# CLINICAL UPDATE:
## MYO-101 FOR LGMD TYPE 2E

# BUSINESS UPDATE:
## MYONEXUS ACQUISITION

Cambridge, MA

February 27, 2019

SAREPTA THERAPEUTICS

# 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 estimated number of patients affected by LGMDs; the potential benefits of AAVrh74, MHCK7, SR2 and SR3; the LGMD programs providing an opportunity to generate a steady stream of gene therapy candidates; the acquisition of Myonexus providing near-term, value-building catalysts for Sarepta; possible read-through of the LGMD2E program's clinical results to other LGMD programs; Sarepta's first five LGMD programs targeting a majority of LGMD2 cases; LGMD2 represents ~80 - 90% of total LGMD; Sarepta's tier 1 global regions representing ~30,000 – 40,000+ of total LGMD (US, EU, BR, JP); Sarepta's manufacturing strategy accounting for steady stream of LGMD therapies; our plan to hold near-term meeting with the FDA to plot path forward to align on next steps for each of the five programs and discuss the potential to dose higher (without impacting timeline); our construct commercial manufacturing strategy for LGMD; and the expectation that the acquisition of Myonexus will accelerate the development of LGMD portfolio.

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 clinical research or commercialization due to a variety of reasons, some of which may be outside of Sarepta's control; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve any significant revenues from the sale of such products; there can be no assurance that Sarepta will be able to complete the acquisition of Myonexus on the anticipated terms, or at all; Sarepta may not realize the anticipated benefits of the acquisition, which involves various risks, including disruption of Sarepta's ongoing business and distraction of its management and employees from other opportunities and challenges, potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges of Myonexus or the product candidates, liability for activities of Myonexus before the acquisition, including intellectual property infringement claims, violations of laws, commercial disputes, tax liabilities, and other known and unknown liabilities; if the actual number of patients suffering from LGMDs is smaller than estimated, our revenue and ability to achieve profitability may be adversely affected; various factors may decrease the market size of our product and product candidates, including the severity of the disease, patient demographics and the response of patients' immune systems to our product candidates; 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; we may not be able to execute on our business plans, including meeting our expected or planned regulatory milestones and timelines, research and clinical development plans, and bringing our product candidates to market, for various reasons including 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 the United States Patent and Trademark Office with respect to patents that cover our product candidates; 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 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.


SAREPTA THERAPEUTICS

# CLINICAL UPDATE:

## MYO-101 BETA-SARCOGLYCANOPATHY GENE THERAPY PROGRAM
## LIMB-GIRDLE MUSCULAR DYSTROPHY TYPE 2E


Louise Rodino-Klapac, Ph.D.

Senior Vice President, Gene Therapy
Sarepta Therapeutics, Inc.


SAREPTA THERAPEUTICS

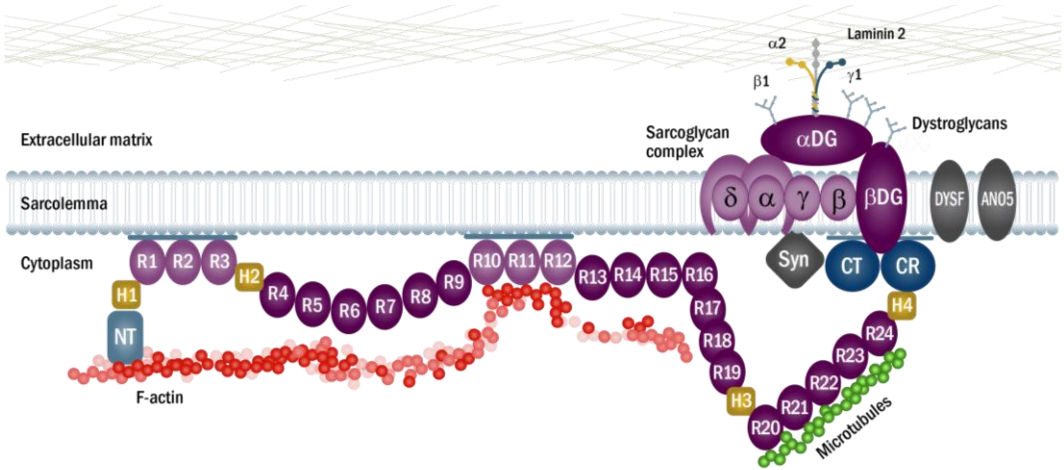
# LGMDS ARE DEVASTATING MUSCULAR DYSTROPHIES

*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
- **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.

