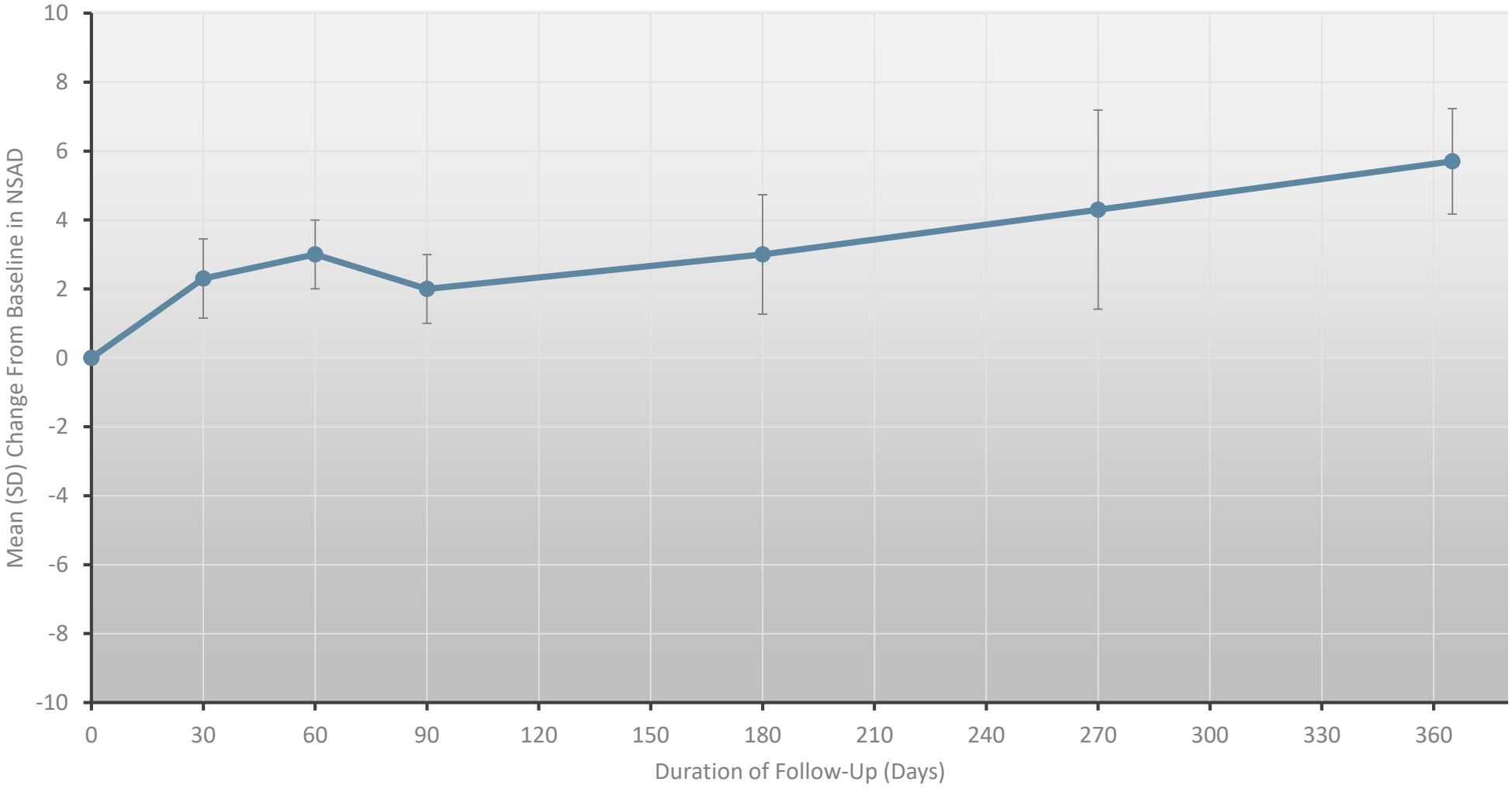
ALL SUBJECTS SHOWED IMPROVEMENT IN ALL FUNCTIONAL MEASURES

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**

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

*Values updated following database transfer

Cohort 1 - Mean Change from Baseline in NSAD



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