CLINICAL UPDATE:

SRP-9003 BETA-SARCOGLYCANOPATHY GENE THERAPY PROGRAM
LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2E FUNCTIONAL DATA

Louise Rodino-Klapac

Senior Vice President, Gene Therapy
Sarepta Therapeutics, Inc.

October 4, 2019

SAREPTA THERAPEUTICS

FORWARD-LOOKING STATEMENTS

This presentation contains "forward-looking statements." Any statements that are not statements of historical fact may be deemed to be forward-looking statements. Words such as “believe,” “anticipate,” “plan,” “expect,” “will,” “may,” “intend,” “prepare,” “look,” “potential,” “possible” and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements relating to the safety profile of SRP-9003 seen to date supporting the ability to dose escalate; the potential benefits of the AAVrh74 vector and the MHCK7 promoter; our clinical programs in LGMD; and our plans regarding dose escalation, selection of final dose for registration trial and engaging with global regulatory agencies to discuss pivotal trial designs.

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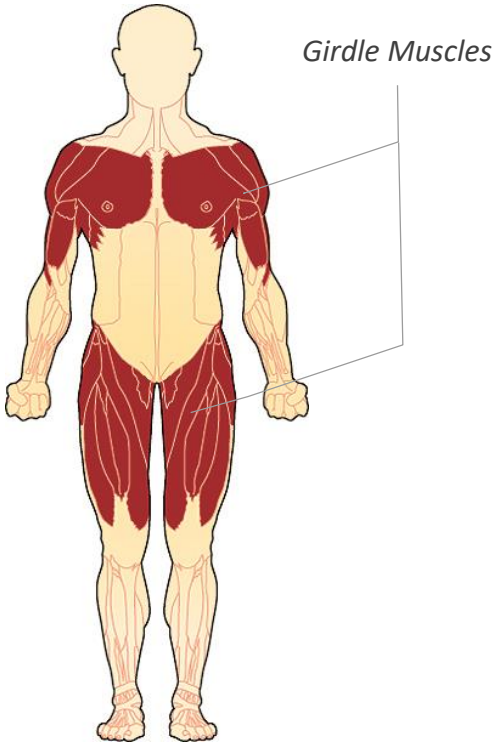
LGMDS ARE DEVASTATING MUSCULAR DYSTROPHIES

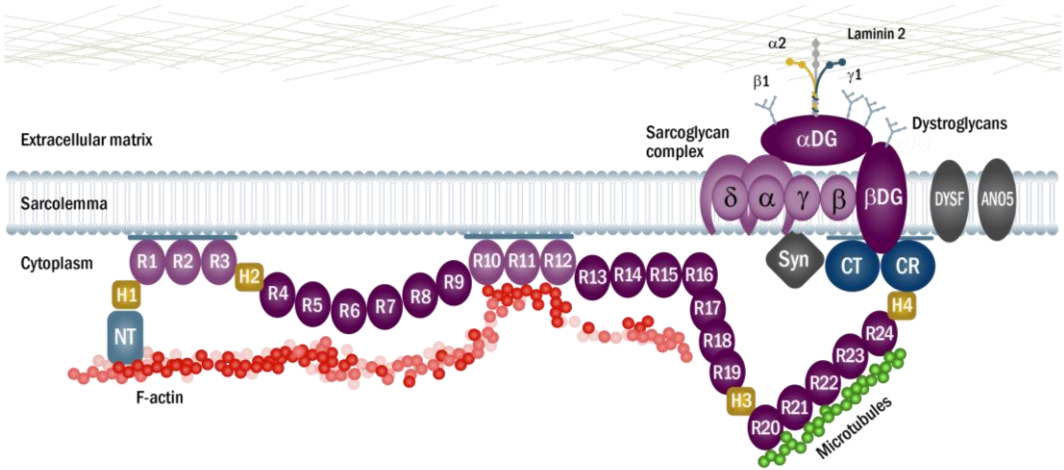
MONOGENIC, RARE NEUROMUSCULAR DISEASES

- **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 teens
  - More severe forms mimic DMD
  - Death can result before age 30
- **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.