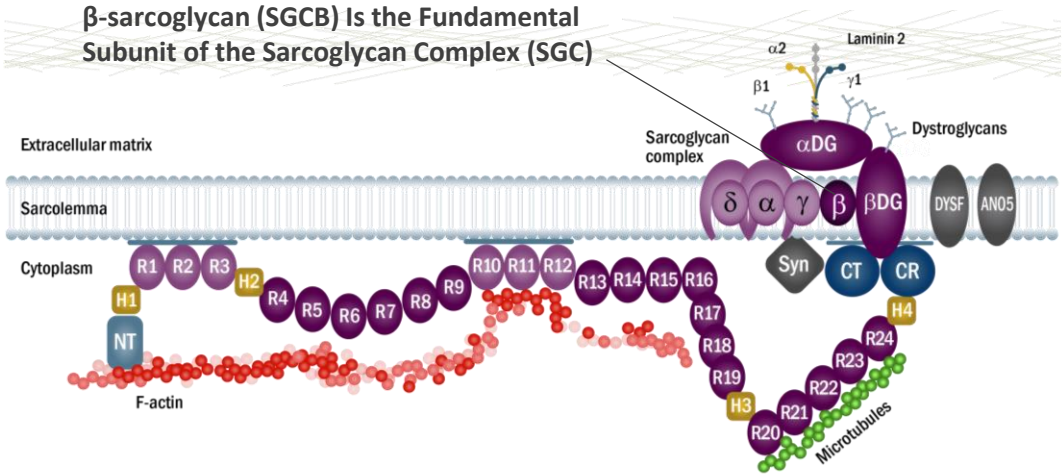
# EACH OF THE 5 MYONEXUS LGMDS IS CAUSED BY A MONOGENIC DEFECT RESULTING IN THE LACK OF ONE OF THE PROTEINS COMPRISING THE DYSTROPHIN-ASSOCIATED PROTEIN COMPLEX




- **Sarcoglycans** prevent muscle damage during contraction
  - All 4 functional sarcoglycans must be present to form a functional sarcoglycan complex (SCG)
    - **β-sarcoglycan (MYO-101)**
    - **α-sarcoglycan (MYO-102)**
    - **γ-sarcoglycan (MYO-103)**
  - Sarcoglycan deficiency leads to dystrophin deficiency
- **Dysferlin** and **ANO5** support muscle membrane repair (MYO-201 and MYO-301)
  - Failed muscle repair leads to chronic muscle degeneration

DYSF, dysferlin; ANO5, anoctamin-5

# EACH OF THE 5 MYONEXUS LGMDS IS CAUSED BY A MONOGENIC DEFECT RESULTING 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 (MYO-101)**
    - **α-sarcoglycan (MYO-102)**
    - **γ-sarcoglycan (MYO-103)**
  - Sarcoglycan deficiency leads to dystrophin deficiency
- **Dysferlin** and **ANO5** support muscle membrane repair (MYO-201 and MYO-301)
  - Failed muscle repair leads to chronic muscle degeneration

DYSF, dysferlin; ANO5, anoctamin-5

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

SAREPTA THERAPEUTICS

# LGMD TYPE 2E OPEN-LABEL TRIAL DESIGN

- **Up to 9 subjects with LGMD**
  - Cohort 1: 3 subjects; 4-15 years of age, **$5x10^{13}$ vg/kg** AAVrh74.MHCK7.SGCB

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

- **60-day muscle biopsy**

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

# ENDPOINTS IN THE LGMD2E STUDY

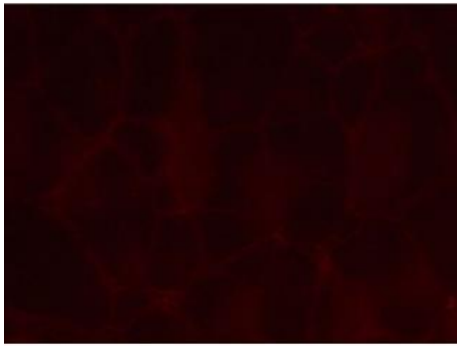
- **Primary endpoints**
  - Expression: **≥20% β–sarcoglycan positive fibers**
  - Safety

- **Secondary endpoints, including:**
  - Decrease in CK
  - Functional endpoints

