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 19, 2018

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)

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

(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 (see General Instructions A.2. below):

☐ 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))

Indicate by check mark whether the registrant is an emerging growth company as defined in 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 19, 2018, Sarepta Therapeutics, Inc. issued a press release announcing that at its first R&D Day, Jerry Mendell, M.D. presented positive preliminary results from the first three children dosed in the Phase 1/2a gene therapy micro-dystrophin trial to treat patients with Duchenne muscular dystrophy. A copy of the press release and the presentation of Jerry Mendell, M.D. and Louise Rodino-Klapac, Ph.D. are furnished as Exhibits 99.1 and 99.2, respectively, and are incorporated herein by reference.

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 Number	Description
99.1	Press release dated June 19, 2018.
99.2	Systemic Delivery of AAVrh74.MHCK7. Micro-dystrophin for Duchenne Muscular Dystrophy, Jerry Mendell, M.D. and Louise Rodino-Klapac, Ph.D.

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 hereunto duly authorized.

Sarepta Therapeutics, Inc.

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

Date: June 19, 2018

Exhibit 99.1

Sarepta Therapeutics Announces that at its First R&D Day, Jerry Mendell, M.D. Presented Positive Preliminary Results from the First Three Children Dosed in the Phase 1/2a Gene Therapy Micro-dystrophin Trial to Treat Patients with Duchenne Muscular Dystrophy

-- Biopsies performed at Day 90 showed robust micro-dystrophin expression in muscle measured by all methods and observed in all three patients --

-- Significant decrease in levels of serum creatine kinase (CK), an enzyme biomarker strongly associated with muscle damage caused by Duchenne muscular dystrophy --

-- No serious adverse events (SAEs) observed --

CAMBRIDGE, Mass., June 19, 2018 (GLOBE NEWSWIRE) -- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), a commercial-stage biopharmaceutical company focused on the discovery and development of precision genetic medicine to treat rare neuromuscular diseases, announced that at the Company's R&D Day, Jerry Mendell, M.D. of Nationwide Children's Hospital presented positive preliminary results from its Phase 1/2a gene therapy clinical trial assessing AAVrh74.MHCK7.micro-Dystrophin in individuals with Duchenne muscular dystrophy (DMD). Dr. Mendell presented the following preliminary data on the first three patients enrolled in the study:

- All patients showed robust expression of transduced micro-dystrophin, which is properly localized to the muscle sarcolemma, as measured by immunohistochemistry. Mean gene expression, as measured by percentage of micro-dystrophin positive fibers was 76.2% and the mean intensity of the fibers was 74.5% compared to normal control.

- All post-treatment biopsies showed robust levels of micro-dystrophin as measured by Western blot, with a mean of 38.2% compared to normal utilizing Sarepta's method, or 53.7% compared to normal pursuant to Nationwide Children's quantification of Sarepta's method that adjusts for fat and fibrotic tissue.

- A mean of 1.6 vector copies per cell nucleus was measured in patients, consistent with the high micro-dystrophin expression levels observed.

- All patients showed significant decreases of serum creatine kinase (CK) levels, with a mean reduction of CK of over 87% at Day 60. CK is an enzyme associated with muscle damage and patients with DMD uniformly exhibit high levels of CK. Indeed, significantly elevated CK is often used as a preliminary diagnosis tool for DMD, which is then followed by confirmatory genetic testing.

- No serious adverse events (SAEs) were observed in the study. Two patients had elevated gamma-glutamyl transferase (GGT) that resolved with increased steroids within a week and returned to baseline levels. There were no other significant laboratory findings. Patients had transient nausea generally during the first week of therapy coincident with increased steroid dosing.

Dr. Mendell, the study's principal investigator, in collaboration with Louise Rodino-Klapac, Ph.D., empirically optimized the AAVrh74.MHCK7 specifically for DMD:

- The AAVrh74 vector can be systemically and robustly delivered to skeletal, diaphragm and cardiac muscle without promiscuously crossing the blood brain barrier, making it an ideal candidate to treat neuromuscular diseases.

- As a rhesus monkey-derived AAV vector, AAVrh74 appears to show lower immunogenicity rates in existing early-stage clinical studies than expected 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 DMD, who typically die from pulmonary or cardiac complications. In preclinical models, micro-dystrophin expression in the heart was observed to be up to 120% of the micro-dystrophin levels observed in skeletal muscles.

- The transgene was designed to maintain spectrin-like repeats 2 and 3, which has been reported to be important for maintaining the protective functional characteristics of dystrophin.

"As a genetic medicine company, our goal is to work with the world's leading clinicians and scientists to advance scientific discoveries to the clinic and, ultimately, to therapies that profoundly improve and extend the lives of those living with Duchenne muscular dystrophy and other rare, fatal diseases," stated Doug Ingram, Sarepta's president and chief executive officer. "Since the discovery of the dystrophin gene in 1986, scientists, clinicians, patient advocates and the biotech ecosystem have tirelessly searched for ways to restore or replace dystrophin and rescue boys with DMD from the damage and early death. Dr. Mendell's results, if confirmed in additional patients, studies, measures and time points, represent a monumental leap forward in the direction of our goal."

Dr. Mendell added, “I have been waiting my entire 49-year career to find a therapy that dramatically reduces CK levels and creates significant levels of dystrophin. Although the data are early and preliminary, these results, if they persist and are confirmed in additional patients, will represent an unprecedented advancement in the treatment of DMD. I look forward to treating more patients in the clinical study to generate the data necessary to bring this therapy to patients with DMD, with the goal of dramatically changing the course of the disease.”

“For years, PPMD has been interested in the potential of gene therapy as a treatment for Duchenne. At a critical moment in development in early 2017 – with the help and support of our amazing community – we were thrilled to be able to fund this important project of Drs. Mendell and Rodino-Klapac. To have reached this moment today is incredible and we are grateful to Sarepta for their investment and partnership in moving this therapeutic approach forward. While these are early days and work remains to fully understand the full potential of gene therapies, these first signals are encouraging. We remain hopeful that this will lead to a viable treatment for Duchenne,” stated Pat Furlong, Parent Project Muscular Dystrophy’s (PPMD) founding president and chief executive officer.

PPMD committed $2.2 million to the trial, with support from additional Duchenne foundations and families.

About Sarepta Therapeutics

Sarepta Therapeutics is a commercial-stage biopharmaceutical company focused on the discovery and development of precision genetic medicine to treat rare neuromuscular diseases. The Company is primarily focused on rapidly advancing the development of its potentially disease-modifying Duchenne muscular dystrophy (DMD) drug candidates. For more information, please visit www.sarepta.com.

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 design and potential benefits of the AAVrh74 vector, including its ability to systemically and robustly being delivered to skeletal, diaphragm and cardiac muscle without promiscuously crossing the blood brain barrier and its potential to show lower immunogenicity rates; the ability of the

MHCK7 promoter to robustly express in the heart; the potential of the transgene to maintain the protective functional characteristics of dystrophin; Sarepta's goal to work with the world's leading clinicians and scientists to advance scientific discoveries to the clinic and, ultimately, to therapies that profoundly improve and extend the lives of those living with DMD and other rare, fatal diseases; and the potential of Dr. Mendell's results to represent a monumental leap forward in the direction of Sarepta's goal, an unprecedented advancement in the treatment of DMD and dramatically change the course of the disease.

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 testing and early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful, and initial results from a clinical trial do not necessarily predict final results; Sarepta's ongoing research and development efforts may not result in any viable treatments suitable for commercialization due to a variety of reasons, some of which may be outside of Sarepta's control, 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, possible limitations of Company 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 with respect to patents that cover Sarepta's product candidates; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve any significant 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, 2017 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 opera-tions and the trading price of Sarepta's common stock. We caution investors not to place considerable reli-ance 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.

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OUR VISION FOR THE FUTURE OF

Precision Genetic Medicine

SAREPTA THERAPEUTICS, INC. 2018 R&D DAY

Systemic Delivery of AAVrh74.MHCK7.Micro-dystrophin for DMD

Jerry Mendell, MD
Center for Gene Therapy
Nationwide Children's Hospital
Columbus, OH

Louise Rodino-Klapac, PhD
Sarepta Therapeutics
Cambridge, MA

Today's Presentation

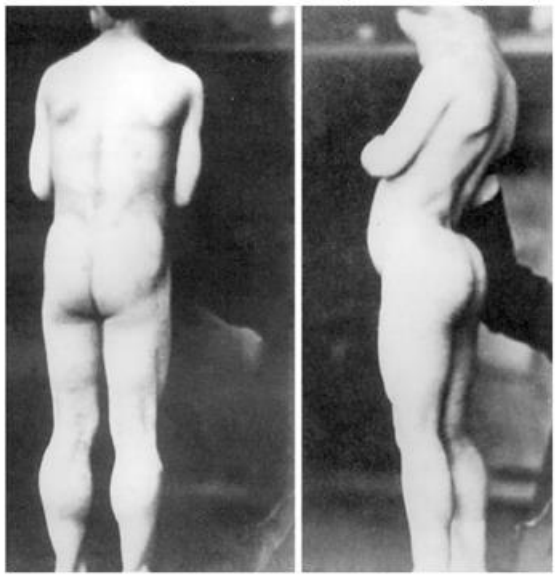
- DMD background and the engineering of micro-dystrophin
- Micro-dystrophin preclinical data
- Evidence of gene therapy efficacy from SMA
- Clinical data of micro-dystrophin gene therapy for DMD

DMD, Duchenne muscular dystrophy; SMA, spinal muscular atrophy.

DMD
Our motivation

- Most common life-threatening childhood muscular dystrophy
- Devastating disease
  - Boys are wheelchair-dependent by 12-13 years old
- Patients die in early 20s-30s from pneumonia and/or cardiomyopathy
- Incidence of 1:3500–5000 male births worldwide
- Elevated CK levels

Picture of DMD patient taken by Duchenne (1863)



CK, creatine kinase.