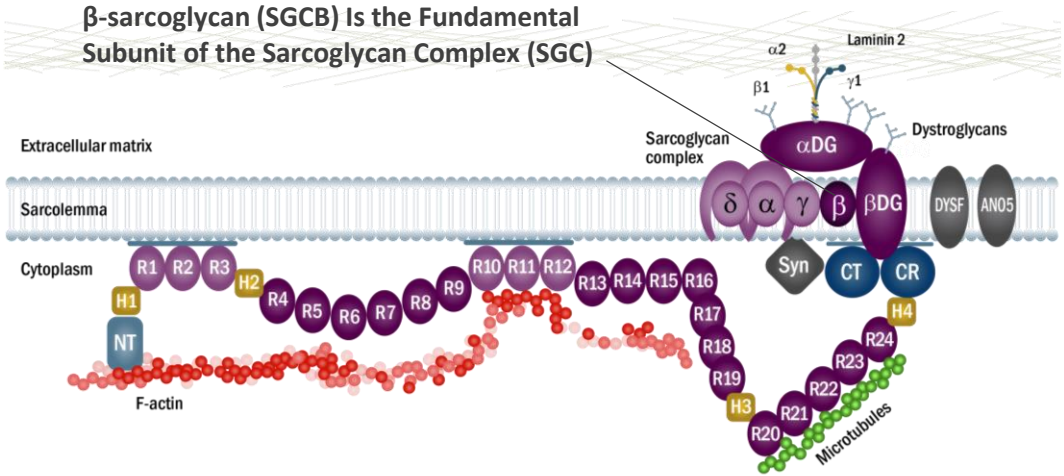
LGMD PORTFOLIO



- **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 (MYO-201 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.

LGMD PORTFOLIO ADDRESSES MONOGENIC MUTATIONS THAT RESULT IN THE LACK OF ONE OF THE PROTEINS COMPRISING THE DYSTROPHIN-ASSOCIATED PROTEIN COMPLEX



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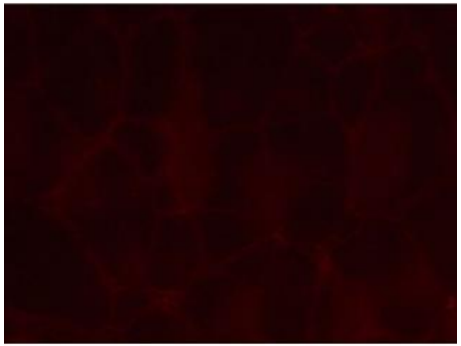
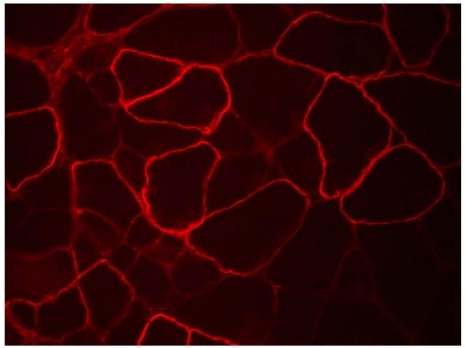
PRE-CLINICAL MODELS CORRELATED EXPRESSION AND FUNCTION

≥20 PERCENT EXPRESSION LEADS TO INCREASED FUNCTION

Pretreatment

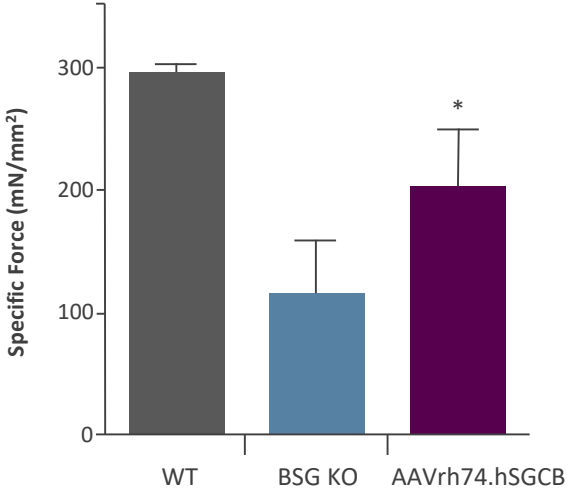


Post Treatment



5x10^{12} vg/kg

Function



LGMD2E PHASE I/II STUDY: COHORT 1 (N=3)

SAREPTA THERAPEUTICS

LGMD TYPE 2E OPEN-LABEL TRIAL DESIGN

- **Up to 6 subjects with LGMD**
  - Cohort 1: 3 subjects; 4-15 years of age, **$5x10^{13}$ vg/kg** AAVrh74.MHCK7.SGCB systemic delivery

- **Inclusion criteria**
  - A confirmed SGCB mutation in both alleles
  - Negative for AAVrh74 antibodies
  - >40% of Normal 100 meter walk test

- **60-day needle muscle biopsy**

- **Prednisone 1 day prior to gene transfer, 30 days 1 mg/kg, taper**

OUTCOME MEASURES

- **Primary endpoint**
  - **≥ 20% β–sarcoglycan expression**
  - Safety
- **Secondary endpoints, including:**
  - Decrease in CK
  - Functional endpoints
    - North Star Assessment for LGMD (NSAD)
    - 100m
    - 10m
    - 4 stairs
    - Time to rise

LGMD2E STUDY EXPRESSION RESULTS: COHORT 1 (N=3)

SAREPTA THERAPEUTICS

LGMD2E SUBJECT DEMOGRAPHICS AT BASELINE[1]

Subject	Age (years)	Mutation	Weight (kg)	CK Levels at Baseline (U/L)
1	13	Exon 3	55	10,727
2	4	Exon 4	17	12,826
3	13	Exon 3	50	10,985