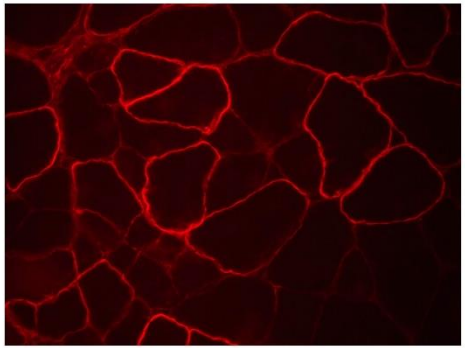
# PRE-CLINICAL MODELS CORRELATED EXPRESSION AND FUNCTION

*≥20 PERCENT EXPRESSION LEADS TO INCREASED FUNCTION*

**Pretreatment**

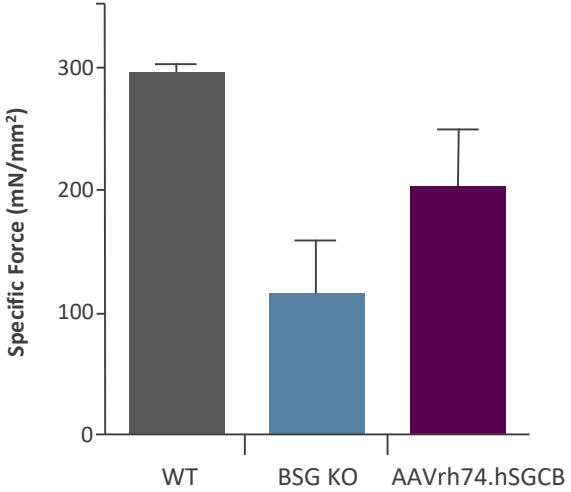


**Post Treatment**



**5x10$^{12}$ vg/kg**

**Function**



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

SAREPTA THERAPEUTICS

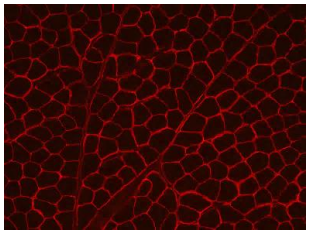
# LGMD2E SUBJECT DEMOGRAPHICS AT BASELINE

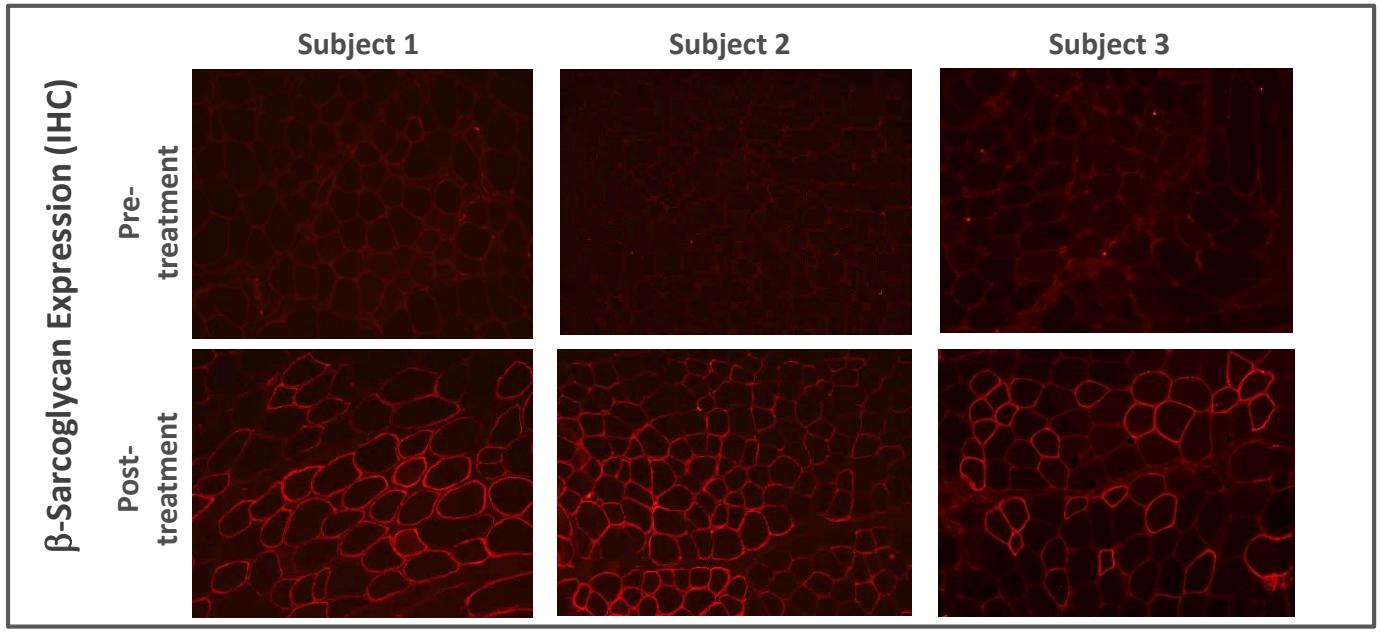
| Subject | Age (years) | Weight (kg) | CK Levels at Baseline (U/L) |
|---|---|---|---|
| 1 | 13 | 55 | 10,727 |
| 2 | 4 | 17 | 12,826 |
| 3 | 13 | 50 | 10,985 |