Dystrophin-associated Protein Complex (DAPC)

- Dystrophin is a core component of the DAPC
- Functions as a "shock absorber" during muscle contraction
- Loss of dystrophin causes disassembly of the entire DAPC
- Normal muscle contraction in DMD causes chronic muscle breakdown
- ***Restore the DAPC complex – restore function***

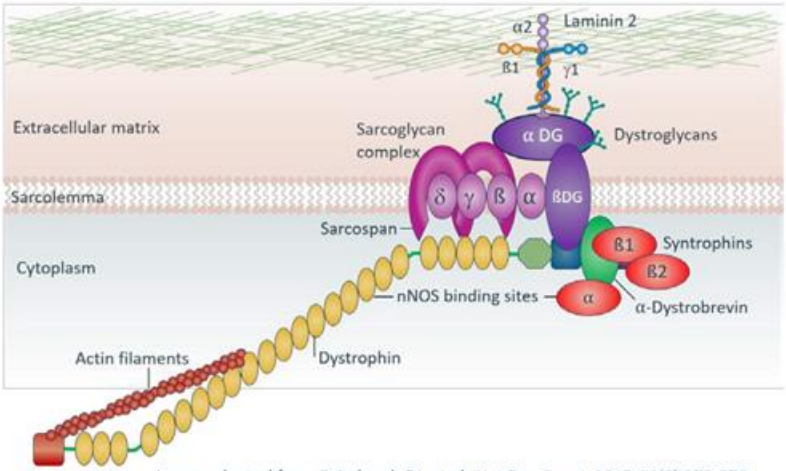
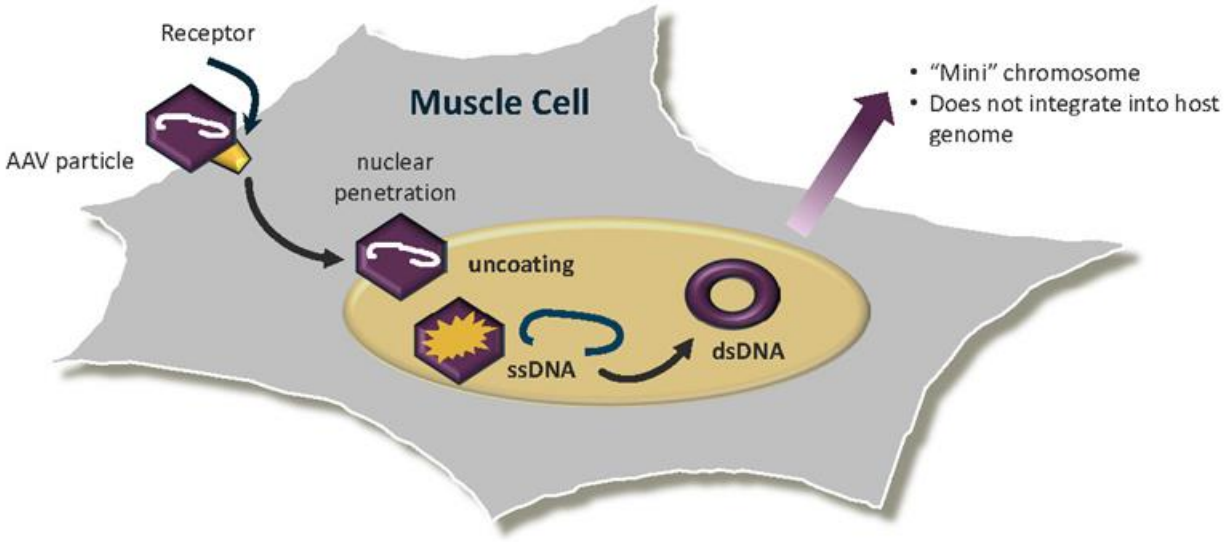


Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

DG, dystroglycan; nNOS, neuronal nitric oxide synthase.

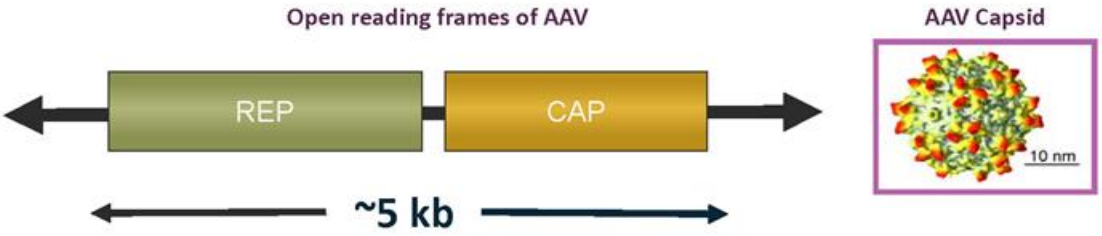
Adeno-associated Virus (AAV) Is a Delivery Vehicle for Dystrophin



DNA, deoxyribonucleic acid; dsDNA, double-stranded DNA; ssDNA, single-stranded DNA.

Adeno-associated Virus (AAV) Is a Delivery Vehicle for Dystrophin

- ssDNA virus
- Does not cause disease in humans
- Long-term persistence in cells

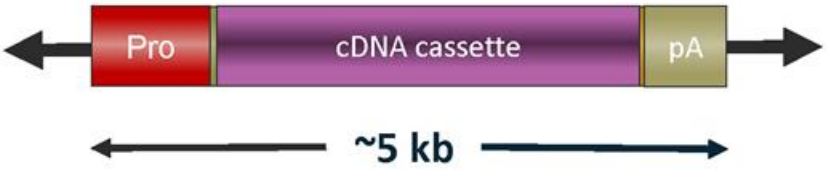


kb, kilobase; nm, nanometer.

Adeno-associated Virus (AAV) Is a Delivery Vehicle for Dystrophin

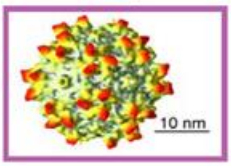
- ssDNA virus
- Does not cause disease in humans
- Long-term persistence in cells
- Gene therapy requires replacement of viral genes with gene of interest

Structure of typical AAV construct with gene of interest



~5 kb

AAV Capsid

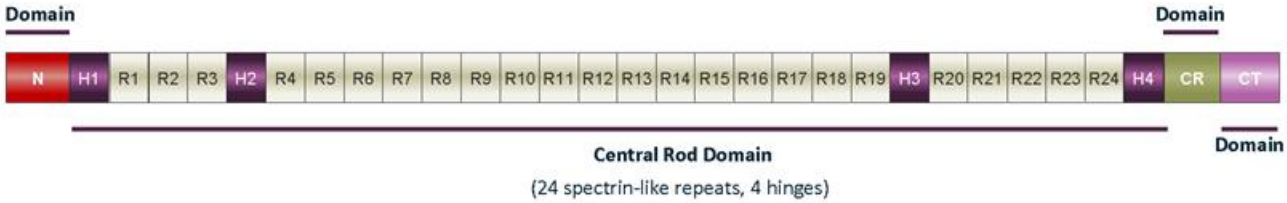


cDNA, complementary DNA; kb, kilobase; pA, polyadenylation signal; nm, nanometer; Pro, promoter sequence.

Pathogenesis of DMD

- Dystrophin is the largest gene in the human genome at 2.6 Mb
  - Poses a critical obstacle for molecular manipulation

Dystrophin encodes a protein with 4 domains



CR, cysteine-rich; CT, carboxy-terminal; H, hinge; Mb, megabase; N, amino-terminal; R, spectrin-like repeat.

How Do We Decrease the Size of the *DMD* Gene?

Birth of the mini-dystrophins

- Clinical observations paved the way for mini-gene therapy
- 61-year-old ambulatory patient with Becker muscular dystrophy had 46% of dystrophin coding region deleted (Del 17-48)[1]

***R2** and **R3** critical for force production.*

***R16** and **R17** are required for the association of nNOS with the DAPC. Not present in this patient.*

1. England SB, et al. *Nature*. 1990;343(6254):180-182.
2. Wells DJ, et al. *Hum Mol Genet*. 1995;4(8):1245-1250.

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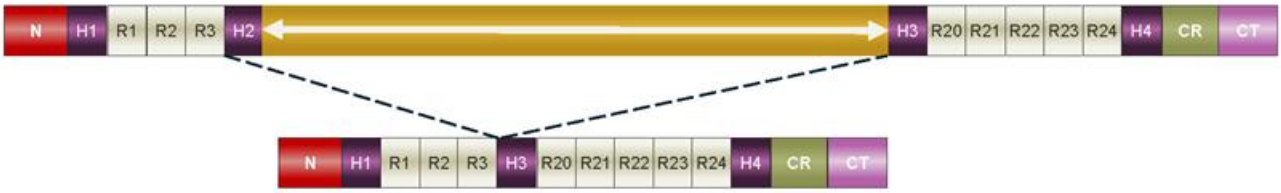

"Mini"-dystrophin[2]
(6 Kb)