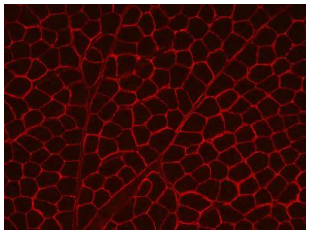
- Exons 3-6 encode for the extracellular domain of SGCB
- Mutations in these exons lead to complete absence of or severely reduced expression of SGCB, and a severe phenotype that includes cardiomyopathy[2]

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

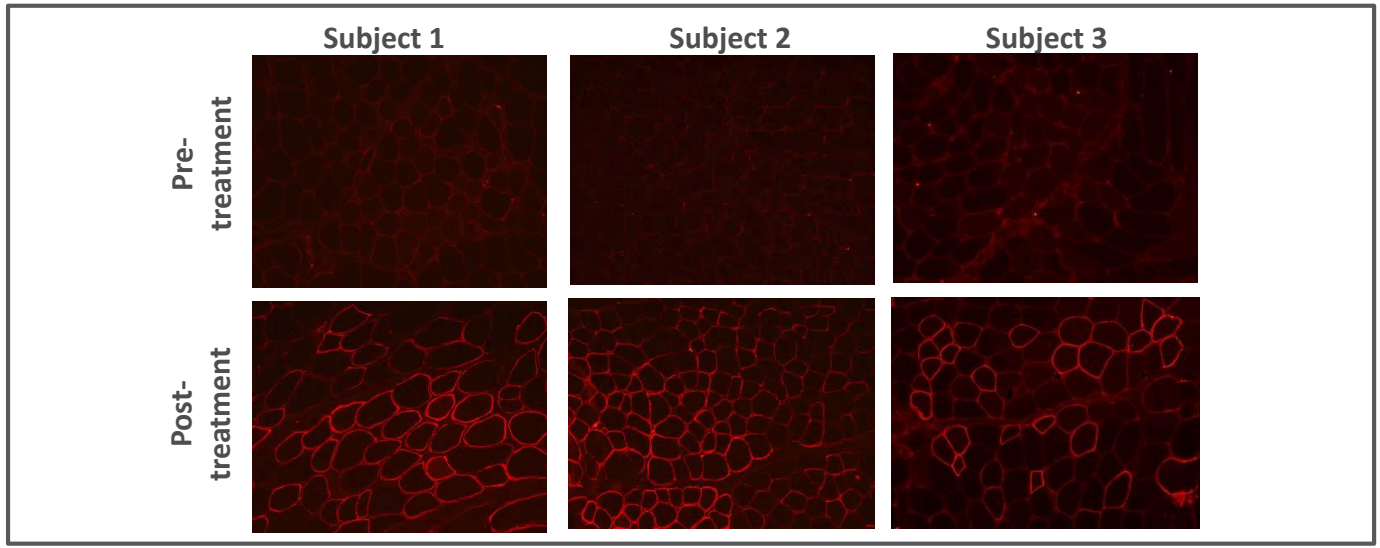
1. Sarepta Therapeutics 2019. Data on file. 2. Semplicini C, et al. *Neurology*. 2015;84(17):1772-1781.

ROBUST β-SARCOGLYCAN EXPRESSION IN MUSCLE BIOPSIES IN ALL 3 SUBJECTS AT A DOSE OF $5X10^{13}$ VG/KG

Normal Control



Beta-Sarcoglycan Expression (IHC)



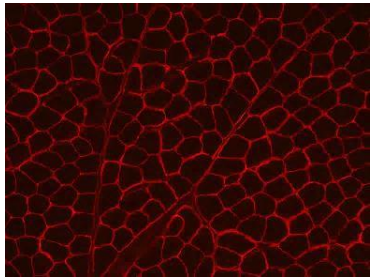
	Percentage of SGCB-positive Fibers	Intensity
Mean (n=3)	51%	47%