ClinicalTrials.gov Identifier: NCT03652259.

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

Normal Control






| | 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%** |

# ROBUST AND CONSISTENT β-SARCOGLYCAN EXPRESSION IN ALL 3 SUBJECTS AS MEASURED BY WESTERN BLOT POST-TREATMENT

| Subject | Mean Beta-Sarcoglycan Expression (N=3) vs Normal |
|---|---|
| 1 | 34.7% |
| 2 | 39.2% |
| 3 | 34.5% |
| **Mean** | **36.1%** |

The gene transfer delivers full length β-sarcoglycan

# THE OPTIMIZED VECTOR AND PROMOTER PROVIDED ROBUST EXPRESSION AT $5X10^{13}$ VG/KG

## Vector Genome Number

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

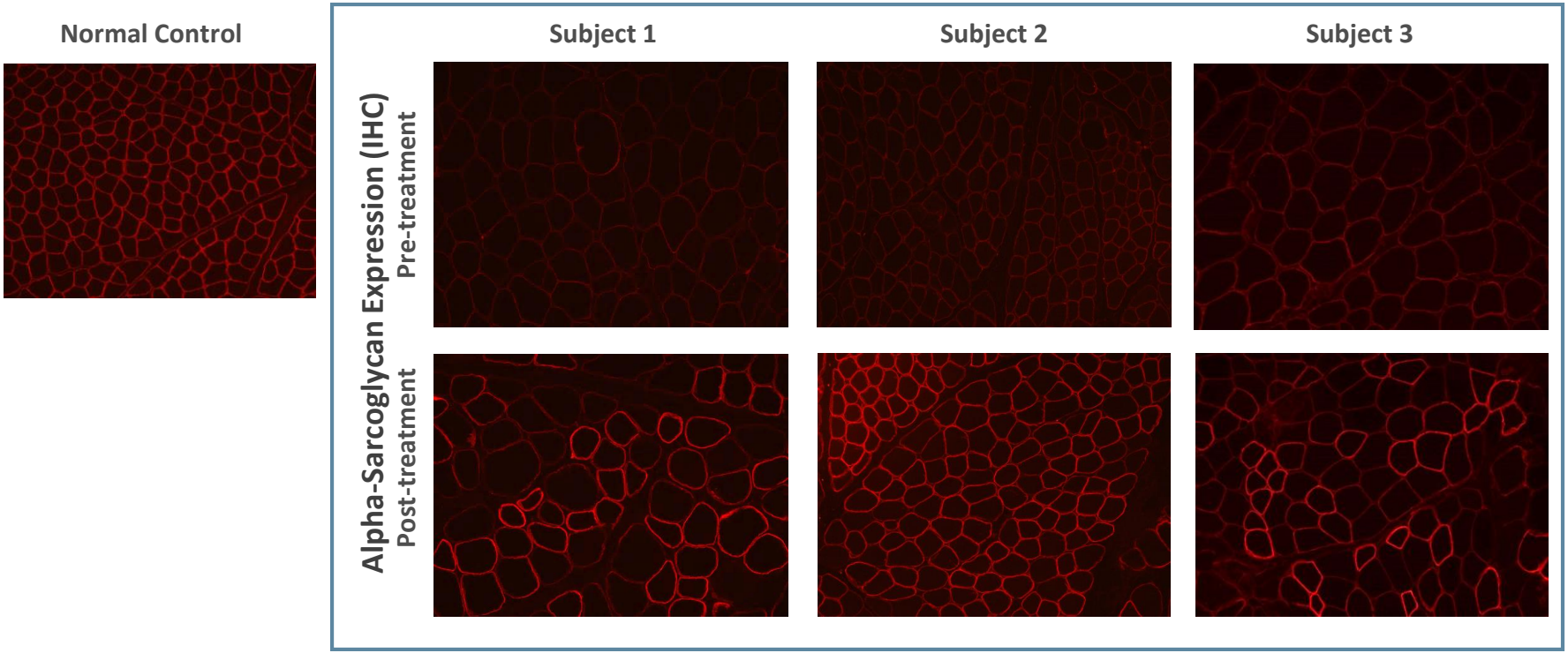
## Beta-Sarcoglycan Expression (IHC)