***R2** and **R3** critical for force production.*

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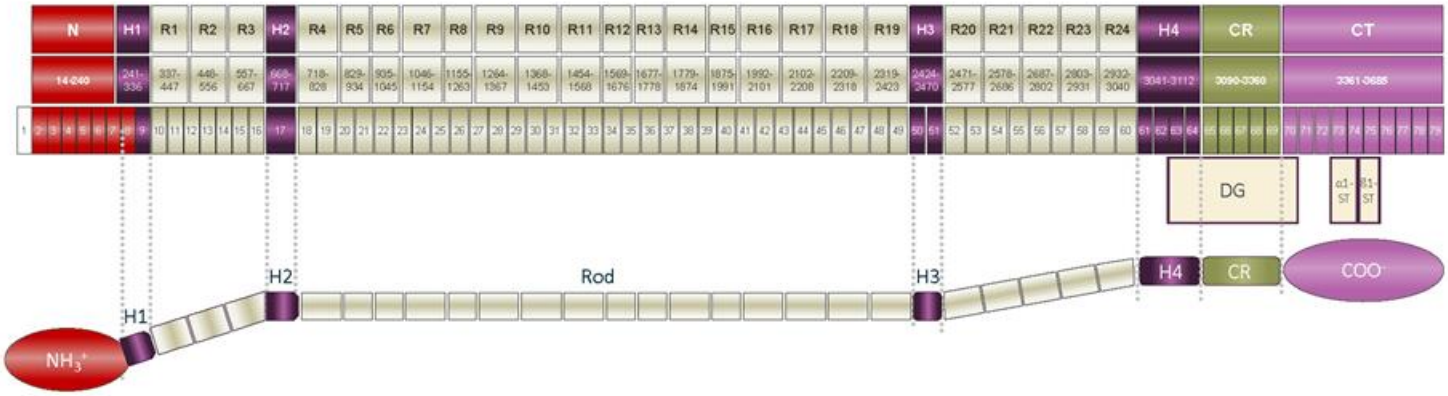
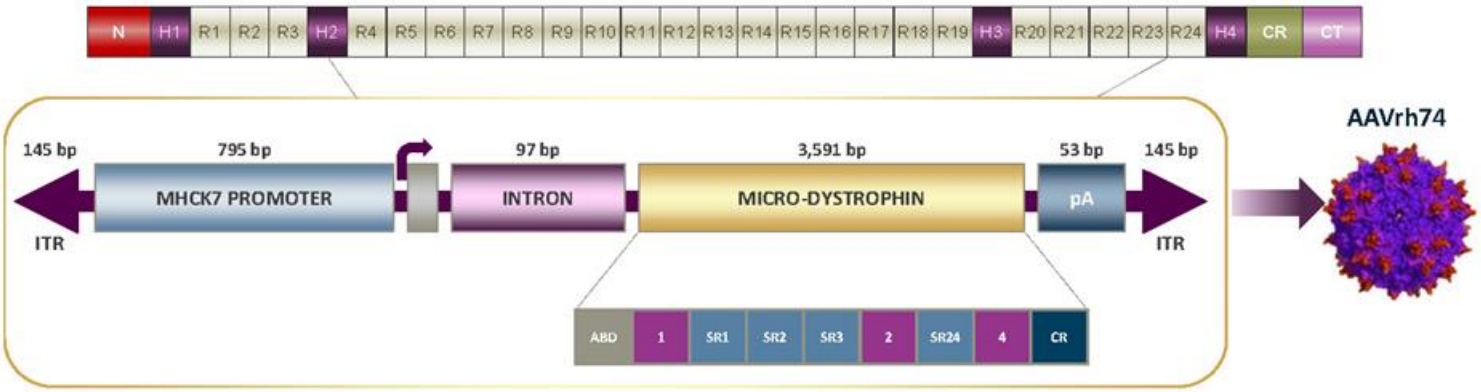
Challenge:
Further Modify Dystrophin to <5 Kb So That It Can Fit in AAV Particle



AAVrh74.MHCK7.Micro-dystrophin

- MHCK7 promoter enables robust dystrophin expression in heart and skeletal muscle
- AAVrh74 provides broad distribution to ***all*** muscle types, including the heart and diaphragm



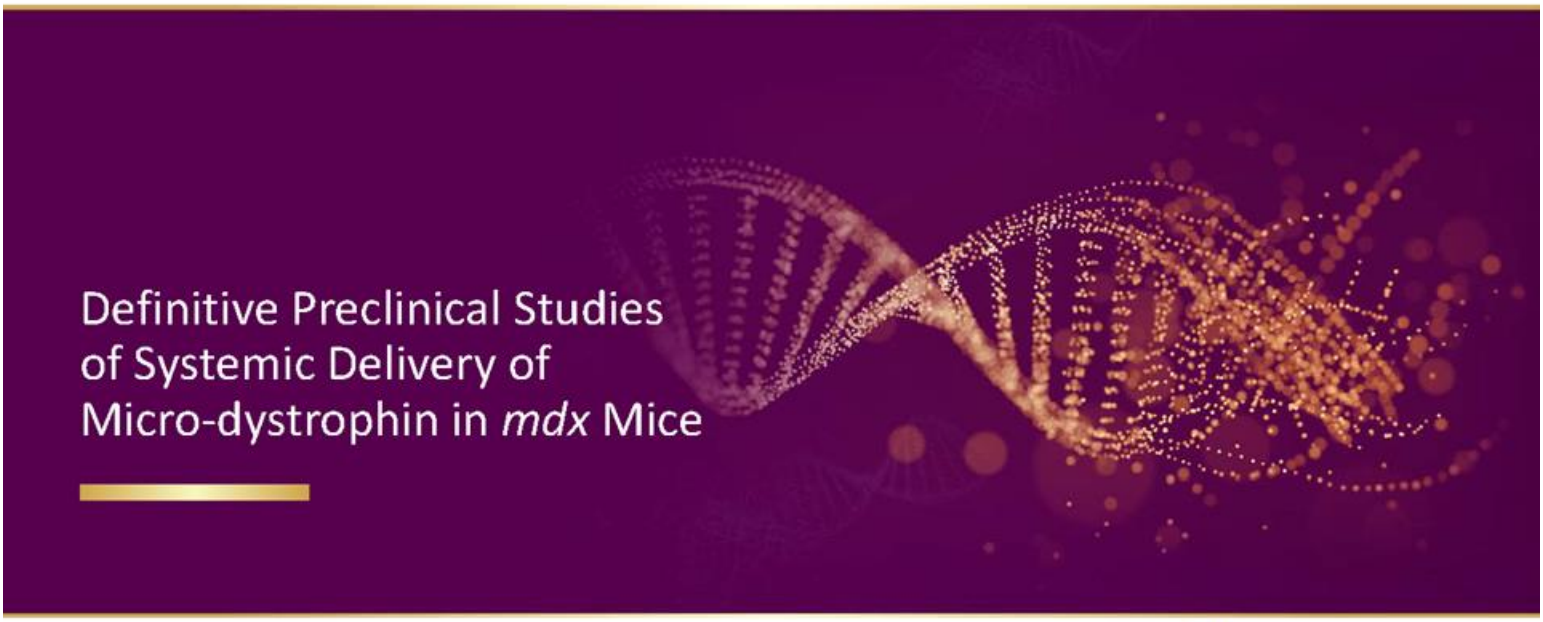
ITR, inverted tandem repeat; SR, spectral-like repeat.

Strong Profile for AAVrh74

- Demonstrated efficacy
  - Ideal systemic biodistribution vs other vectors in preclinical testing
  - Widespread high-level gene expression after IV infusion in preclinical animal models
  - Gene expression in Phase 1 trials across multiple diseases by IM and IV delivery*
  - **Low pre-existing immunogenicity**: Nonhuman serotype guards against pre-existing immunity (still under evaluation; currently <15%)
- Demonstrated safety
  - **No observed adverse effect level (NOAEL)** in primates and mice
    - GLP toxicity studies: IM, n=5; ILP, n=3; IV, n=2
  - **14 human subjects** dosed (IM, n=4; IV, n=10) without vector-related adverse effects
  - **6 approved INDs**

GLP, good laboratory practice; ILP, isolated limb perfusion; IM, intramuscular; IND, investigational new drug; IV, intravenous.
*Unpublished data based on screening of approximately 70 patients with Limb girdle muscular dystrophy (LGMD) or DMD.

Definitive Preclinical Studies of Systemic Delivery of Micro-dystrophin in *mdx* Mice



SAREPTA THERAPEUTICS

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Preclinical IV Study Design for the Delivery of AAVrh74.MHCK7.Micro-dystrophin

2 x 10^{12} vg total dose
(8 x 10^{13} vg/kg)

6 x 10^{12} vg total dose
(2 x 10^{14} vg/kg)

1.2 x 10^{13} vg total dose
(6 x 10^{14} vg/kg)

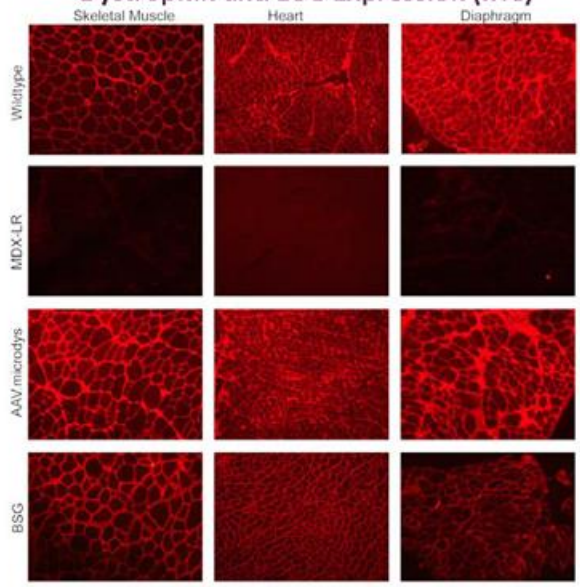
Assess efficacy and safety 12 weeks after gene delivery

- Transgene expression and biodistribution
- Western blot and qPCR
- Histological analysis
- Functional benefit
- Safety and toxicity

qPCR, quantitative polymerase chain reaction; vg, viral genomes.

Reassembly of the Dystrophin-associated Protein Complex With Micro-dystrophin

Dystrophin and BSG Expression (IHC)



BSG, β-sarcoglycan; IHC, immunohistochemistry; LR, locoregional.