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%**

SGCB EXPRESSION SIGNIFICANTLY UPREGULATED SGC COMPLEX AT A DOSE OF 5 X 10^{13} VG/KG

Normal Control



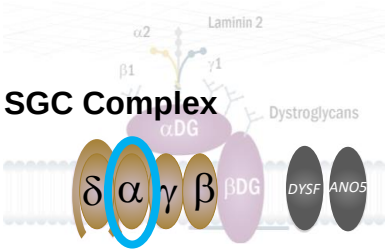
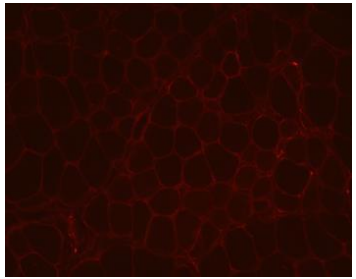
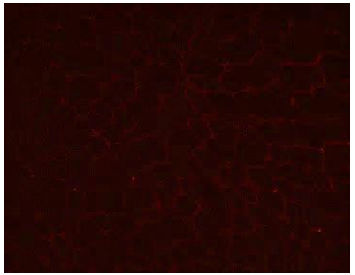
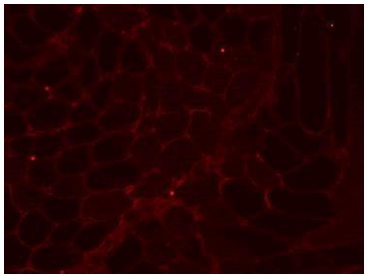
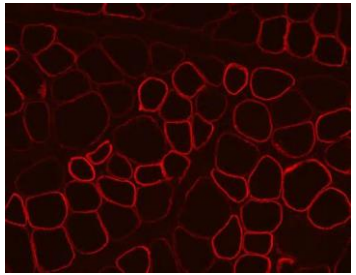
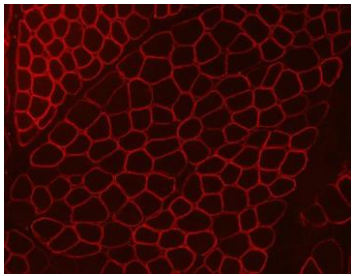
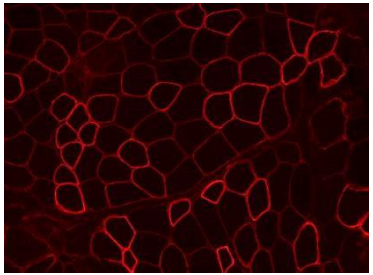


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

α-Sarcoglycan Expression (IHC)

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

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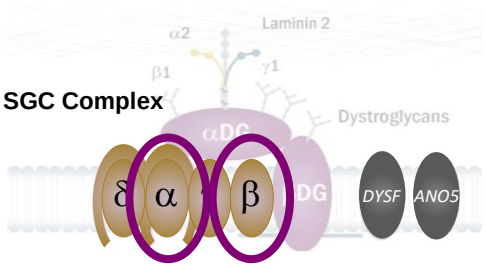
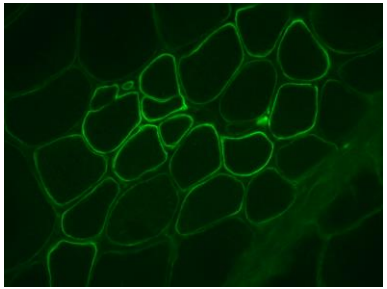
Sarepta Therapeutics 2019. Data on file. ClinicalTrials.gov: NCT03652259.

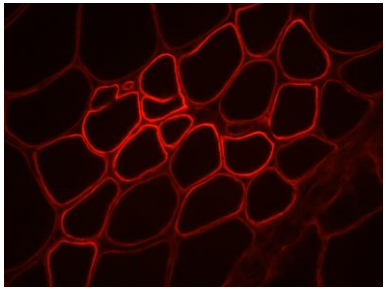
SGCB EXPRESSION SIGNIFICANTLY UPREGULATED SGC COMPLEX PROTEIN AT A DOSE OF $5x10^{13}$ VG/KG



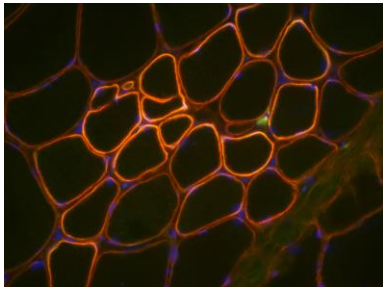
β-sarcoglycan



α-sarcoglycan



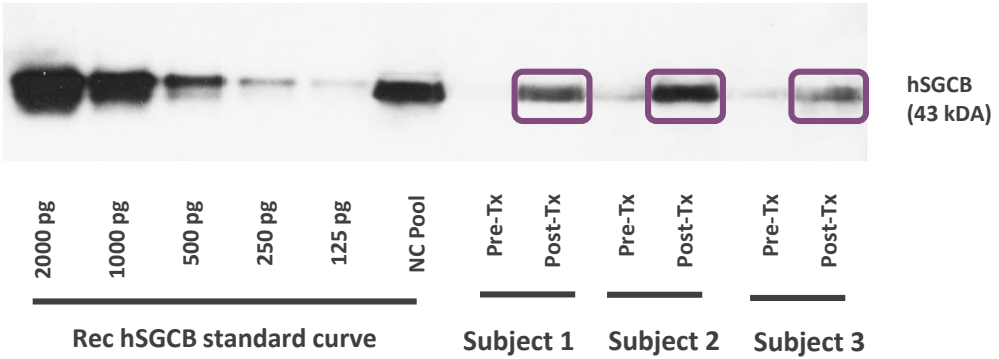
Colocalization (Merge)



β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority.
Sarepta Therapeutics 2019. Data on file. ClinicalTrials.gov: NCT03652259. Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2012;14(6):373-378.

