2019 PPMD ANNUAL CONFERENCE

Douglas S. Ingram
President and Chief Executive Officer

June 28, 2019

CALEB
Living with Duchenne
Muscular Dystrophy

A NEW ERA OF MEDICINE IS UPON US

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," "would," "should," "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 potential benefits of our technologies and scientific approaches, including the potential benefits of AAVrh74, MHCK7 and the micro-dystrophin transgene; and our plans for the future and expected milestones, including the SRP-9001 clinical development plan, our plan to initiate a commercial supply, multi-center, trial for SRP-9001 by the end of 2019, our goal to expand the inclusion criteria for SRP-9001 and our goal of treating 100% of individuals with DMD.

These forward-looking statements involve risks and uncertainties, many of which are beyond our control and are based on our current beliefs, expectations and assumptions regarding our business. Actual results and financial condition could materially differ from those stated or implied by these forward-looking statements as a result of such risks and uncertainties and could materially and adversely affect our business, results of operations and trading price. Potential known risk factors include, among others, the following: our data for our different programs, including micro-dystrophin, may not be sufficient for obtaining regulatory approval; our product candidates, including those with strategic partners, may not result in viable treatments suitable for commercialization due to a variety of reasons including the results of future research may not be consistent with past positive results or may fail to meet regulatory approval requirements for the safety and efficacy of product candidates; even if our programs result in new commercialized products, we may not achieve any significant revenues from the sale of such products; success in preclinical testing and early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; our dependence on our manufacturers to fulfill our needs for our clinical trials and commercial supply, including any inability on our part to accurately anticipate product demand and timely secure manufacturing capacity to meet product demand, may impair the availability of products to successfully support various programs, including research and development and the potential commercialization of our gene therapy product candidates; we may not be able to successfully scale up manufacturing of our product candidates in sufficient quality and quantity or within sufficient timelines; current reimbursement models may not accommodate the unique factors of our gene therapy product candidates; 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 such as expanding inclusion criteria, and bringing our product candidates to market, for various reasons including possible limitations of our financial and other resources, manufacturing limitations that may not be anticipated or resolved for in a timely manner, and regulatory, court or agency decisions, such as decisions by the United States Patent and Trademark Office; and those risks identified under the heading "Risk Factors" in Sarepta's 2018 Annual Report on Form 10-K or and most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in its other SEC filings.

For a detailed description of risks and uncertainties Sarepta faces, you are encouraged to review Sarepta's filings with the SEC. We caution investors not to place considerable reliance on the forward-looking statements contained in this presentation. The forward-looking statements in this presentation are made as of the date of this presentation only and, other than as required under applicable law, Sarepta does not undertake any obligation to publicly update its forward-looking statements.

SAREPTA THERAPEUTICS

NEWPORT BEACH


BOSTON

OUR MISSION

Armed with the most advanced science in genetic medicine, we are in a daily race to rescue lives otherwise stolen by rare disease.

At Sarepta, every day is another 24 hours to stand up for patients, advance technology, challenge convention and ***drag tomorrow into today***.

DIVERSE PRECISION GENETIC MEDICINE PIPELINE

15 DUCHENNE PROGRAMS CURRENTLY IN DEVELOPMENT

RNA

PMO | PPMO

11

PROGRAMS

GENE THERAPY

Nationwide Children's | GENETHON Cure through innovation

3

PROGRAMS

GENE EDITING

Duke University

1

PROGRAM

Saturday afternoon *Gilmore O'Neill*	TODAY'S FOCUS	Saturday morning *Charlie Gersbach (Duke)*