Schematic of the DAPC

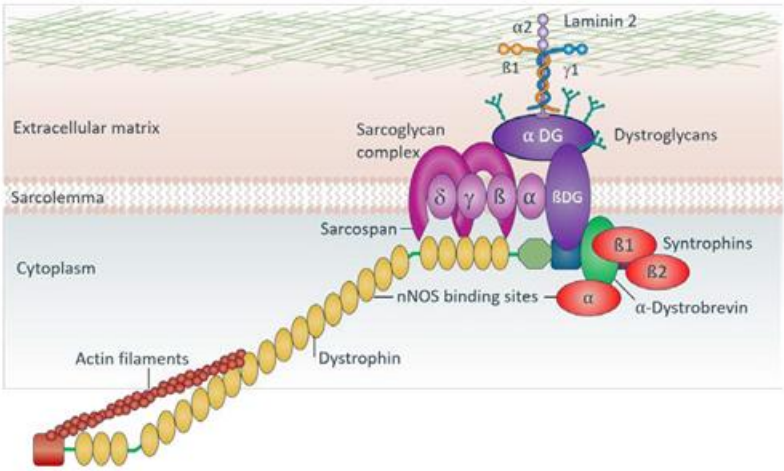
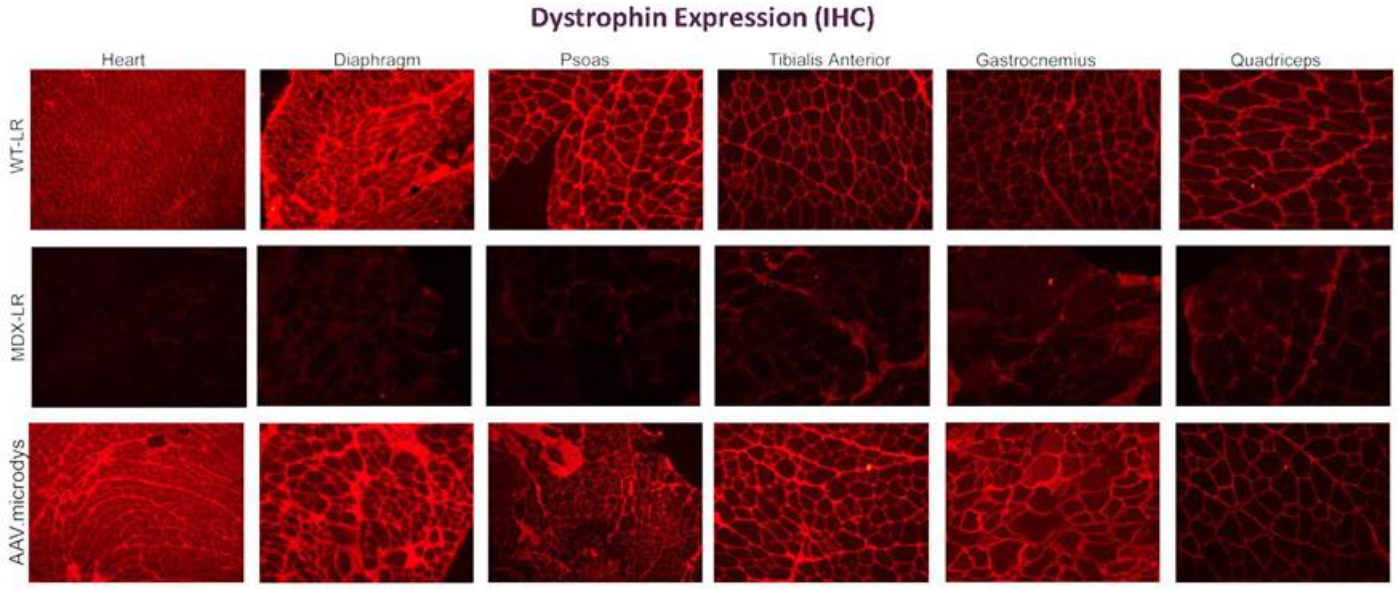


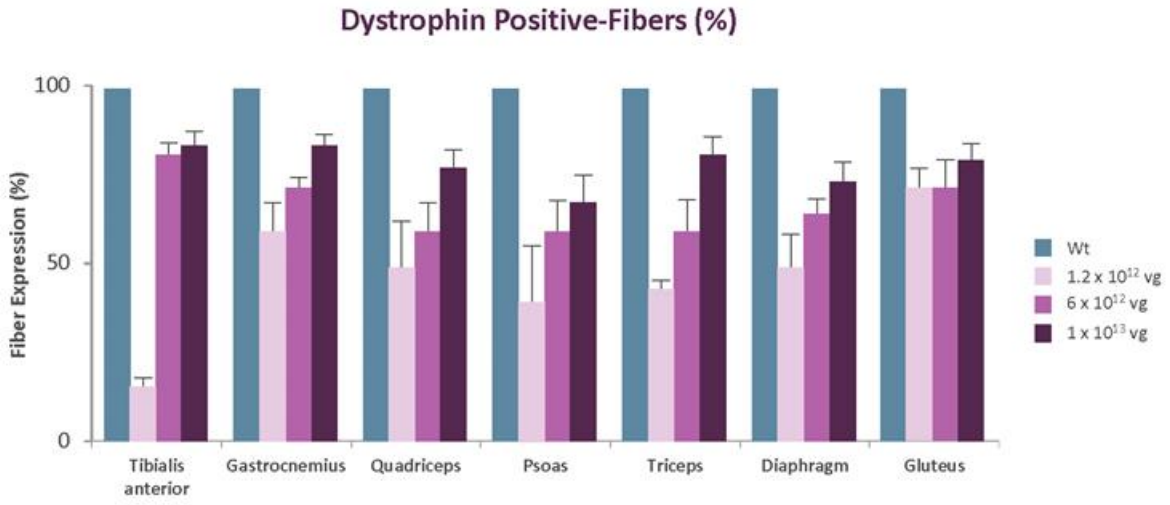
Image adapted from Fairclough RJ, et al. *Nat Rev Genet*. 2013;14(6):373-378.

Widespread Expression After Micro-dystrophin Gene Delivery



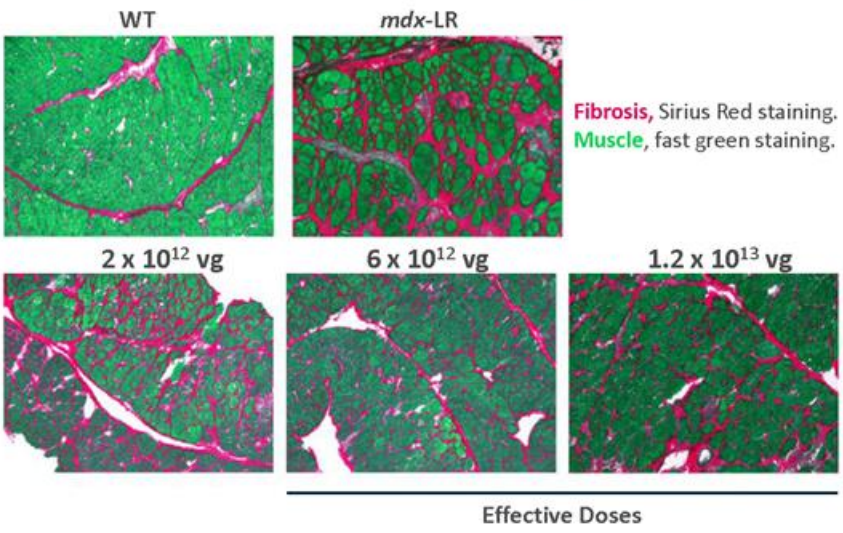
WT, wild-type.

Widespread Expression After Micro-dystrophin Gene Delivery

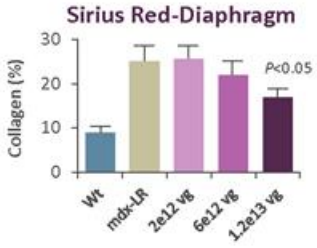


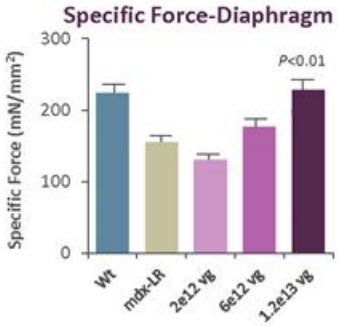
Reduced Fibrosis Accompanies Functional Improvement in the Diaphragm

Evaluation of Fibrosis in the Diaphragm (IHC)



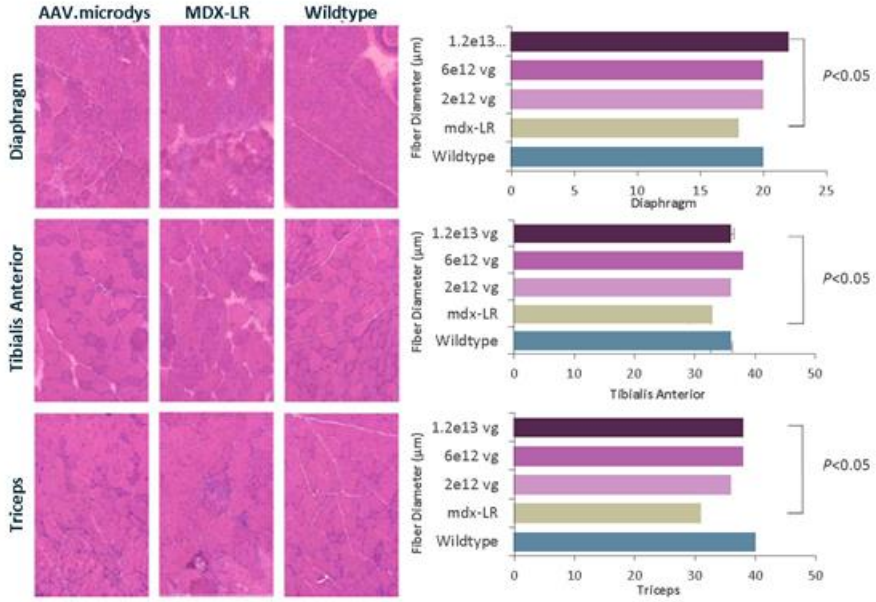
Fibrosis, Sirius Red staining.
Muscle, fast green staining.





mN, milliNewtons.