DETECTION OF β-SARCOGLYCAN EXPRESSION BY WESTERN BLOT POST-TREATMENT IN ALL 3 SUBJECTS AT DAY 60

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

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β-SARCOGLYCAN EXPRESSION IS SUPPORTED BY VECTOR GENOME COUNTS

Beta-Sarcoglycan Expression (IHC)

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

Beta-Sarcoglycan (Western Blot)

	Percent of Normal
Mean (n=3)	36.1%

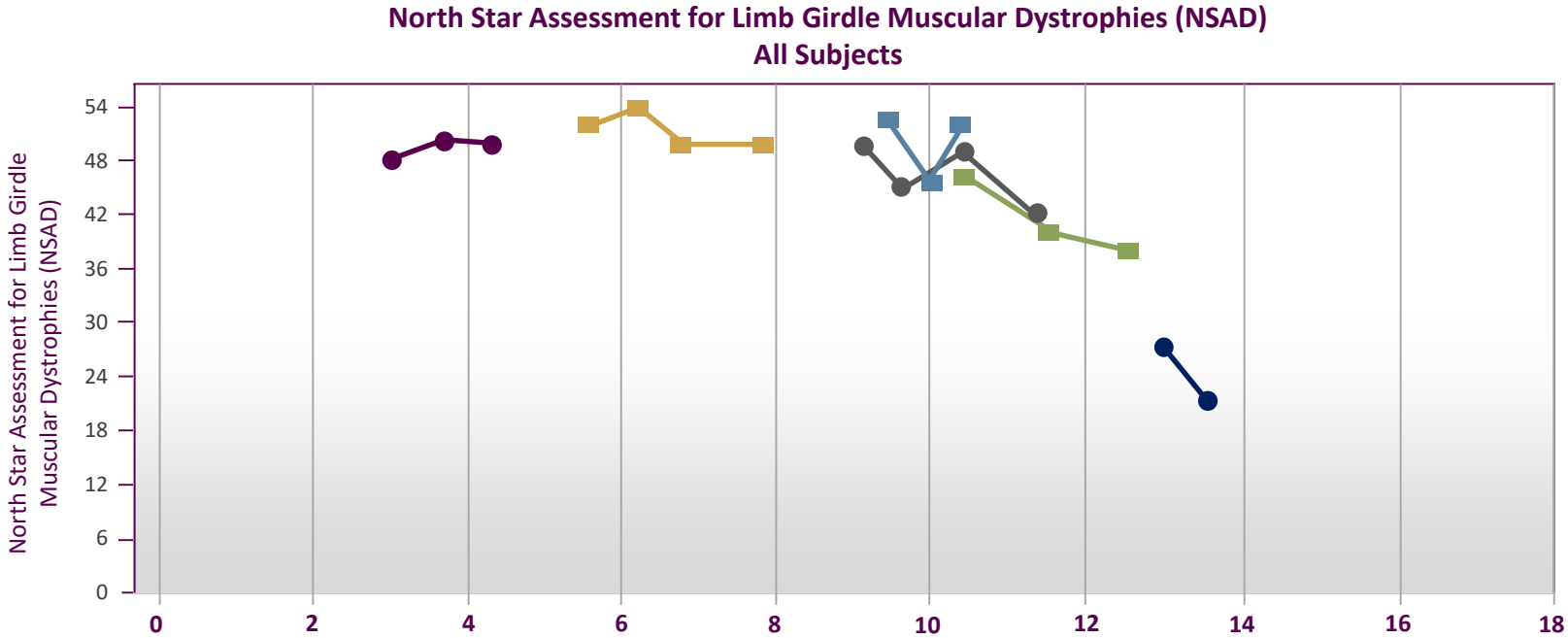
Vector Genome Number

	Vector Copies/µg DNA	Copies per Nucleus
Mean (n=3)	8.4E04	0.60

LGMD2E STUDY
FUNCTIONAL DATA SUMMARY:
COHORT 1 (n=3)

SAREPTA THERAPEUTICS

LGMD2E NATURAL HISTORY DATA GENERATED BY LINDA LOWES & LINDSAY ALFANO AT NATIONWIDE CHILDREN'S HOSPITAL



Patients are assessed every 6 months

CREATINE KINASE (CK) LEVELS ARE REDUCED WITH β-SARCOGLYCAN GENE THERAPY

		CK Levels (U/L)					
Subject	**Age (years)**	**Baseline**	**Day 30**	**Day 60**	**Day 90**	**Day 180**	**Day 270**
1	13	10,727	619	2257	1135	1553	2300
2	4	12,826	4795	910	2159	5070	2665
3	13	10,985	687	2061	2392	10,055	1295

9 Months: 82% Reduction in CK

ClinicalTrials.gov Identifier: NCT03652259

SUMMARY OF CLINICAL DATA AT 9 MONTHS

ALL SUBJECTS SHOWED IMPROVEMENT IN ALL FUNCTIONAL MEASURES

Subject	Assessment	NSAD	Time to Rise (sec)	4 Stairs Up (sec)	100 m (sec)	10 m (sec)
1	Baseline	40	5.0	2.4	49.3	5
	Day 270	41	4.1	2.3	43.2	4.5
2	Baseline	48	1.5	1.6	59.3	3.4
	Day 270	54	1.2	1.3	48.4	3.2
3	Baseline	41	3.5	2.8	49.9	5.2
	Day 270	47	3.0	1.9	48.6	4.3