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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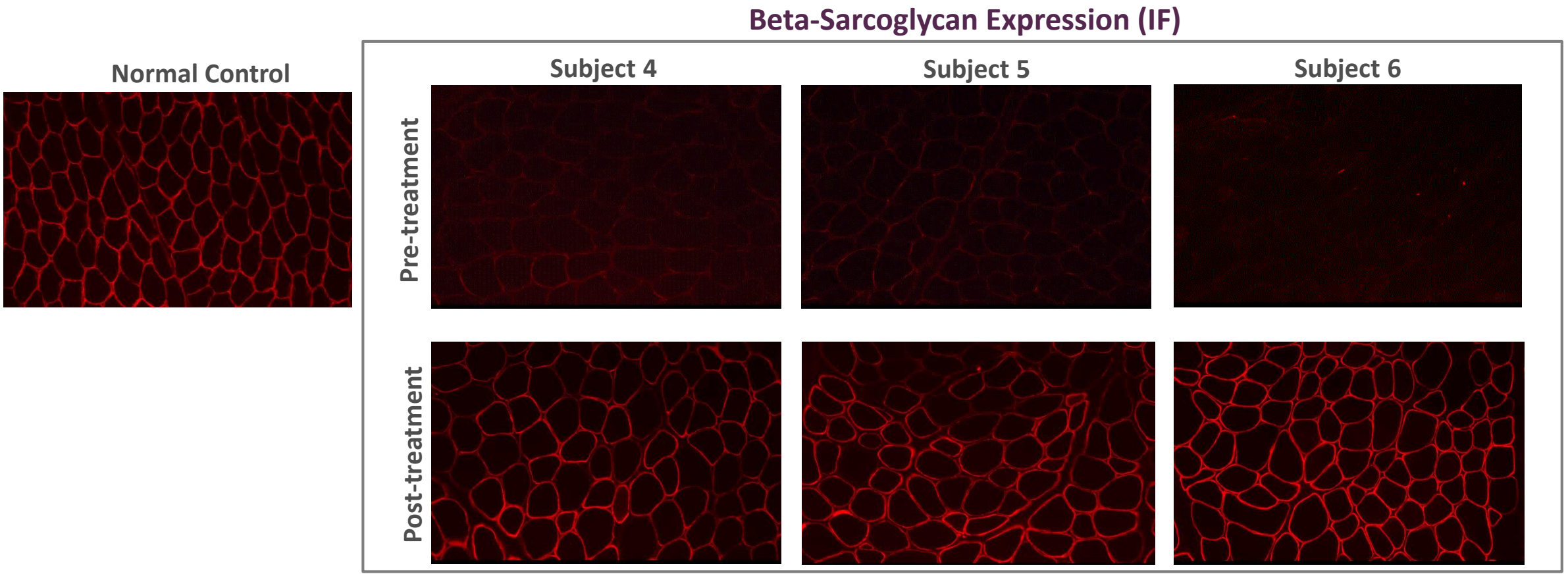
1. Baseline is Baseline/Screening visit measurement.

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

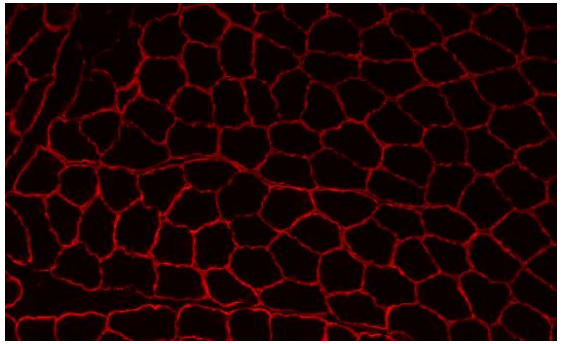
Cohort 2 - Robust β-Sarcoglycan Expression in Muscle Biopsies in All 3 Subjects at a Dose of $2x10^{14}$ vg/kg