Histological Improvement in Muscles Treated With AAVrh74.MHCK7.Micro-dystrophin



Pathologist Conclusions

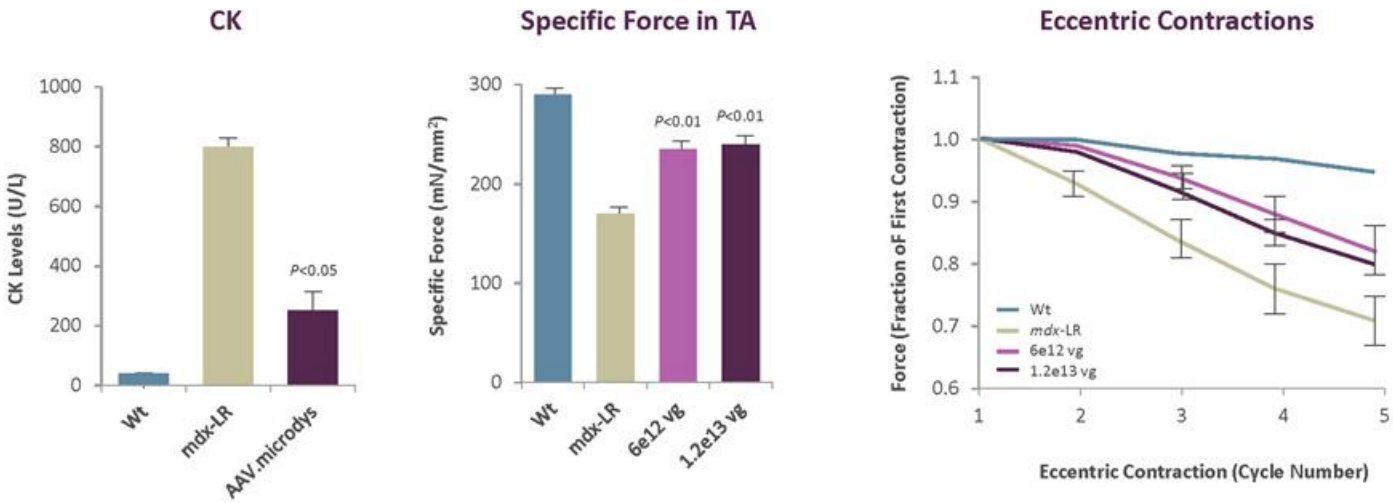
Efficacy

- Injection of *mdx* mice with the test article ***substantially reduced in a dose-dependent manner*** the skeletal myopathy that developed in vehicle-treated, age-matched *mdx* mice

Safety

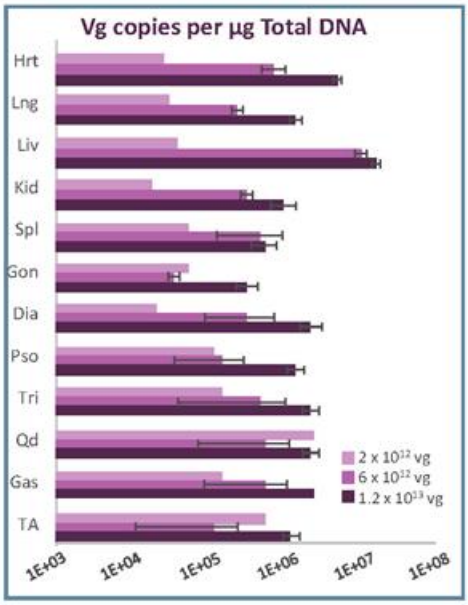
- The test article AAVrh74.MHCK7.Micro-dystrophin (administered at 2 x 10^{12}, 6 x 10^{12}, or 1.2 x 10^{13} vg total dose by IV injection at 4-6 weeks of age) ***did not induce anatomic lesions*** in muscles of male *mdx* knockout mice at 12 weeks after administration

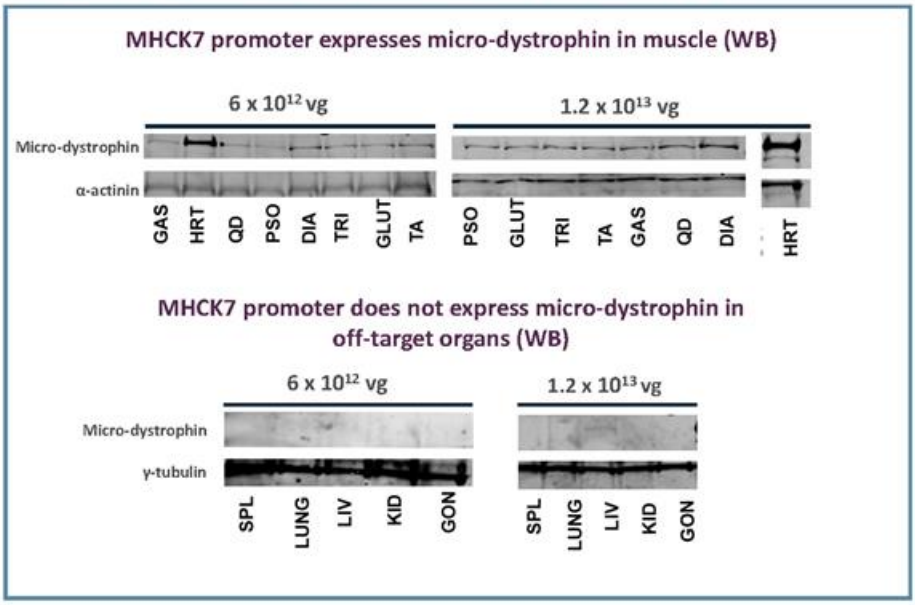
CK Reduction, Muscle Strength, and Stamina Improvement in *mdx* Mice Treated With AAVrh74.MHCK7.Micro-dystrophin



- No difference in fatigue in the 6 x 10^{12} vg and 1.2 x 10^{13} vg doses

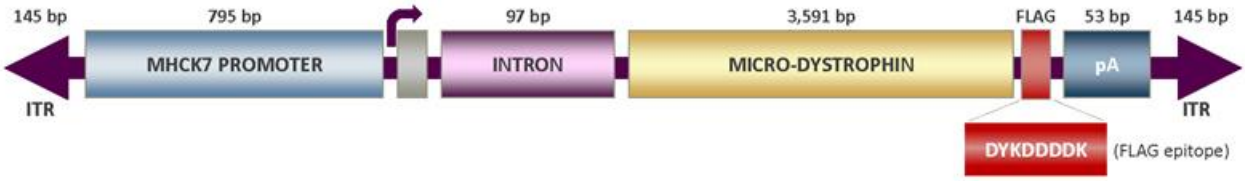
Widespread Biodistribution Throughout 8 Different Muscle Groups With Systemic Delivery of Micro-dystrophin in the *mdx* Mouse Model



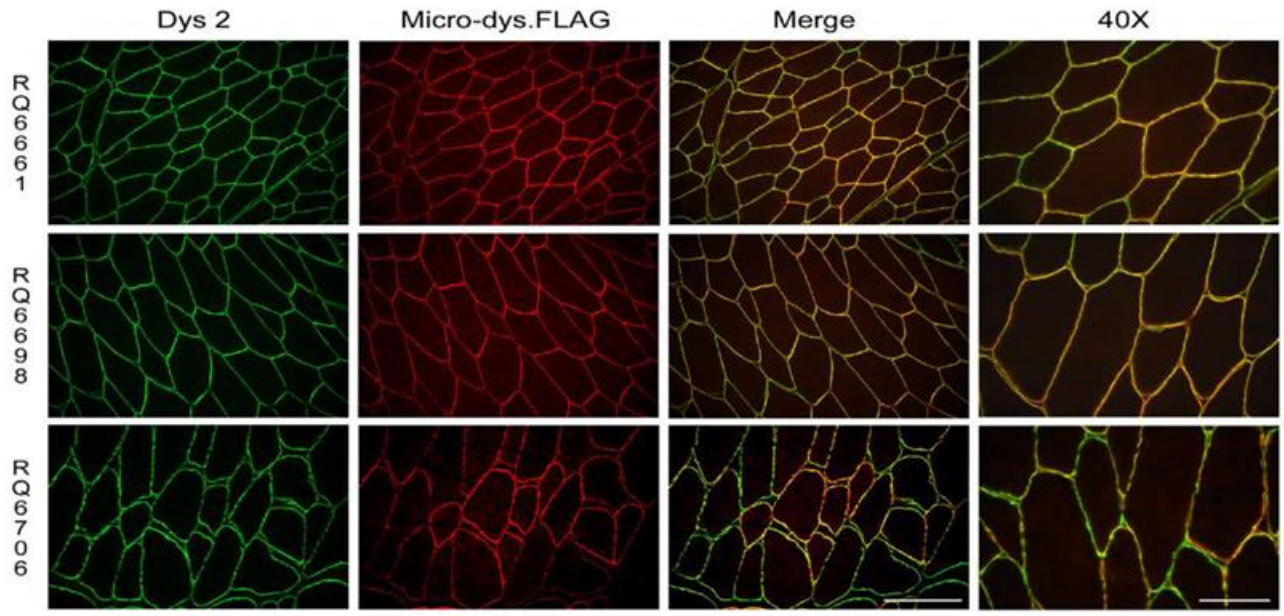


Dia, diaphragm; Gas, gastrocnemius, Gon, gonadal; Hrt, heart; kDA, kilodaltons; Kid, kidney; Liv, liver; Lng, lung; Pso, Psoas; Qd, quadriceps; Spl, spleen; Tri, triceps, WB, Western Blot.