SUMMARY OF CLINICAL DATA AT 9 MONTHS

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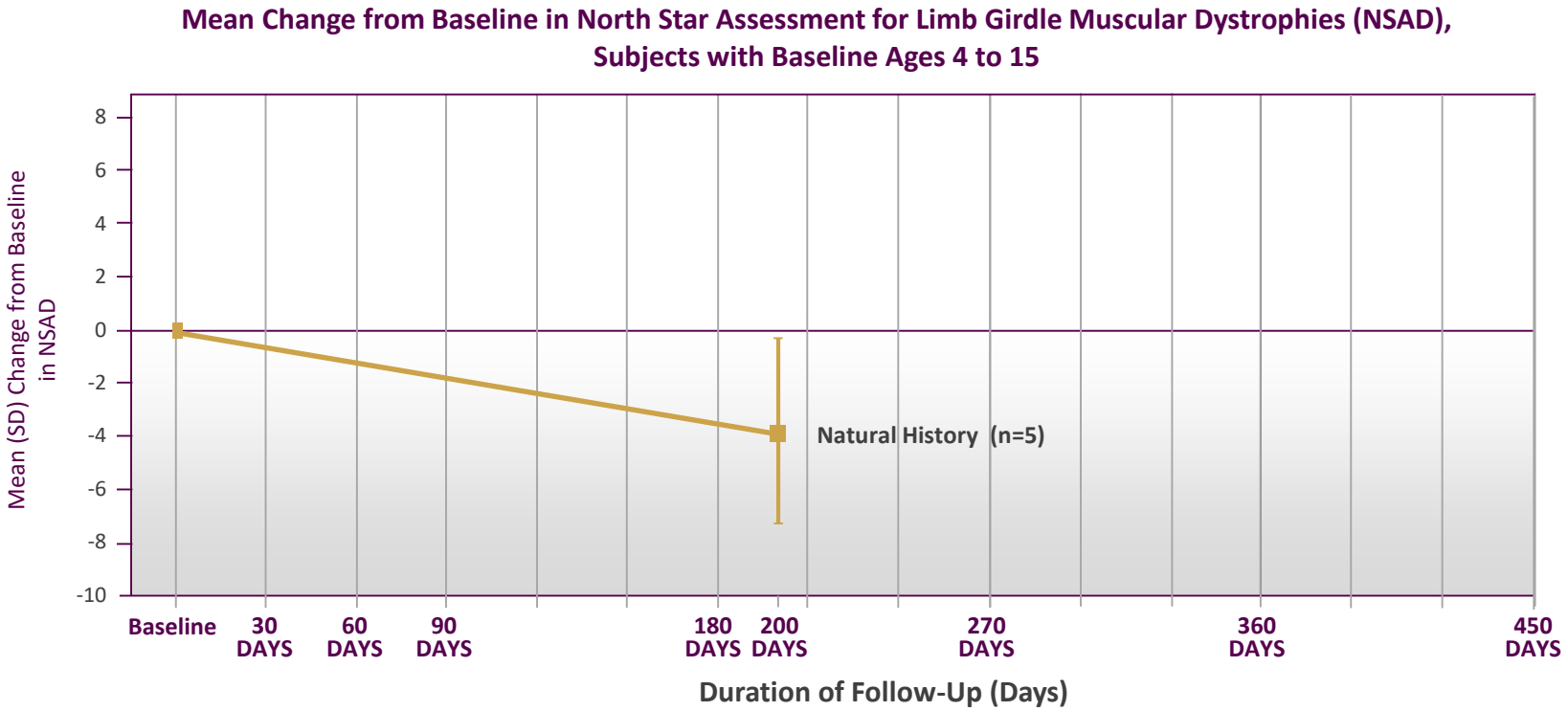
	Day 270	54	1.2	1.3	48.4	3.2
3	Baseline	41	3.5	2.8	49.9	5.2
	Day 270	47	3.0	1.9	48.6	4.3