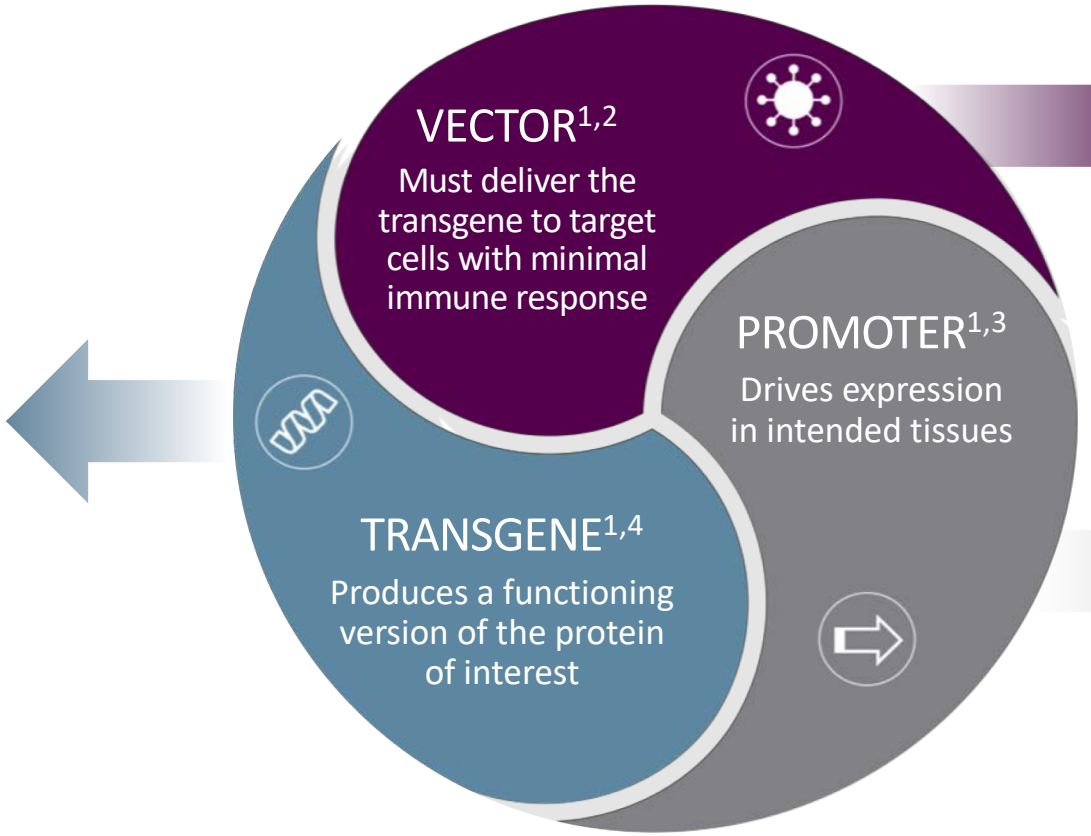
SAREPTA THERAPEUTICS

MICRO-DYSTROPHIN GENE THERAPY

RYAN
Living with Duchenne
Muscular Dystrophy

Micro-Dystrophin is investigational and has not been FDA reviewed or approved.

ESSENTIAL COMPONENTS OF GENE THERAPY



TISSUE TARGETING
(SKELETAL + CARDIAC + DIAPHRAGM)

CORRECT LOCALIZATION
(MICRO-DYSTROPHIN + important binding partners - DAPC)

SELECTIVE GENE EXPRESSION

1. Naso MF, et al. *BioDrugs*. 2017;31(4):317-334. 2. U.S. National Library of Medicine. Help Me Understand Genetics: *Gene Therapy*. Bethesda, Maryland: 2013. https://ghr.nlm.nih.gov/primer/therapy/genetherapy. Accessed November 15, 2018. 3. Zheng C, Baum BJ, *Methods Mol Biol*. 2008;434:205-219. 4. Chamberlain K, et al. *Hum Gene Ther Methods*. 2016;27(1):1-12.

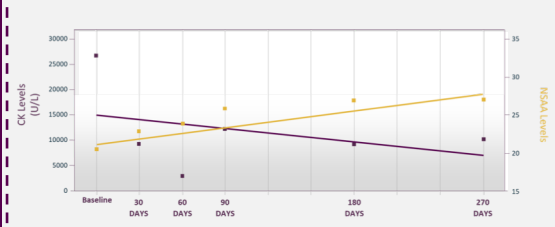
SAREPTA THERAPEUTICS

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

GENE THERAPY IS A ONE-TIME TREATMENT

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

INFORMATION YOU SHOULD KNOW

	1	2	3	4	5
QUESTION	Is **micro-dystrophin** safe and tolerable?	Is **micro-dystrophin DNA** inside muscle cells?	Is **micro-dystrophin protein** made?	Is **micro-dystrophin** at the cell membrane? How much is there?	Is **function** improved?
EXPERIMENT	**Safety**	**Western Blot:** 1. It is the accepted standard for dystrophin quantification. 2. It is the only measure that is in every study protocol. 3. Done properly, Western blot is accurate with a good standard deviation: • CV is approximately 20%			**Assessments could include:** **CK** **North Star Ambulatory Assessment (NSAA)**
EXAMPLE	*AEs, SAEs, Tolerability, and Other Signals*				

1. Sarepta Therapeutics Western blot validated method version 3 on file.

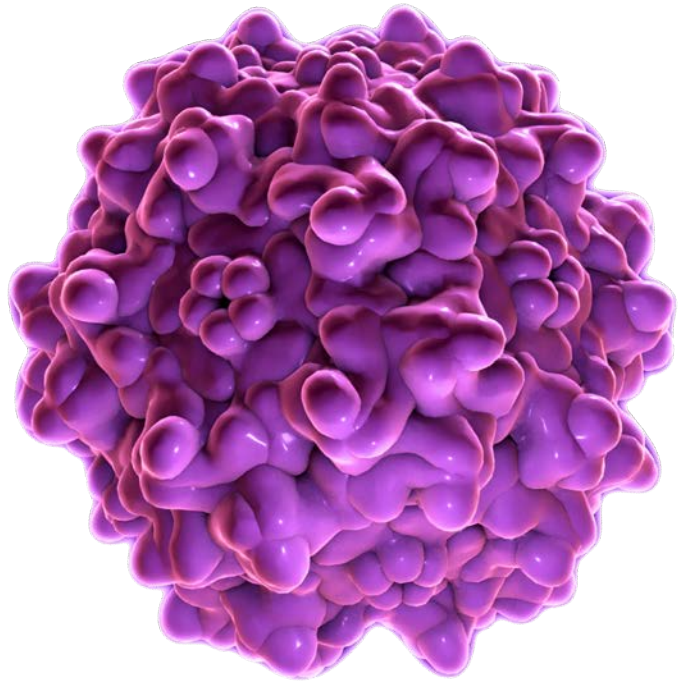
Micro-Dystrophin is investigational and has not been FDA reviewed or approved