Micro-dystrophin With FLAG Tag Will Reveal Transgene Distribution in Nonhuman Primates (NHPs)

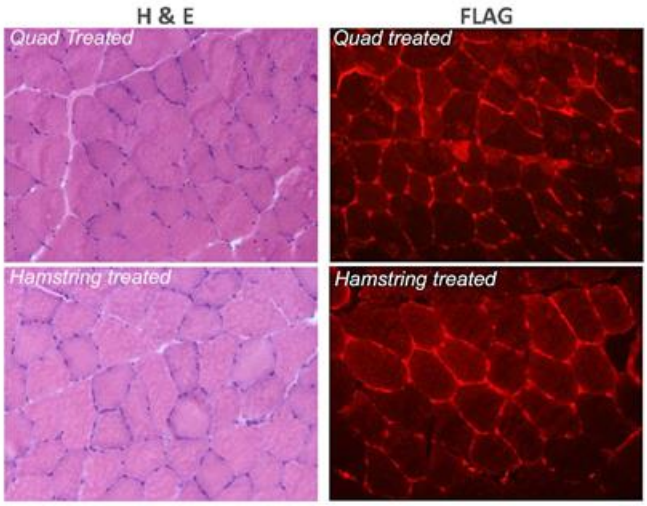


Endogenous Dystrophin and Micro-dystrophin.FLAG Colocalize to the Sarcolemma in NHPs

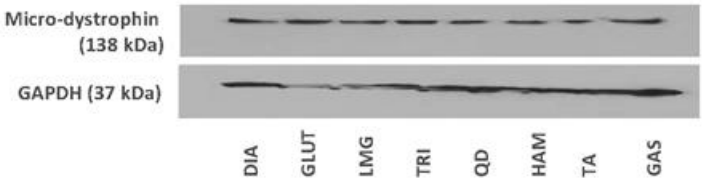


Widespread Biodistribution With Systemic Delivery of Micro-dystrophin in NHPs

Micro-dystrophin Tissue Expression (IHC)



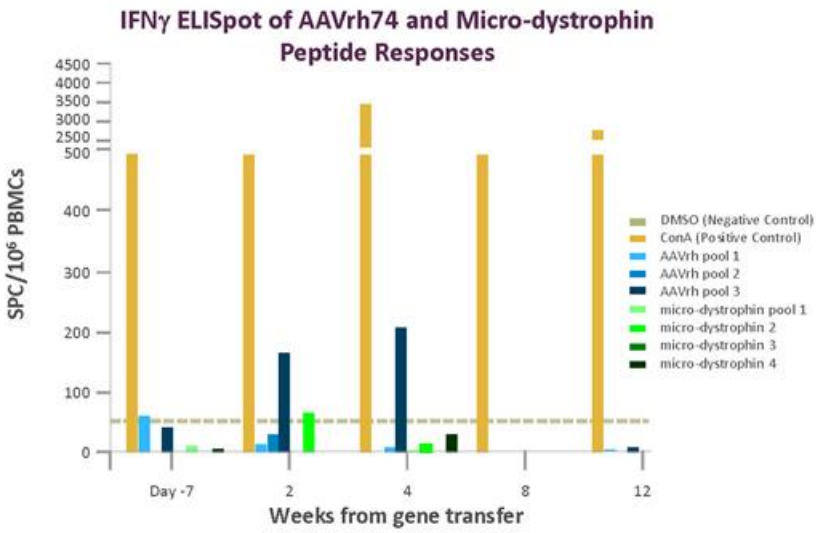
Micro-dystrophin Tissue Expression (WB)

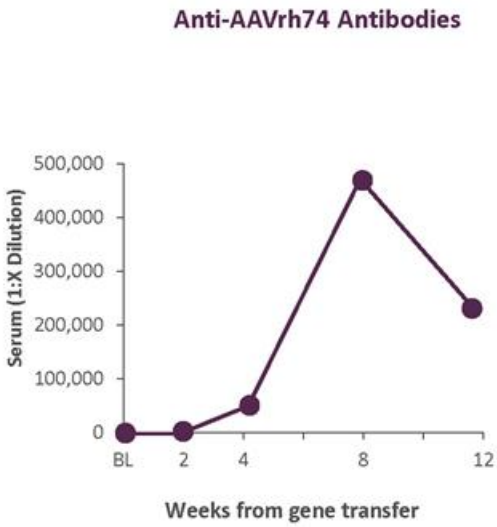


- NHPs were treated with 2 x 10^{14} vg/kg with AAVrh74.MHCK7.Micro-dystrophin

GAPDH, glyceraldehyde 3-phosphate dehydrogenase; H & E, hematoxylin and eosin; HAM, hamstring; LMG, left adductor magnus.

No Abnormal Immunological Responses Were Observed With Systemic Delivery of Micro-dystrophin in NHPs*†





BL, baseline; CBC, cell blood count; ConA, concanavalin A; ELISpot, enzyme-linked immunospot; DMSO, dimethyl sulfoxide; IFNγ, interferon gamma; PBMC, peripheral blood mononuclear cell; SFC, spot-forming cells.

*CBC/Chemistries Performed at Charles Rivers and histopathology formally reviewed by a veterinary pathologist (GEMpath Inc.).

†Systemic delivery of AAVrh74.MHCK7.micro-dystrophin did not induce any anatomic lesions.

Conclusions

Construct optimized for use in DMD

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

Preliminary preclinical results

- Widespread micro-dystrophin expression across all muscle types
- Reduction in CK
- Improved functional measures
- No toxicity

Evidence From Spinal Muscular Atrophy

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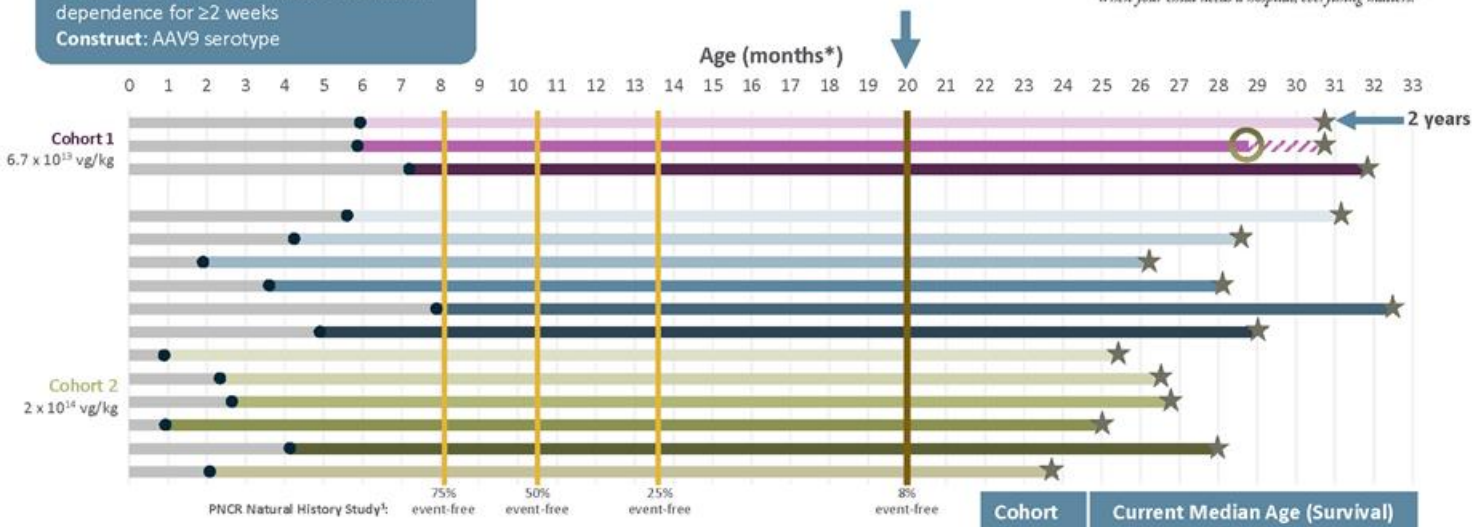
AVXS-101: Survival Data (as of Feb 2018)

Outcome: death or >16 hr/day of ventilator dependence for ≥2 weeks
Construct: AAV9 serotype



Cohort	Current Median Age (Survival) (months*)
1	47
2	33

PNCR, Pediatric Neuromuscular Clinical Research Network.
*Month defined as 30 days.
1. Finkel RS, et al. *Neurology*. 2014;83(9):810-817.