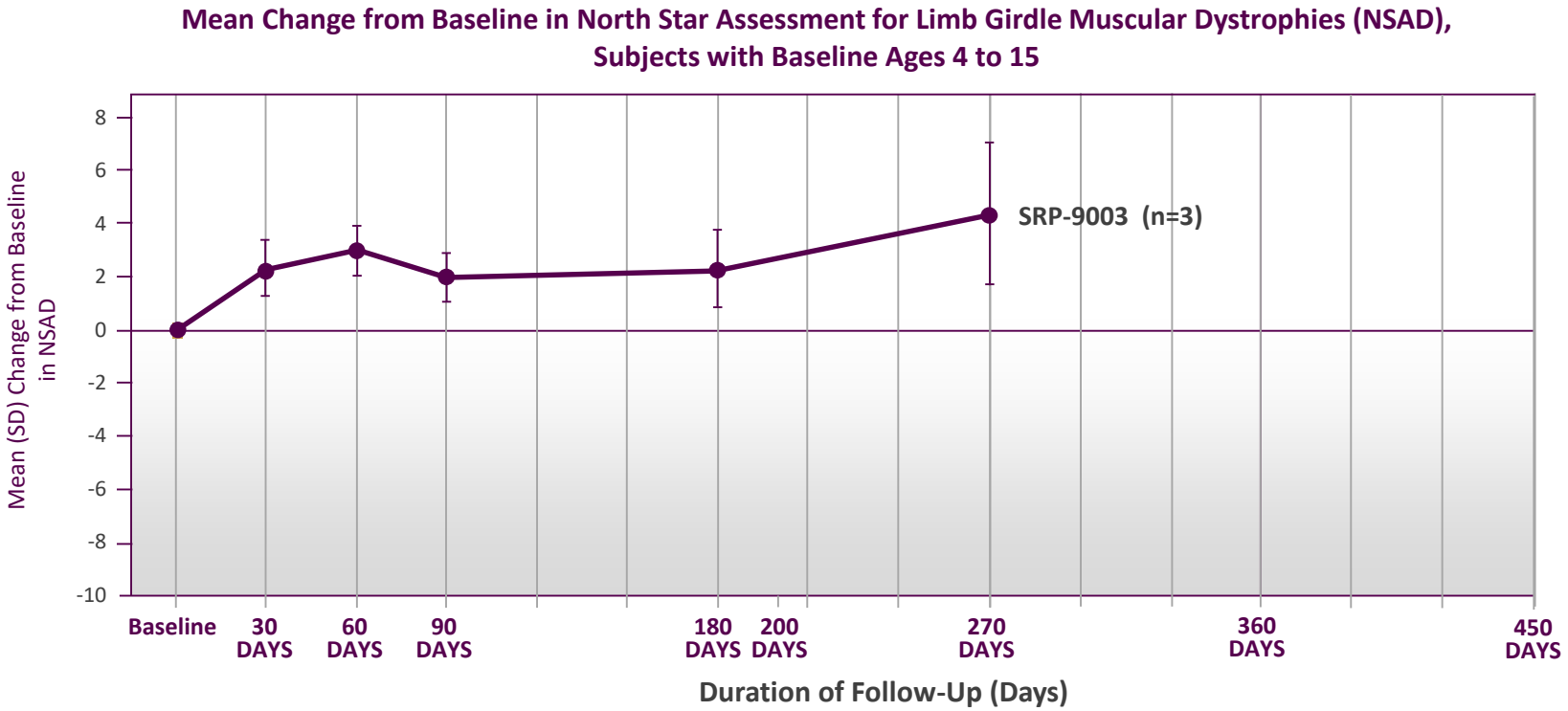
BASELINE DEMOGRAPHICS OF AGE-MATCHED LGMD2E NATURAL HISTORY GROUP (4-15 YEARS)

Subject	Age (years)
1	5
2	12
3	10
4	9
5	9

AGE-MATCHED LGMD2E NATURAL HISTORY COHORT



SRP-9003 TREATED LGMD2E PATIENTS (LOW DOSE COHORT 1)