OUR VECTOR – AAVrh74

***Vector** – Must deliver the transgene to target cells with minimal immune response*[1,2,3]

Rationale for selecting AAVrh74:

- Originally isolated from non-human primate
- Robust affinity for muscle cells in animal models
- Relatively low level of pre-existing immunity
- Does not promiscuously cross the blood brain barrier
- Different than AAV9



1. Naso MF, et al. *BioDrugs*. 2017;31(4):317-334. 2. U.S. National Library of Medicine. Help Me Understand Genetics: *Gene Therapy*. Bethesda, Maryland: 2013. https://ghr.nlm.nih.gov/primer/therapy/genetherapy. Accessed November 15, 2018. 3. Zygmunt D, et al. *Hum Gene Ther.* 2017;28(9):737-746.

SAREPTA THERAPEUTICS

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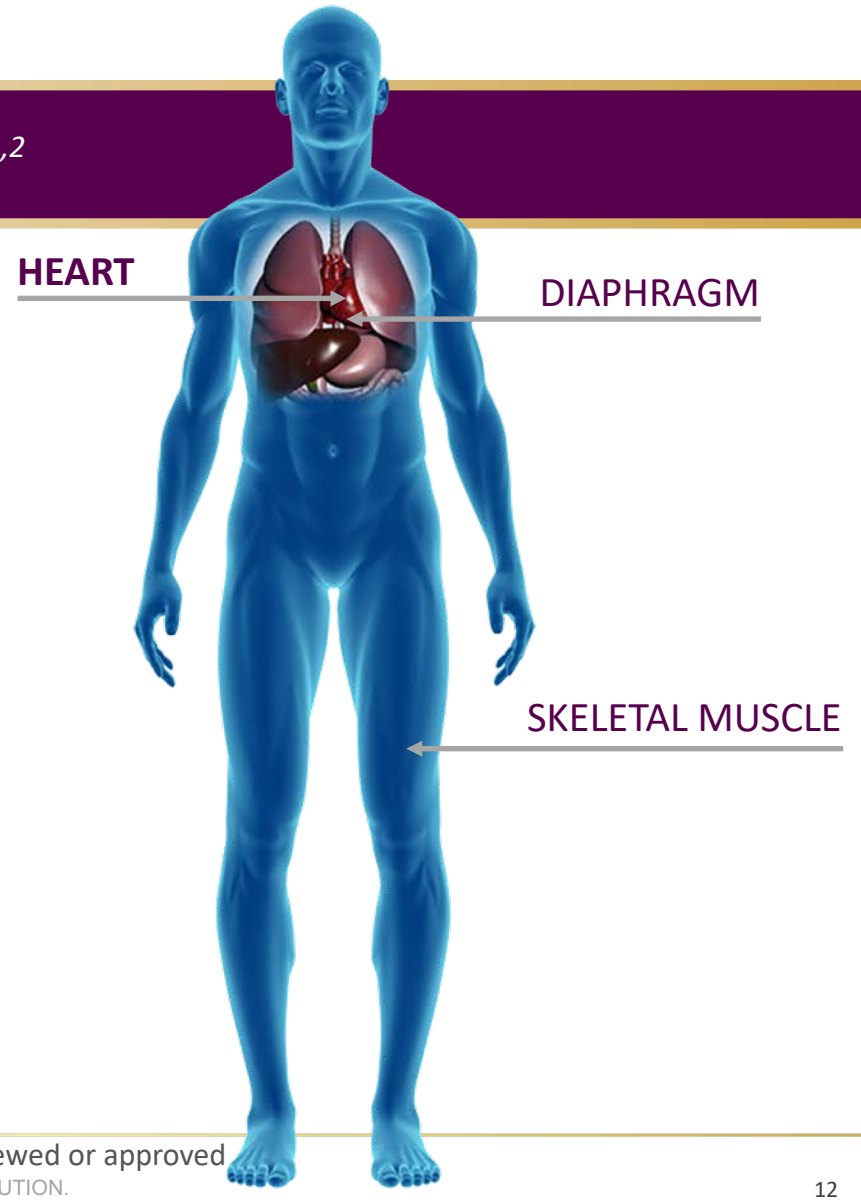
MHCK7 PROMOTER – DESIGNED TO ENHANCE CARDIAC ACTIVITY

Promoter *– drives expression in intended tissues*[1,2]

MHCK7 Promoter[3]:

- Engineered by design for muscular dystrophy
- Specific to skeletal muscle, cardiac muscle and diaphragm
- Designed to enhance expression in cardiac muscle



1. Naso MF, et al. *BioDrugs*. 2017;31(4):317-334. 2. Zheng C, Baum BJ, *Methods Mol Biol*. 2008;434:205-219.
3. Salva MZ, et al. Mol Ther 2007;15(2):320-329