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

## Beta-Sarcoglycan Expression (Western Blot)

| | Percent of Normal |
|---|---|
| **Mean (n=3)** | **36.1%** |

# ROBUST β-SARCOGLYCAN EXPRESSION SIGNIFICANTLY UPREGULATED SARCOGLYCAN COMPLEX AT A DOSE OF 5X10$^{13}$ VG/KG



# 90% 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 (U/L) |
|---|---|---|---|
| 1 | 13 | 10,727 | 1135 |
| 2 | 4 | 12,826 | 2159 |
| 3 | 13 | 10,985 | 320 |

90% Mean Reduction in CK

ClinicalTrials.gov Identifier: NCT03652259

# STEROIDS HAD NO IMPACT ON CK LEVELS IN A PRIOR, LOWER DOSE, NON-SYSTEMIC LGMD 2D STUDY

| Subject | Age (years) | CK Levels at Baseline (U/L) | CK Levels at Day 90 (U/L) |
|---|---|---|---|
| 1* | 49 | 440 | 336 |
| 2 | 11 | 5191 | 4680 |
| 3 | 15 | 4722 | 4709 |
| 4 | 10 | 16654 | 21740 |
| 5 | 13 | 2500 | 3912 |
| 6 | 9 | 5734 | 7547 |
| Mean | 18 | 5874 | 7154 |

ClinicalTrials.gov Identifier: NCT01976091

*non-ambulant patient

**LGMD 2E and 2D study share the same steroid protocol**

# SAFETY (N=3)

- All patients doing well, patients 1,2: 90 days follow up, patient 3: 60 days follow up
- Two patients had elevated liver enzymes, one of which was designated a serious adverse event (SAE), as the patient had associated transient increase in bilirubin
  - Both events occurred when the patients were tapered off oral steroids
  - Elevated liver enzymes returned to baseline and symptoms resolved within days following supplemental steroid treatment
- No other clinically significant laboratory findings
  - **No decreases in platelet counts observed**
- Two 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

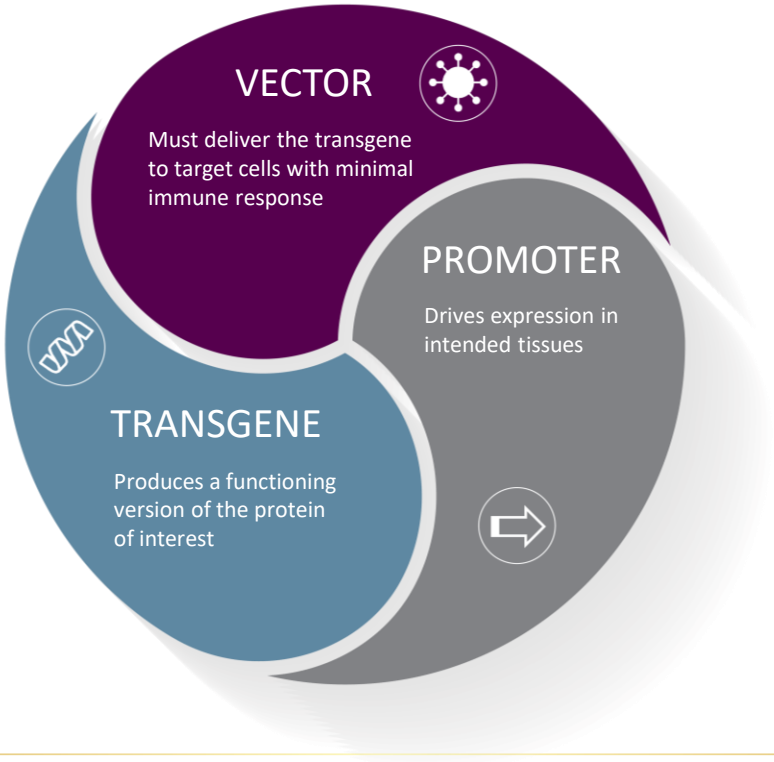
# BUSINESS UPDATE:
# MYONEXUS ACQUISITION


## Doug Ingram

President and CEO
Sarepta Therapeutics, Inc.