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



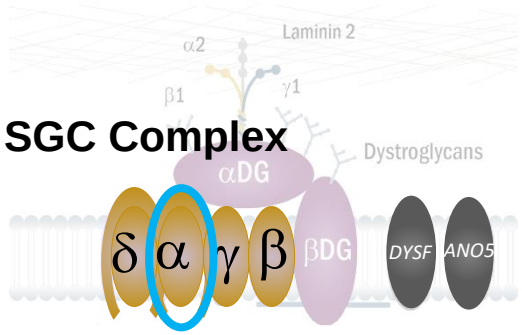
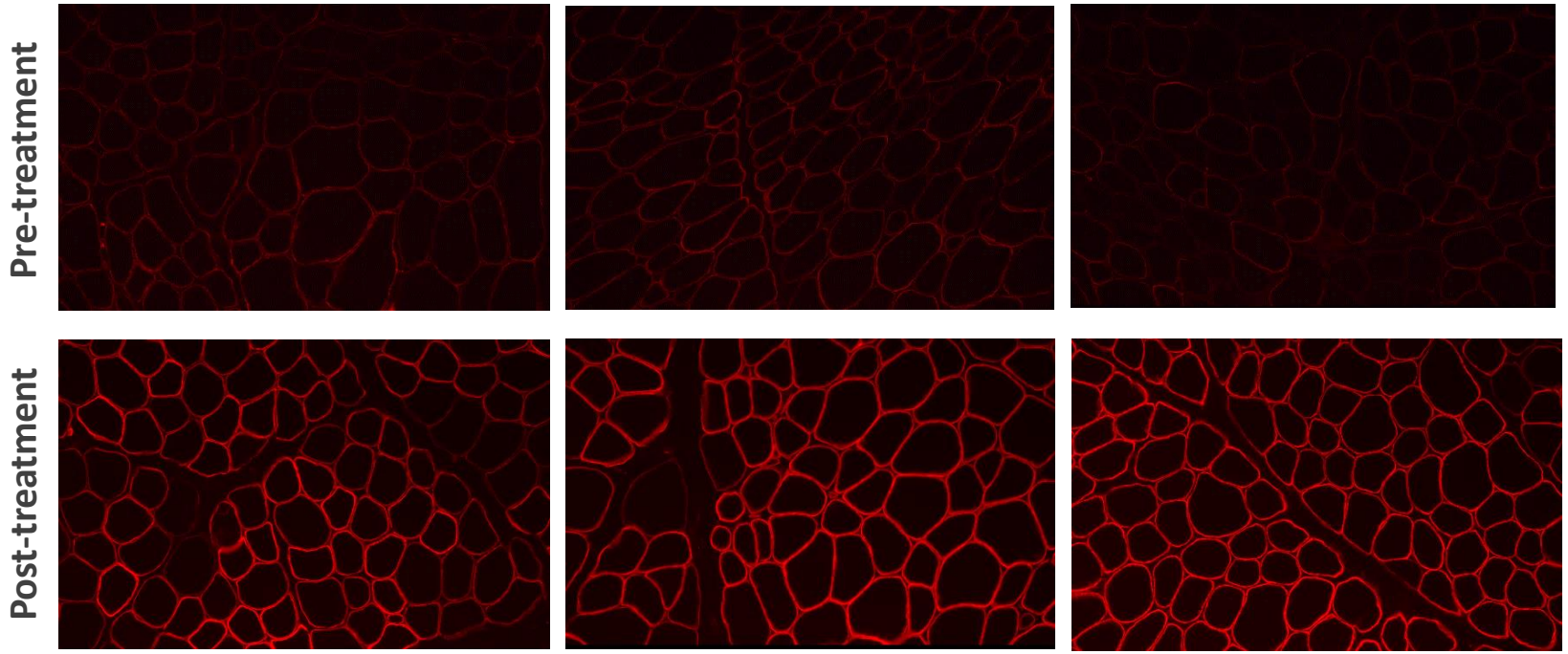