SAREPTA THERAPEUTICS

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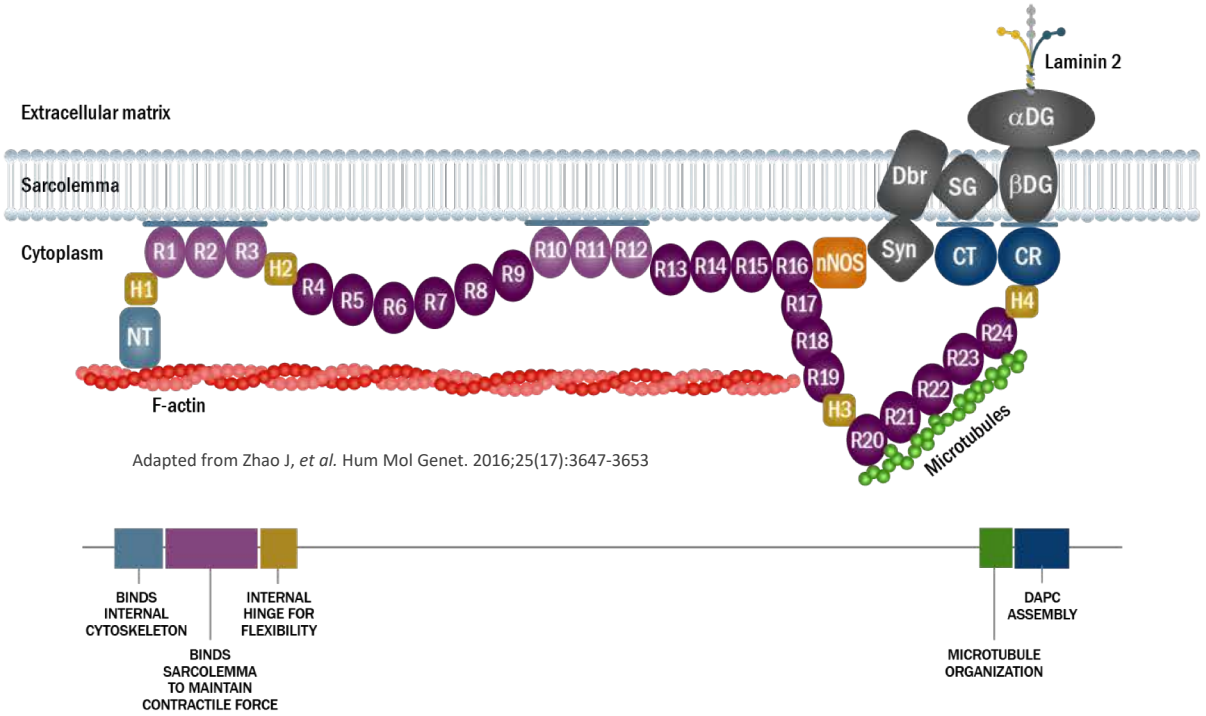
SAREPTA MICRO-DYSTROPHIN RETAINS CRITICAL ELEMENTS OF DYSTROPHIN[3-7]

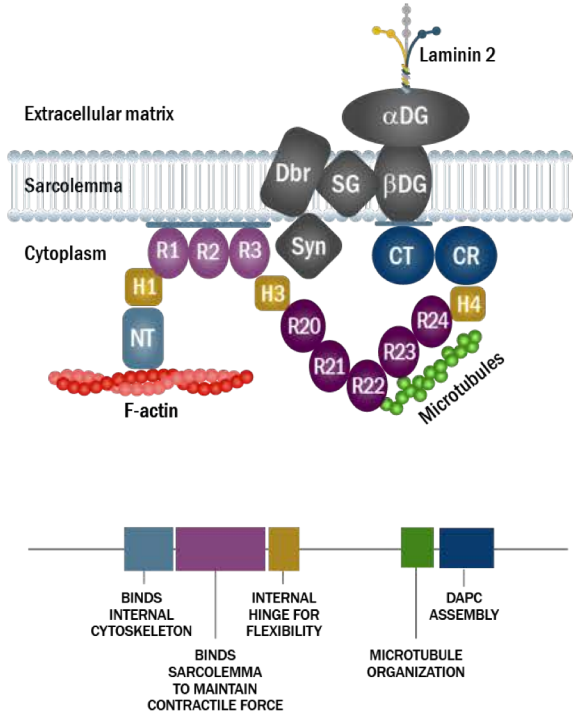
Transgene *– Produces a functioning version of the protein of interest*[1,2]

NORMAL MUSCLE[3-7]

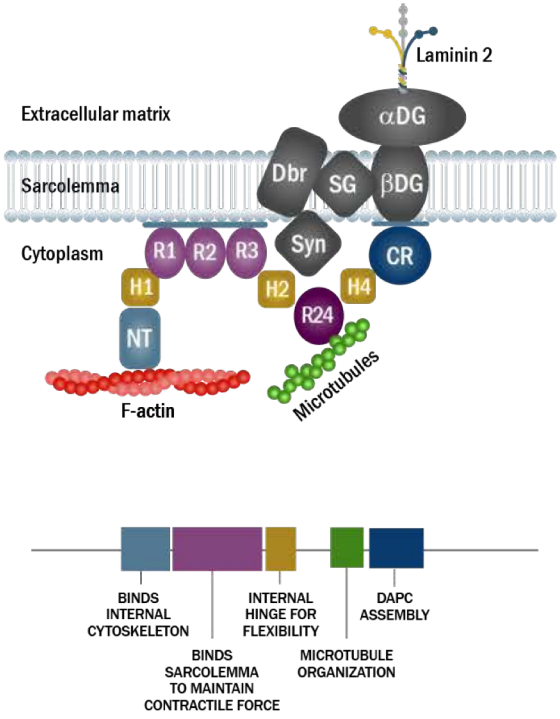


Adapted from Zhao J, *et al.* Hum Mol Genet. 2016;25(17):3647-3653

61 YoA AMBULATORY PATIENT[8-9]



SAREPTA MICRO-DYSTROPHIN[3-7]