SAREPTA THERAPEUTICS

# CRITICAL COMPONENTS OF SAREPTA'S GENE THERAPY ENGINE



# SAREPTA'S GENE THERAPY ENGINE AT WORK – DUCHENNE MUSCULAR DYSTROPHY (DMD)

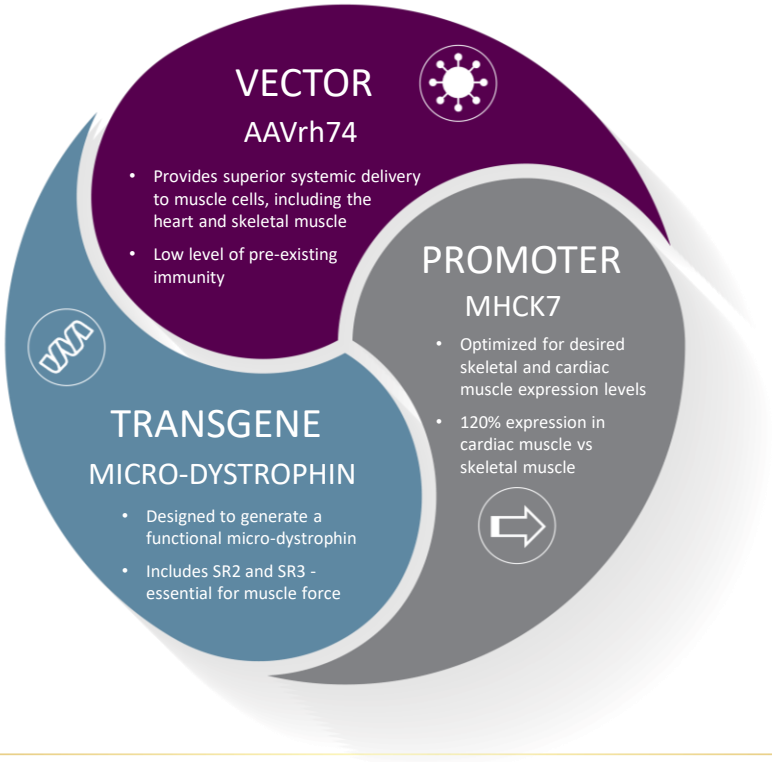
EARLY CLINICAL RESULTS*
MICRO-DYSTROPHIN GENE THERAPY FOR DMD

**81%**
Robust expression of micro-dystrophin in muscle fibers

**96%**
Robust expression of micro-dystrophin measured by signal intensity

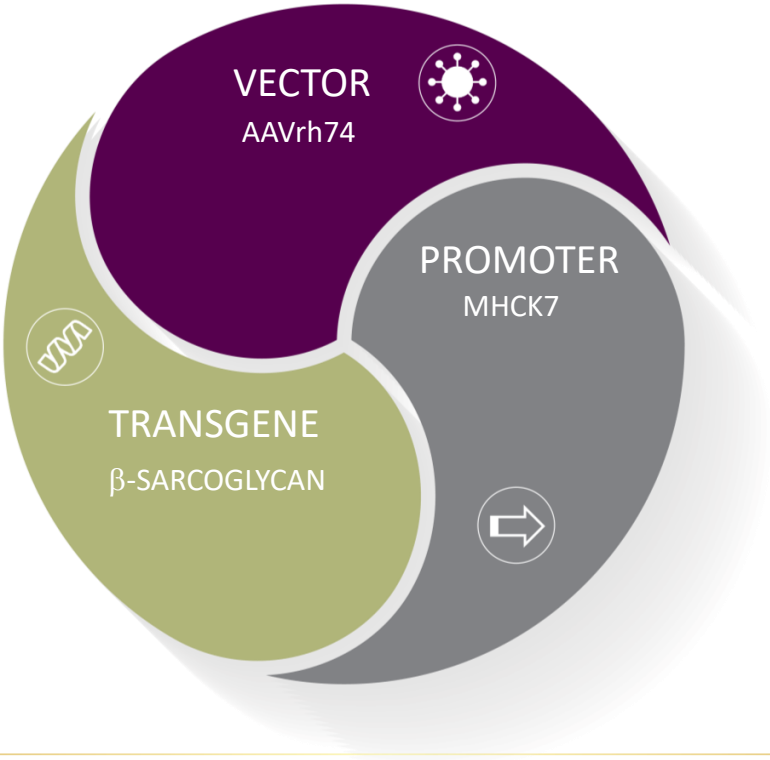
**96%**
Robust expression of micro-dystrophin measured by Western blot**