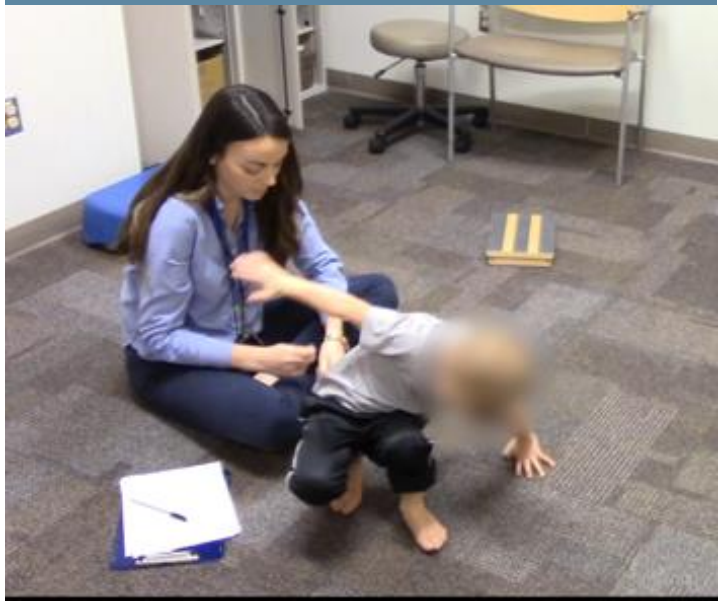
PATIENT 1: GETTING UP FROM SITTING

Baseline Getting up from Sitting

9 months post gene therapy

PATIENT 2: TRUNK CONTROL

Baseline
Poor Trunk Control

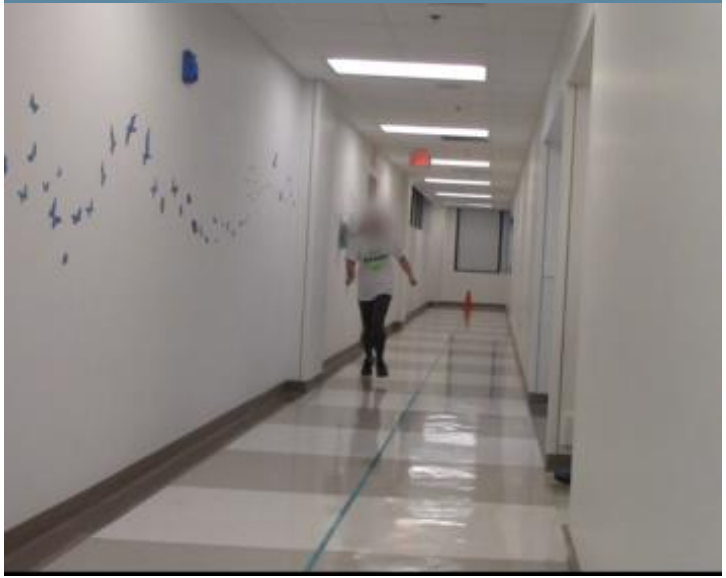


9 months Post Gene Therapy
Clinic Visit

PATIENT 3: 100M RUNNING

100 m baseline running
Limited hip extension/flexion

100 m 9 months post gene therapy
Good hip extension/flexion; faster speed



SAFETY TO DAY 270 (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

SUMMARY

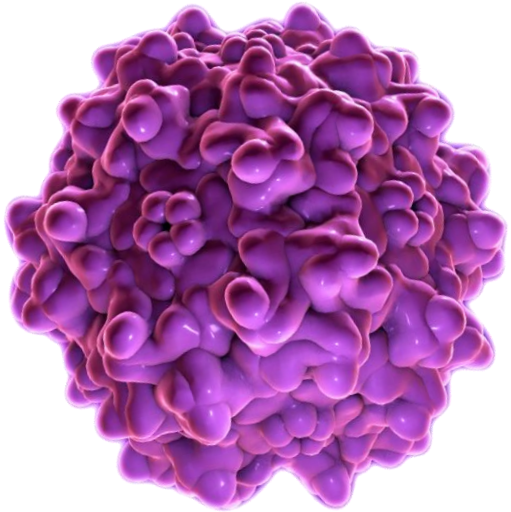
Construct optimized for use in LGMD

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

Preliminary clinical results

- Widespread beta-sarcoglycan expression across all patients at a systemic dose of **$5x10^{13}$ vg/kg**
- Substantial reduction in CK
- Consistent improvement in all functional measures in all patients
- Safety profile supports dose escalation

FUTURE CLINICAL DEVELOPMENT:
DOSE ESCALATION TO IDENTIFY REGISTRATIONAL TRIAL DOSE



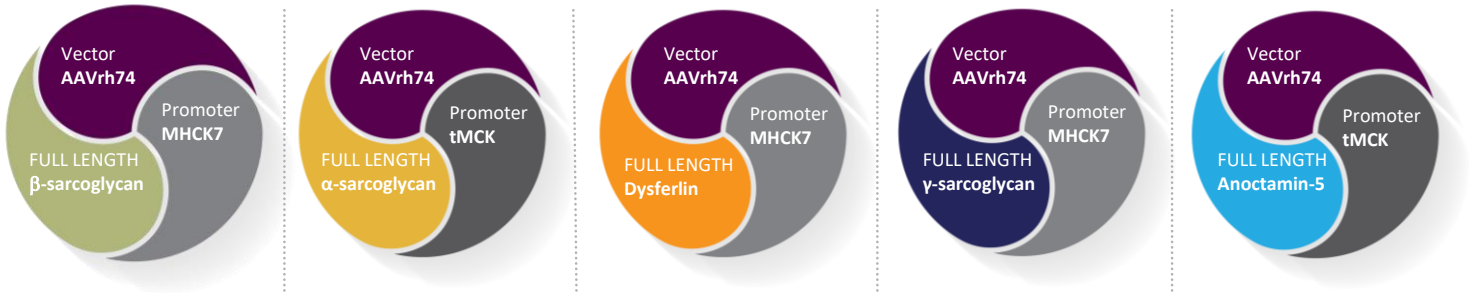
AAVrh74.MHCK7.SGCB
(SRP-9003)

Next Steps:

- Dose Escalation: 4-fold increase
- Final dose for registration trial will be selected from 2 doses studied
- Engagement with global regulatory agencies to discuss pivotal trial designs

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	MYO-201	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.
Sarepta Therapeutics 2019. Data on file

QUESTIONS & ANSWERS

SAREPTA THERAPEUTICS

CLINICAL UPDATE:

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LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2E FUNCTIONAL DATA

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