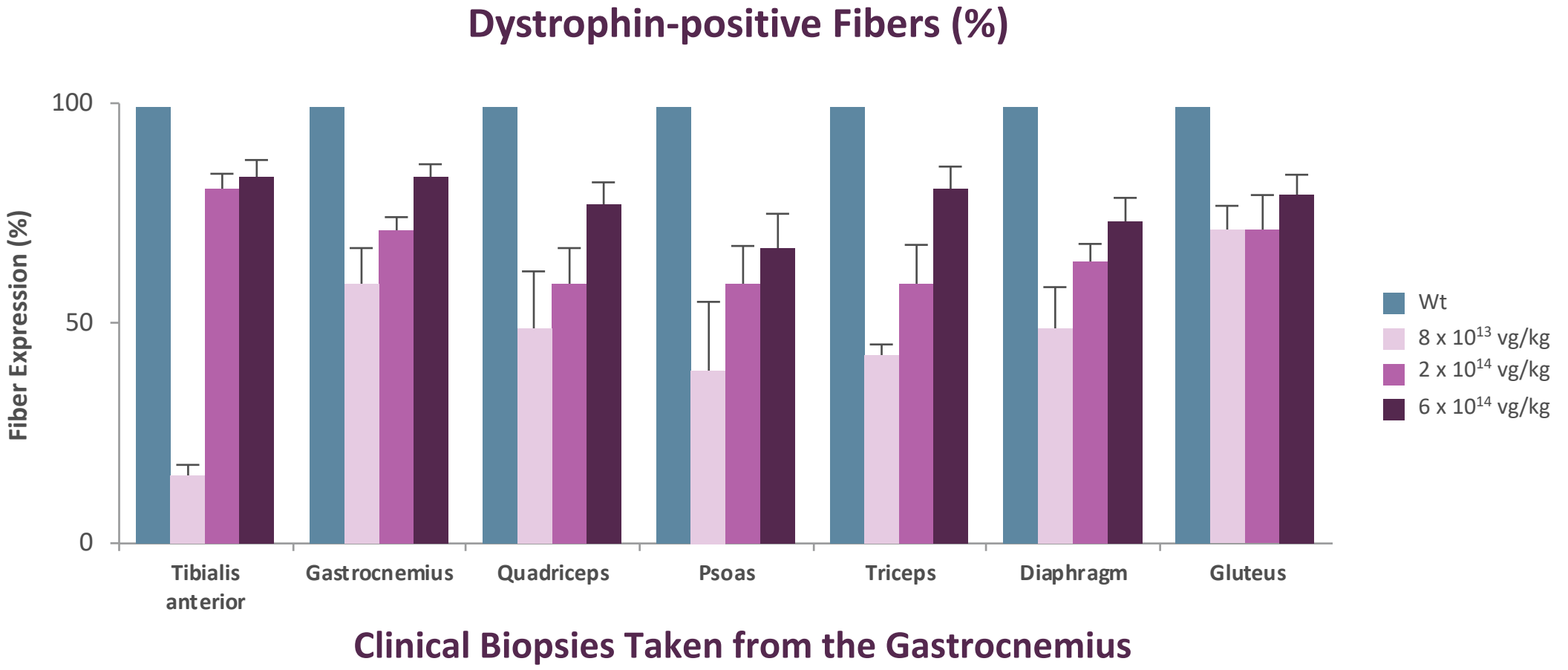
Dbr, dystrobrevin; DG, dystroglycan; f-actin; filamentous; nNOS, neuronal nitric oxide synthase; NT, amino terminal; SG, sarcoglycan; Syn, syntrophin.

1. Naso MF, et al. *BioDrugs*. 2017;31(4):317-334. 2. Chamberlain K, et al. *Hum Gene Ther Methods*. 2016;27(1):1-12. 3. Gao Q *et al*. *Compr Physiol.* 2015 July 1; 5(3):1223. 4. Harper SQ *et al. Nature Med.* 2002 March; 8(3):253. 5. Nelson DM *et al. Human Molec Genetics.* 2018 27(12):2090. 6. Fairclough RJ, *et al*. *Nat Rev Genet* 2013;14:373-8. 7. Aartsma-Rus, A., et al., *Muscle Nerve*, 2006. 34(2): p. 135-44. 8. England SB, et al. *Nature*. 1990;343(6254):180-182. 9. Wells DJ, et al. *Hum Mol Genet*. 1995;4(8):1245-1250.

SAREPTA THERAPEUTICS

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

AAVRH74.MHCK7.MICRO-DYSTROPHIN WIDESPREAD EXPRESSION AFTER GENE DELIVERY IN *MDX* MICE



Sarepta Therapeutics Data on File.