**78%**
Reduction of creatine kinase




* Data from the 4 patients dosed in Study NCT03375164
**NCH Western blot method
***North Star Ambulatory Assessment (NSAA), Time to Rise, 4 Stairs Up, and 100M

# SAREPTA'S GENE THERAPY ENGINE AT WORK – LIMB-GIRDLE MUSCULAR DYSTROPHY (LGMD)




PRELIMINARY CLINICAL RESULTS
β-SARCOGLYCAN GENE THERAPY
FOR LIMB GIRDLE MUSCULAR
DYSTROPHY TYPE 2E

**51%**
Robust expression of β-sarcoglycan in muscle fibers

**47%**
Robust expression of β-sarcoglycan measured by signal intensity

**36%**
Robust expression of β-sarcoglycan measured by Western blot**

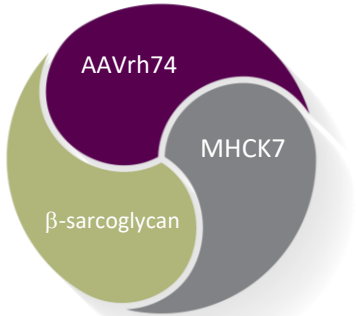
**90%**
Reduction of creatine kinase

* Data from the 3 patients dosed in Study NCT03652259
**NCH Western blot method
***North Star Ambulatory Assessment (NSAA), Time to Rise, 4 Stairs Up, and 100M