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

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

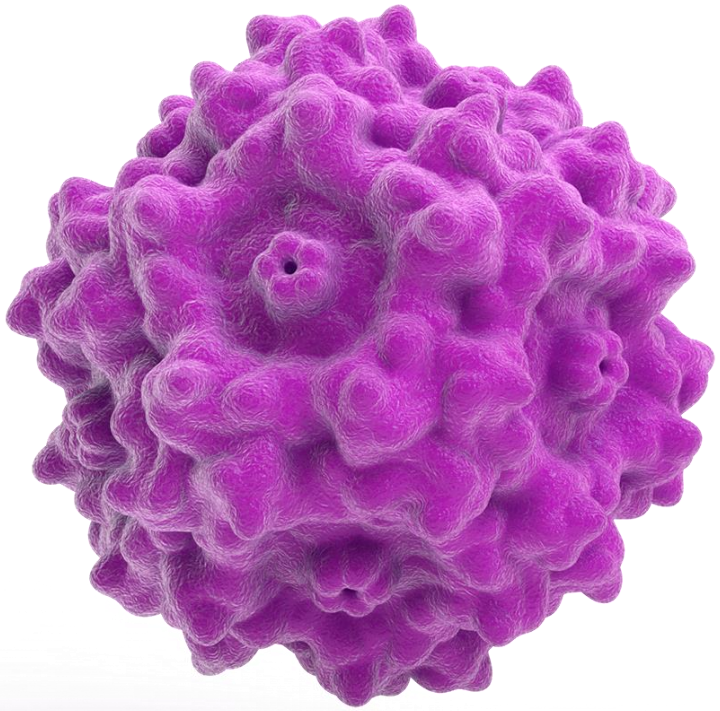
- AAVrh74 efficiently transduces all muscle types
- MHCK7 promoter allows for cardiac and skeletal transgene muscle expression
- Low pre-existing immunity for AAVrh74

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

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

Next Steps for Clinical Development



AAVrh74.MHCK7.SGCB
(SRP-9003)

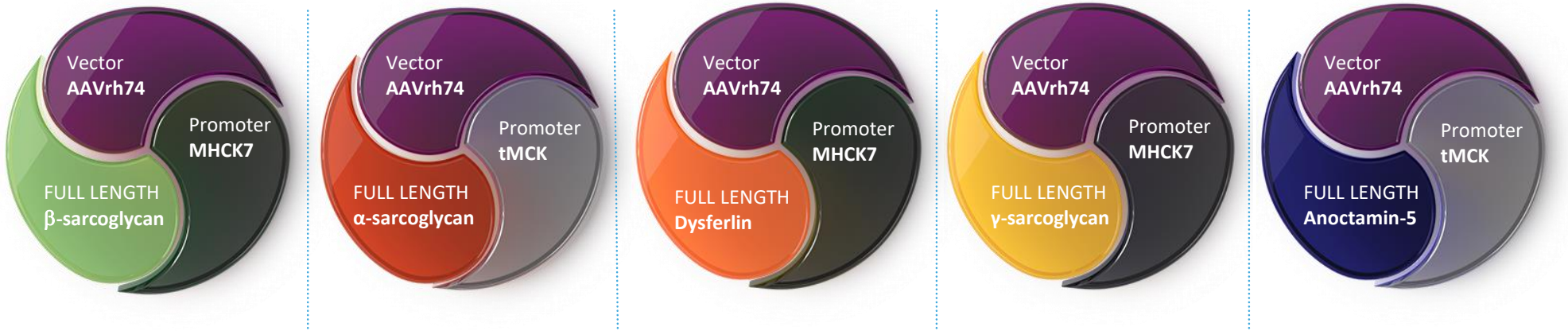
- Final dose for registration trial will be selected by Q3
- Engagement with global regulatory agencies to discuss pivotal trial designs
- Commenced run on commercial manufacturing process to support further clinical development
- Initiation of registrational study in 2021

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.

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

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