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

SRP-9001 MICRO-DYSTROPHIN

Clinical Data

Micro-Dystrophin is investigational and has not been FDA reviewed or approved.

LIAM
Living with Duchenne Muscular Dystrophy

TRIAL 1: OPEN-LABEL TRIAL DESIGN (NO PLACEBO GROUP)

Study Overview

- 4 subjects with DMD – open-label trial (no placebo group)
  - 4-7 years of age
  - Confirmed *DMD* mutation within exons 18 to 58
  - Negative for AAVrh74 antibodies
- Stable steroid dosing for at least 3 months (range: 6 months to 2 years)
- Subjects were put on prednisone 1 mg/kg daily dosing starting 1 day before treatment for ≥30 days
  - Found to effectively reduce immune response to AAV

Primary endpoint

- Safety

Secondary endpoints

- Change in micro-dystrophin expression pre- vs post-treatment
- Decrease in CK
- 100-meter timed test (100 m)
- North Star Ambulatory Assessment (NSAA; 10-meter timed test included)
- Ascend and descend 4 steps
- Timed up and go
- Hand-held dynamometry
- Cardiac magnetic resonance imaging (at 1 year)

ClinicalTrials.gov Identifier: NCT03375164.

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

SAFETY TO DATE (N=4)

TRIAL 1
4 patients
Nationwide Children's

QUESTION

1. Is **micro-dystrophin** safe and tolerable?
2. Is **micro-dystrophin DNA** inside muscle cells?
3. Is **micro-dystrophin protein** made?
4. Is **micro-dystrophin** at the cell membrane? How much is there?
5. Is **function** improved?

- No serious adverse events in this study to date
- 3 subjects had elevated γ-glutamyl transpeptidase, which resolved with steroid treatment
- Subjects had transient nausea generally within the first week coincident with increased steroid dosing
  - Did not correlate with liver enzyme elevations or any other abnormality
- No decrease in blood platelet count
- No indications of failure to thrive
- No other clinically significant laboratory findings

These preliminary outcomes need to be confirmed

ClinicalTrials.gov Identifier: NCT03375164. Sarepta Therapeutics Data on File.

SAREPTA THERAPEUTICS

Micro-Dystrophin is investigational and has not been FDA reviewed or approved.

MICRO-DYSTROPHIN EXPRESSION IS SUPPORTED BY A VECTOR GENOME COUNT IN ALL 4 SUBJECTS

TRIAL 1
4 patients
Nationwide Children's

QUESTION

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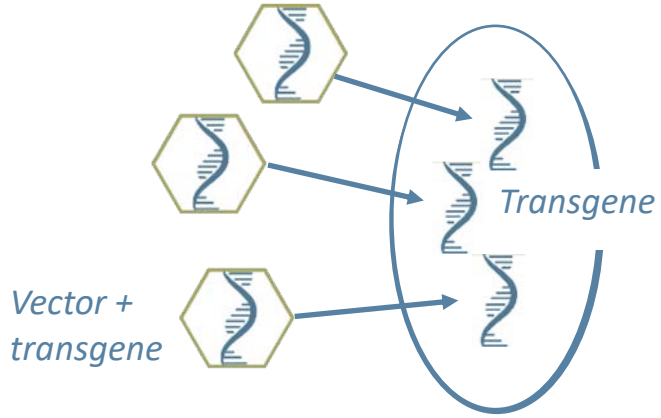

Vector Genome Number

	Vector Copies/µg DNA	Copies per Nucleus
Mean (n=4)	$>10^5$	3.3

ClinicalTrials.gov Identifier: NCT03375164.

Presented at the 23rd Annual Meeting of the World Muscle Society. Precision Genetic Medicines for Neuromuscular Diseases (Sarepta Therapeutics). 3 October 2018. Mendoza, Argentina.