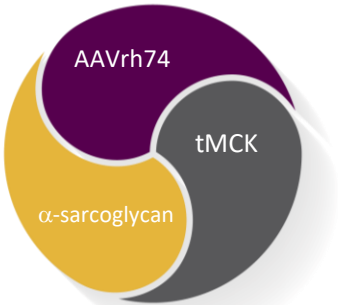
# GENE THERAPY ENGINE AT WORK ACROSS LGMD PORTFOLIO

OPPORTUNITY TO GENERATE A STEADY STREAM OF GENE THERAPY CANDIDATES

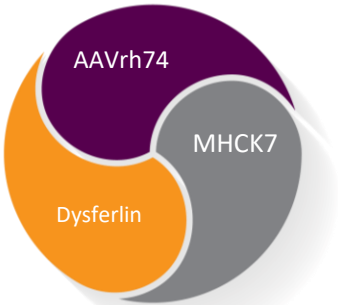
## LGMD PORTFOLIO



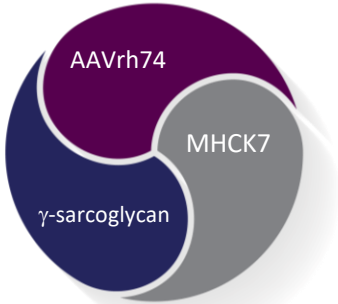

LGMD2E



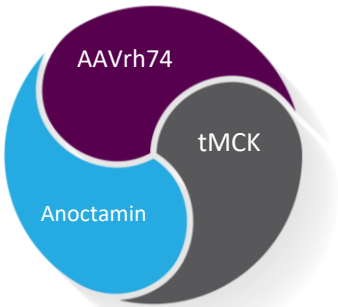

LGMD2D




LGMD2B




LGMD2C




LGMD2L

# ACQUISITION OF MYONEXUS THERAPEUTICS PROVIDES NEAR-TERM, VALUE-BUILDING CATALYSTS FOR SAREPTA

***Aligns to Sarepta's mission of rapidly and urgently bringing important therapies to patients around the world***

| | |
|---|---|
| POSITIVE PRELIMINARY CLINICAL RESULTS – LEAD PROGRAM (LGMD2E) | • Clinical results have the potential to read-through to other LGMD programs<br>• Differentiated science/scientific approach |
| FULL RIGHTS TO ALL FIVE LGMD PROGRAMS | • Sarepta's first five programs target a majority of LGMD2 cases<br>• LGMD2 represents ~80 - 90% of total LGMD |
| UNTAPPED AND GROWING OPPORTUNITY | • Estimated LGMD worldwide population - ~200K – 300K<br>• As LGMD genes of interest have been identified, diagnosis of LGMD patients worldwide is expected to accelerate<br>• Sarepta's tier 1 global regions are believed to represent up to ~30,000 – 40,000+ of total LGMD (US, EU, BR, JP) |
| EXPERTISE / INFRASTRUCTURE SUPPORT RAPID ADVANCEMENT OF PROGRAMS | • Aligned with gene therapy thought leaders – Drs. Jerry Mendell and Louise Rodino-Klapac<br>• Manufacturing strategy designed for steady stream of LGMD therapies |
| FINANCIALLY ADVANTAGEOUS | • Early opt resulted in savings (net value), an attractive purchase price ($165M cash), and ability to rapidly advance programs<br>• Effective use of cash given potential commercial opportunity of LGMD portfolio |

# NEXT STEPS – LGMD PORTFOLIO

## HOLD NEAR-TERM MEETING WITH FDA TO OUTLINE PATH FORWARD

- Align on next steps for each of the five programs
- Potential to dose higher for enhanced expression in additional cohort (without impacting timeline)

## CONSTRUCT COMMERCIAL MANUFACTURING STRATEGY AND TIMELINE

- Approach similar to micro-dystrophin program
  - Transfer from Nationwide Children's to commercial process
  - Move from mammalian adherent stack process to more scalable adherent iCellis process

# GENE THERAPY ENGINE AT WORK ACROSS PIPELINE PROGRAMS

OPPORTUNITY TO GENERATE A STEADY STREAM
OF GENE THERAPY CANDIDATES

DUCHENNE
MUSCULAR DYSTROPHY

LIMB-GIRDLE
MUSCULAR DYSTROPHY

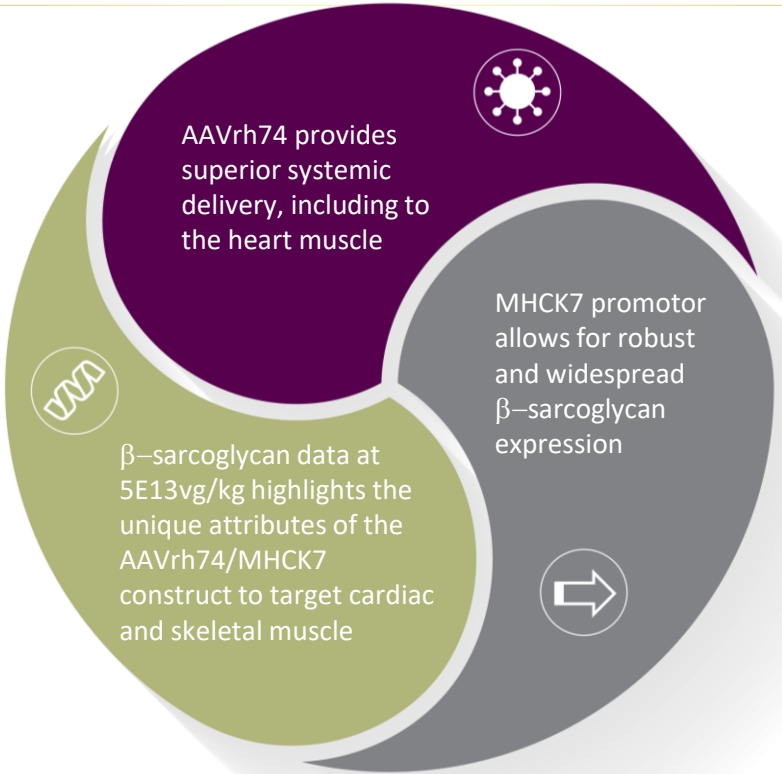
CHARCOT-MARIE-TOOTH
DISEASE

MUCOPOLYSACCHARIDOSIS

POMPE DISEASE

# FULL STEAM AHEAD

## RESULTS REINFORCE SAREPTA'S GENE THERAPY ENGINE




ACQUISITION OF MYONEXUS WILL ACCELERATE THE DEVELOPMENT OF LGMD PORTFOLIO

# QUESTIONS & ANSWERS

SAREPTA THERAPEUTICS