AVXS-101: Motor Milestones

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Two children are able to crawl, pull to a stand, and stand and walk independently

Cohort 2 2×10^{14} vg/kg	Age at gene therapy (months)	Motor Milestone Achievement							
							Sitting Unassisted		
		Brings hand to mouth	Head control	Partial roll*	Roll†	Sitting with assistance	≥5 seconds‡	≥10 seconds§	≥30 seconds‖
E.04	6	✓	✓	✓	✓	✓	✓		
E.05	4	✓	✓	✓	✓	✓	✓	✓	✓
E.06	2	✓	✓	✓	✓	✓	✓	✓	✓
E.07	4	✓	✓	✓	✓	✓	✓	✓	
E.08	8	✓							
E.09	5	✓	✓	✓	✓	✓	✓	✓	✓
E.10	1	✓	✓	✓	✓	✓	✓	✓	✓
E.11	2	✓	✓	✓	✓	✓	✓	✓	✓
E.12	3	✓	✓	✓	✓	✓	✓	✓	✓
E.13	1	✓	✓	✓	✓	✓	✓	✓	✓
E.14	4	✓	✓	✓	✓	✓	✓	✓	✓
E.15	2	✓	✓	✓	✓	✓	✓	✓	✓

*Bayley Scales of Infant and Toddler Development, item #20, rolls a minimum 180° from back in only one direction. †Bayley Scales of Infant and Toddler Development, item #20, rolls a minimum 180° from back to both left and right. ‡Sitting unassisted for ≥5 seconds is in accordance with the criteria of item 22 in the Bayley Scales of Infant and Toddler Development – gross motor subtest and surpasses the 3-second count used as a basis for sitting (test item 1) in the Hammersmith Functional Motor Scale – Expanded for SMA (HFMSE). §Sitting unassisted for ≥10 seconds is in accordance with the criteria in the World Health Organization – MultiCentre Growth Reference Study. ‖Sitting unassisted for ≥30 seconds defines functional independent sitting and is in accordance with the criteria of item 26 in the Bayley Scales of Infant and Toddler Development – gross motor subtest.

Gene Transfer at 4 Weeks

Gene Transfer at 4 Weeks

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Open-label Trial Design

- 12 subjects with DMD – open trial
  - Cohort A: 6 subjects; 3 months-3 years of age
  - Cohort B: 6 subjects; 4-7 years of age
- Inclusion criteria
  - Confirmed *DMD* mutation between exons 18-58, inclusive
  - Negative for AAVrh74 antibodies

Cohort B (4-7 years of age) Endpoints

- **Primary endpoint**:
  - Safety
- **Secondary endpoints**:
  - Change in micro-dystrophin expression pre- vs post-treatment
  - Decrease in CK
  - 100-meter timed test (100m)
  - North Star Ambulatory Assessment (NSAA; 10-meter timed test included)
  - Timed Up and Go (TUG)
  - Ascend and descend 4 steps
  - Hand-held Dynamometry (HHD)
  - Cardiac MRI (at 1 year)

MRI, magnetic resonance imaging.

Clinical Study Results From Cohort B

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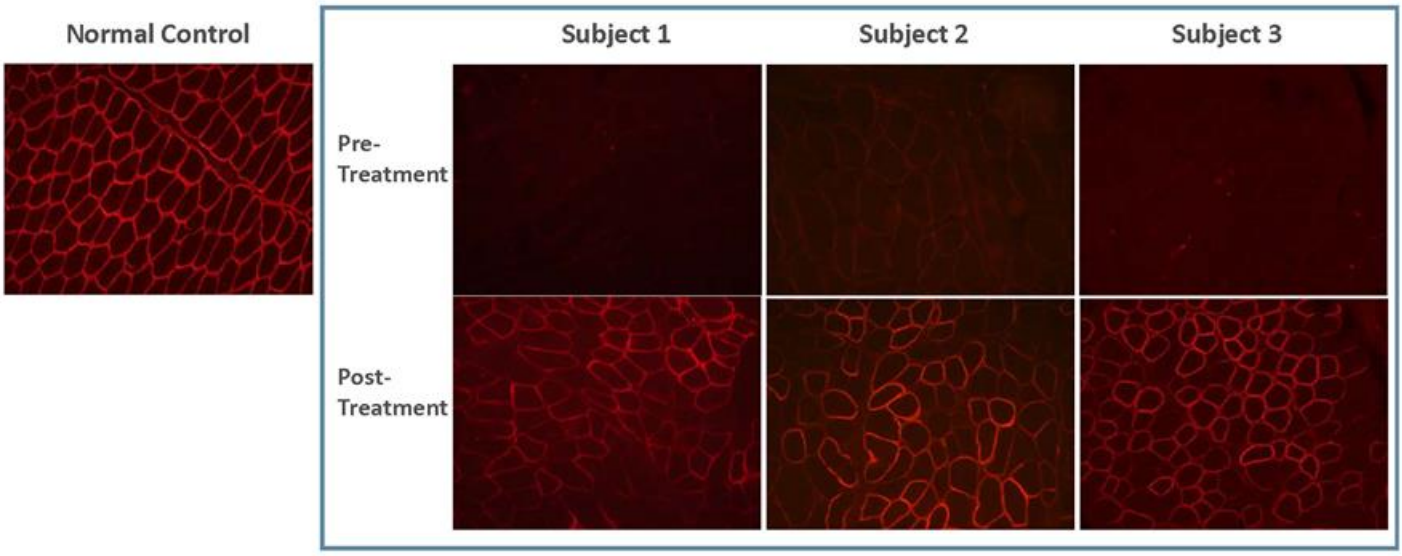
Subject Demographics at Baseline

Subject	Age (years)	CK Levels at Baseline (U/L)
1	5	20,691
2	4	23,414
3	6	34,942
4	4	29,210

Robust Micro-dystrophin Expression in Muscle Fibers from the Gastrocnemius

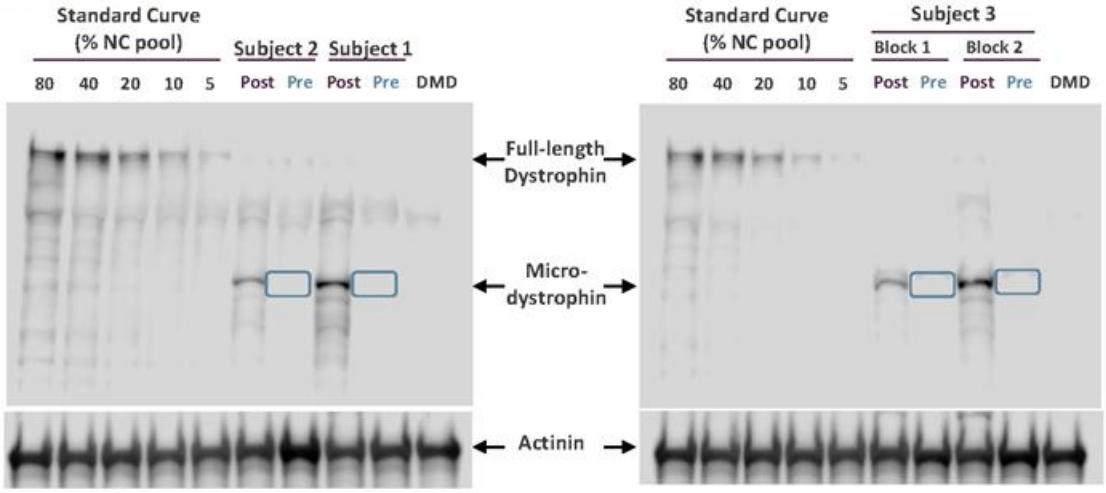
Micro-dystrophin expression (IHC)



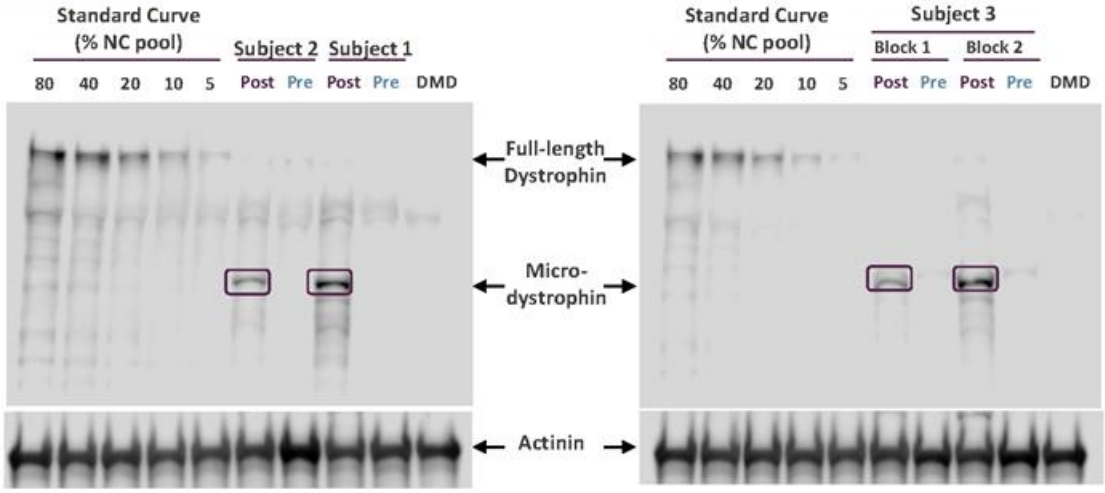
Robust Micro-dystrophin Expression in Muscle Fibers from the Gastrocnemius

Subject	Mean Intensity	Percentage of Dystrophin-Positive Fibers
1	82.0 %	78.0 %
2	59.0 %	73.5 %
3	83.0 %	77.0 %
Mean	**74.5 %**	**76.2 %**

Detection of Micro-dystrophin Expression by Western Blot Post-Treatment



Detection of Micro-dystrophin Expression by Western Blot Post-Treatment



Western quantitation method	Mean micro-dystrophin expression compared vs normal
Sarepta	**38.2%** (not adjusted for fat and fibrotic tissue)
Nationwide	**53.7%** (adjusted for fat and fibrotic tissue)

Vector Genome Copy Number Is >1 Copy Per Nucleus, Consistent With Micro-dystrophin Expression Levels

Subject	Vector Copies/µg DNA	Copies per Nucleus*
1	$>10^5$	1.7
2	$>10^5$	1.3
3	$>10^5$	1.9

*1 vector copy per nuclei translates to ~50% micro-dystrophin positive fibers

Creatine Kinase (CK) in DMD

- Increased permeability of the sarcolemma leads to the leakage of CK from muscle fibers
- Increased serum CK values are the hallmark of muscle damage, and are elevated in DMD (and other muscle diseases)
  - Markedly elevated CK values are diagnostic of DMD
- Peak serum CK values are usually observed in patients with DMD who are between the ages of 2 to 5 years[1]