SAREPTA THERAPEUTICS

Micro-Dystrophin is investigational and has not been FDA reviewed or approved

DETECTION OF MICRO-DYSTROPHIN EXPRESSION BY WESTERN BLOT POST-TREATMENT IN ALL 4 SUBJECTS AT DAY 90

TRIAL 1
4 patients
Nationwide Children's

QUESTION

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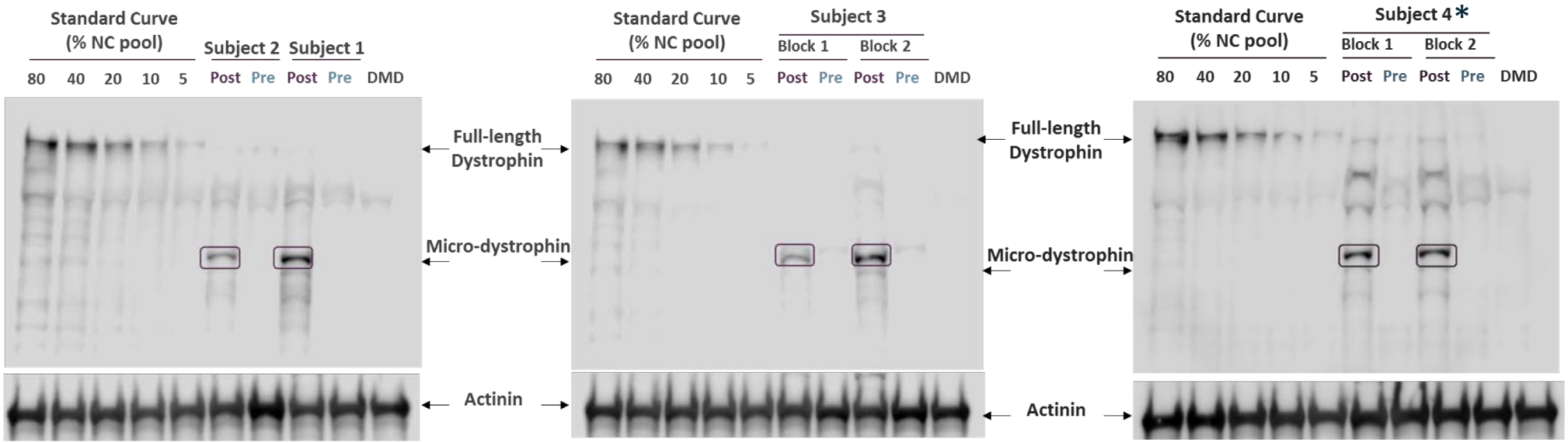

Western Quantitation Method	Mean Micro-dystrophin Expression (N=4) vs Normal	
Nationwide	**95.8%**	(adjusted for fat and fibrotic tissue)

NC, normal control; ULOQ, upper limit of quantitation. *Samples diluted 1:4 because ULOQ (>80%) was exceeded in initial analysis. Mean values were multiplied by correction factor for final value compared with NC.
ClinicalTrials.gov Identifier: NCT03375164. Presented at the 23rd Annual Meeting of the World Muscle Society. Precision Genetic Medicines for Neuromuscular Diseases (Sarepta Therapeutics). 3 October 2018. Mendoza, Argentina.

SAREPTA THERAPEUTICS

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MICRO-DYSTROPHIN EXPRESSION IN MUSCLE FIBERS FROM THE GASTROCNEMIUS IN ALL 4 SUBJECTS POST-TREATMENT

TRIAL 1
4 patients
Nationwide Children's

QUESTION

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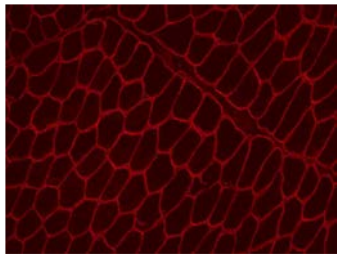
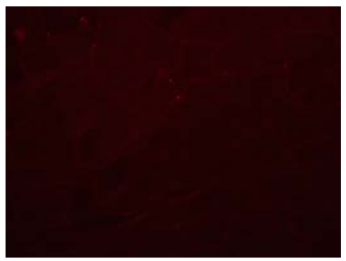
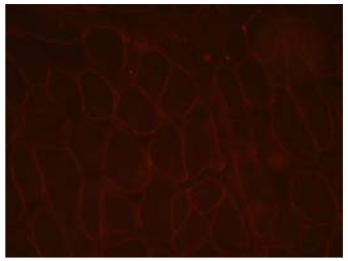
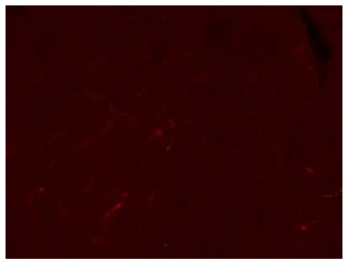
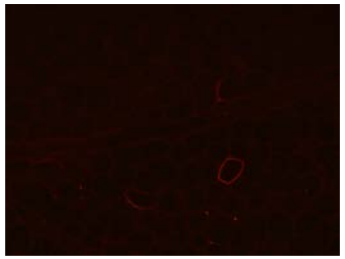
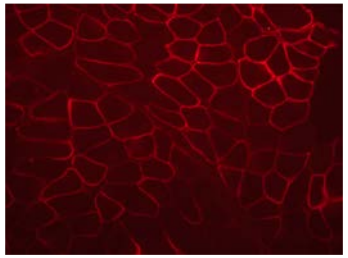
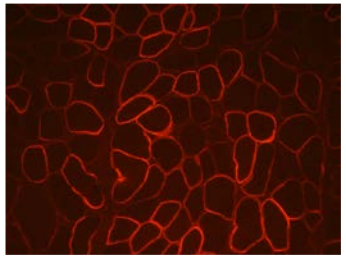
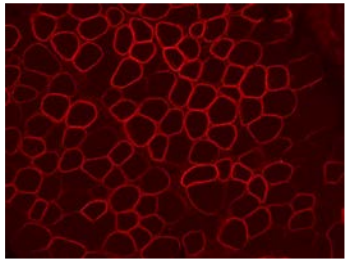
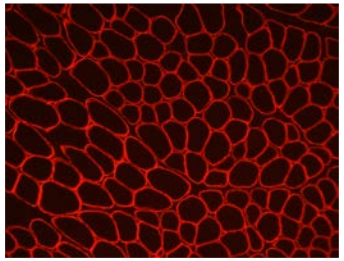
Micro-dystrophin Expression (IHC)

Normal Control



	Subject 1	Subject 2	Subject 3	Subject 4
Pre-treatment				
Post-treatment				

	Percentage of Dystrophin-positive Fibers	Intensity
Mean (n=4)	81.2%	96.0%

ClinicalTrials.gov Identifier: NCT03375164. Sarepta Therapeutics Data on File.

SAREPTA THERAPEUTICS

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SUMMARY OF NSAA DATA FOR ALL 4 PATIENTS

Change from Baseline to Day 270

TRIAL 1
4 patients
Nationwide Children's

QUESTION

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4. Is **micro-dystrophin** at the cell membrane? How much is there?
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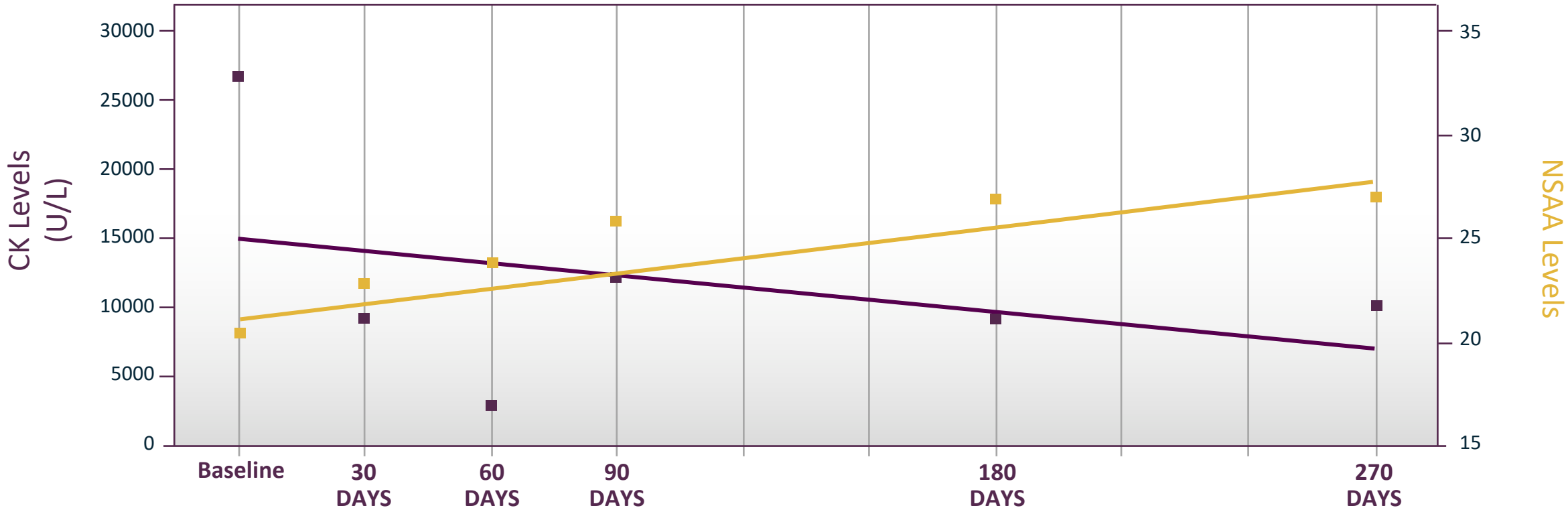

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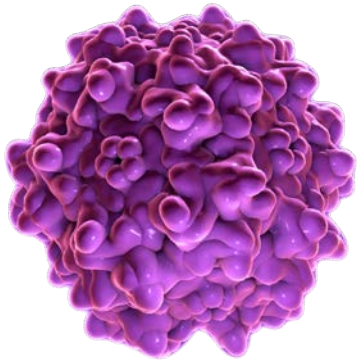
NEXT STEPS IN CLINICAL DEVELOPMENT

Micro-Dystrophin is investigational and has not been FDA reviewed or approved.

GRAYSEN
Living with Duchenne Muscular Dystrophy

SRP-9001 CLINICAL DEVELOPMENT PLAN



AAVrh74.MHCK7.
Micro-dystrophin
(SRP-9001)

TRIAL 1
4 patients
NATIONWIDE CHILDREN'S

TRIAL 2
24 patients
Placebo-controlled

COMMERCIAL SUPPLY TRIAL

Trial 1
NCT03375164

Dosing Complete
Clinical supply

Trial 2
NCT03769116

Dosing began Dec ’18
Clinical supply

Commercial Supply Trial
TBD

SAREPTA THERAPEUTICS

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FUTURE CLINICAL DEVELOPMENT

Our goal is to expand inclusion criteria, as we continue studying the safety and efficacy of SRP-9001, including:

- Expanded age range
- Expanded range of *DMD* genetic mutations
- Inclusion of individuals who are non-ambulatory

SAREPTA THERAPEUTICS

OUR GOAL

Sarepta Therapeutics' goal is to develop life-changing precision genetic medicine to treat ***100% of individuals with Duchenne muscular dystrophy***

2019 PPMD ANNUAL CONFERENCE

Douglas S. Ingram
President and Chief Executive Officer

June 28, 2019

FINN
Living with Duchenne
Muscular Dystrophy

A NEW ERA OF MEDICINE IS UPON US

SAREPTA THERAPEUTICS