1. Zatz M, et al. *J Neurol Sci*. 1991;102:190–196.

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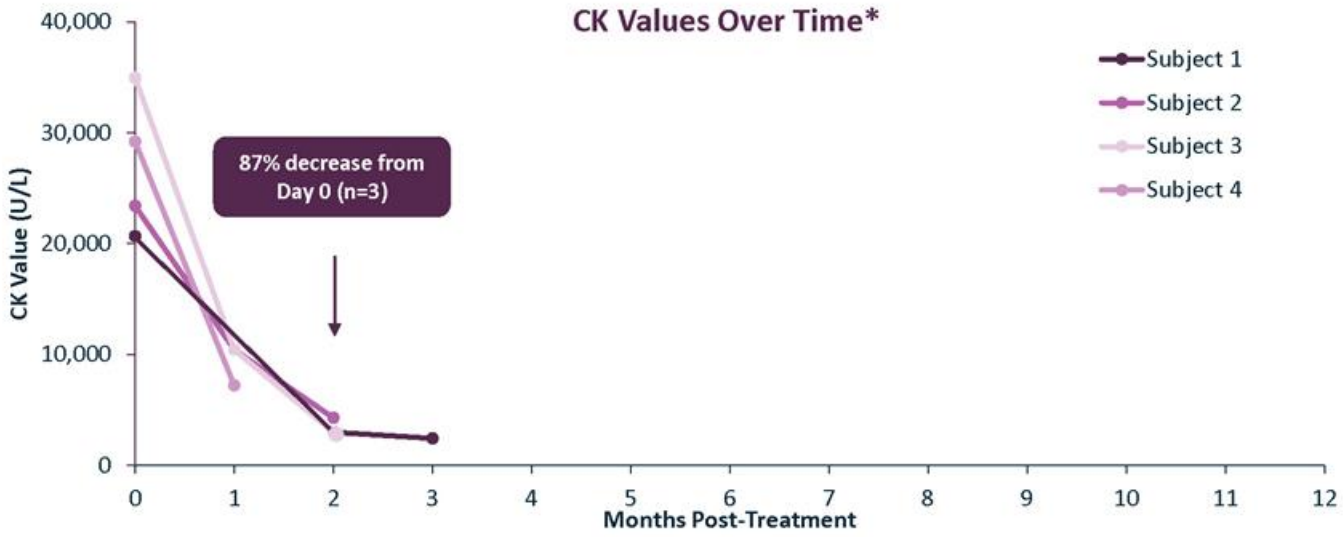
  - Serum CK values decline at a rate of ~8% per year in patients who are >7 years of age
- The rate of serum CK values decrease is impacted by the extent of disease progression
  - The serum CK values of wheelchair-dependent patients, and patients with advanced muscle loss, decrease more slowly than other DMD patients

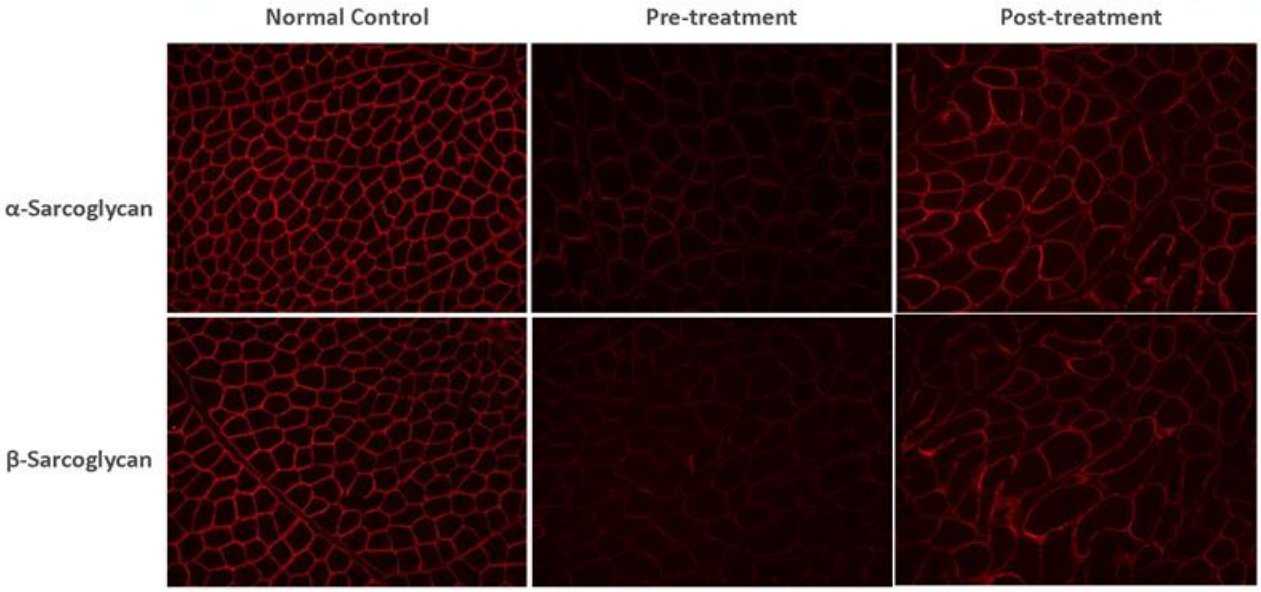
1. Zatz M, et al. *J Neurol Sci*. 1991;102:190–196.

CK Levels Are Dramatically Reduced with Micro-dystrophin Therapy



Micro-dystrophin Gene Therapy Upregulates DAPC Proteins

Expression of DAPC Proteins in Muscle Fibers from the Gastrocnemius of Subject 2 (IHC)



Patient Videos

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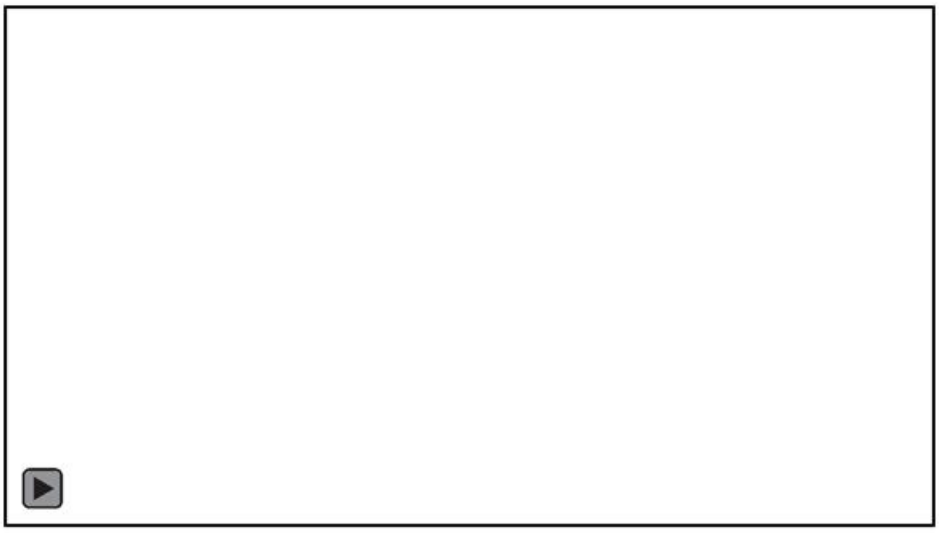
Patient Home Video: Stair Climbing

2 days post-treatment

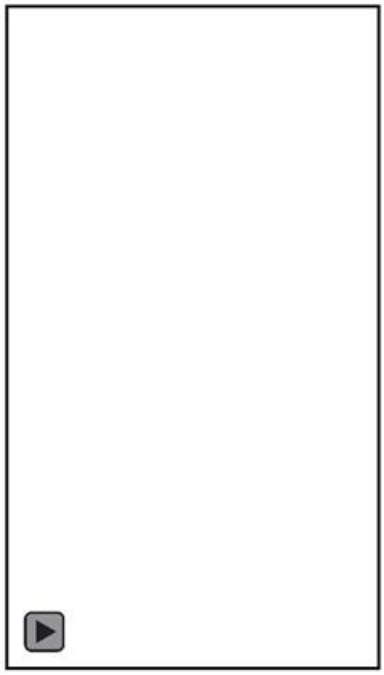
60 days post-treatment

Patient Video

Post-treatment



Patient Home Video:
90 Days Post-Treatment



Safety

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Safety (n=4)

- No Serious Adverse Events (SAEs) in this study
- 2 subjects had elevated GGT that resolved with increased steroids within a week and returned to baseline levels
- No other clinically significant laboratory findings
- Patients had transient nausea generally within the first week coincident with increased steroid dosing
  - Did not correlate with liver enzyme elevations or any other abnormality

GGT, gamma-glutamyltranspeptidase.

Adaptive Clinical Study Design

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Cohort C (4-7 years of age): Addition of Placebo-controlled Study Cohort

Subjects

- Treatment arm, n=12
- Placebo arm, n=12
  - Crossover at 1 year

Endpoints

- **Primary**:
  - Safety
  - Demonstration of micro-dystrophin protein expression
- **Secondary**:
  - Decrease in CK
  - Time to rise
  - Ascend 4 steps
  - NSAA
  - 10-meter timed test
  - 100-meter timed test

Summary

Preliminary Clinical Results

- Consistent with preclinical results
- Widespread micro-dystrophin expression
- Upregulation of the DAPC complex
- Reduction in CK is unprecedented
- Vector genome copy levels (>1 copy/nucleus) are consistent with robust micro-dystrophin protein expression
- Use of the MHCK7 promoter will significantly alter DMD disease course in the heart
- New placebo-controlled study design could serve as the basis for registration