CLINICAL UPDATE:
SRP-9003 BETA-SARCOCGLYCANOPATHY 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
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.

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 the following: 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; the data presented in this presentation may not be consistent with the final data set and analysis thereof or result in a safe or effective treatment benefit; different methodologies, assumptions and applications Sarepta utilizes to assess particular safety or efficacy parameters may yield different statistical results, and even if Sarepta believes the data collected from clinical trials of its product candidates are positive, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities; 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, 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 decisions by the United States Patent and Trademark Office with respect to patents that cover our 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, 2018 or most recently filed 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. You should not place undue reliance on forward-looking statements. Sarepta does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof, except to the extent required by applicable law or SEC rules.
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

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 **ANOS** support muscle membrane repair (MYO-201 and SRP-9006)
  - Failed muscle repair leads to chronic muscle degeneration

ANOS, 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

- **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 **ANOS** support muscle membrane repair (MYO-201 and SRP-9006)
  - Failed muscle repair leads to chronic muscle degeneration
PRE-CLINICAL MODELS CORRELATED EXPRESSION AND FUNCTION

≥20 PERCENT EXPRESSION LEADS TO INCREASED FUNCTION

**Function**

<table>
<thead>
<tr>
<th></th>
<th>Specific Force (mN/mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td>300</td>
</tr>
<tr>
<td>BSG KO</td>
<td>100</td>
</tr>
<tr>
<td>AAVrh74.hSGCB</td>
<td>*</td>
</tr>
</tbody>
</table>

5x10^{12} vg/kg
LGMD2E PHASE I/II STUDY: COHORT 1 (N=3)
LGMD TYPE 2E OPEN-LABEL TRIAL DESIGN

- **Up to 6 subjects with LGMD**
  - Cohort 1: 3 subjects; 4-15 years of age, $5 \times 10^{13} \text{vg/kg}$ 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**
  - $\geq 20\%$ $\beta$-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)
LGMD2E SUBJECT DEMOGRAPHICS AT BASELINE

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Mutation</th>
<th>Weight (kg)</th>
<th>CK Levels at Baseline (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>Exon 3</td>
<td>55</td>
<td>10,727</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>Exon 4</td>
<td>17</td>
<td>12,826</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>Exon 3</td>
<td>50</td>
<td>10,985</td>
</tr>
</tbody>
</table>

- 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

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

ROBUST \( \beta \)-SARCOGLYCAN EXPRESSION IN MUSCLE BIOPSIES IN ALL 3 SUBJECTS AT A DOSE OF \( 5 \times 10^{13} \) VG/KG

**Beta-Sarcoglycan Expression (IHC)**

<table>
<thead>
<tr>
<th></th>
<th>Subject 1</th>
<th>Subject 2</th>
<th>Subject 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-treatment</strong></td>
<td><img src="post-treatment-subject1.png" alt="Image" /></td>
<td><img src="post-treatment-subject2.png" alt="Image" /></td>
<td><img src="post-treatment-subject3.png" alt="Image" /></td>
</tr>
<tr>
<td><strong>Post-treatment</strong></td>
<td><img src="post-treatment-subject1.png" alt="Image" /></td>
<td><img src="post-treatment-subject2.png" alt="Image" /></td>
<td><img src="post-treatment-subject3.png" alt="Image" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Percentage of SGCB-positive Fibers</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (n=3)</strong></td>
<td>51%</td>
<td>47%</td>
</tr>
</tbody>
</table>
**ROBUST β-SARCOGLYCAN EXPRESSION IN MUSCLE BIOPSIES IN ALL 3 SUBJECTS AT A DOSE OF 5x10^{13} VG/KG**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Percentage of SGCB-Positive Fibers</th>
<th>Mean Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63%</td>
<td>47%</td>
</tr>
<tr>
<td>2</td>
<td>49%</td>
<td>57%</td>
</tr>
<tr>
<td>3</td>
<td>42%</td>
<td>38%</td>
</tr>
<tr>
<td>Mean</td>
<td>51%</td>
<td>47%</td>
</tr>
</tbody>
</table>
SGCB expression significantly upregulated SGC complex at a dose of $5 \times 10^{13}$ VG/kg

Normal Control

SGC Complex

α-Sarcoglycan Expression (IHC)

Subject 1  Subject 2  Subject 3

Pre-treatment

Post-treatment

β-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority. Sarepta Therapeutics 2019. Data on file. ClinicalTrials.gov: NCT03652259.
SGCB EXPRESSION SIGNIFICANTLY UPREGULATED SGC COMPLEX PROTEIN AT A DOSE OF $5 \times 10^{13}$ VG/KG

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

### Mean SGCB Expression vs Normal

<table>
<thead>
<tr>
<th>Subject</th>
<th>Mean SGCB Expression vs Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34.7%</td>
</tr>
<tr>
<td>2</td>
<td>39.2%</td>
</tr>
<tr>
<td>3</td>
<td>34.5%</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>36.1%</strong></td>
</tr>
</tbody>
</table>

**The gene transfer delivers full-length SGCB**

$\beta$-sarcoglycan gene therapy is investigational and has not been reviewed or approved by any regulatory authority.

### β-Sarcoglycan Expression is Supported by Vector Genome Counts

**Beta-Sarcoglycan Expression (IHC)**

<table>
<thead>
<tr>
<th></th>
<th>Percentage of Beta-Sarcoglycan-positive Fibers</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (n=3)</td>
<td>51%</td>
<td>47%</td>
</tr>
</tbody>
</table>

**Beta-Sarcoglycan (Western Blot)**

<table>
<thead>
<tr>
<th></th>
<th>Percent of Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (n=3)</td>
<td>36.1%</td>
</tr>
</tbody>
</table>

**Vector Genome Number**

<table>
<thead>
<tr>
<th></th>
<th>Vector Copies/μg DNA</th>
<th>Copies per Nucleus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (n=3)</td>
<td>8.4E04</td>
<td>0.60</td>
</tr>
</tbody>
</table>
LGMD2E STUDY
FUNCTIONAL DATA SUMMARY:
COHORT 1 (n=3)
LGMD2E NATURAL HISTORY DATA GENERATED BY LINDA LOWES & LINDSAY ALFANO AT NATIONWIDE CHILDREN’S HOSPITAL

North Star Assessment for Limb Girdle Muscular Dystrophies (NSAD)

All Subjects

Patients are assessed every 6 months
CREATINE KINASE (CK) LEVELS ARE REDUCED WITH β-SARCOGLYCAN GENE THERAPY

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Baseline (U/L)</th>
<th>Day 30 (U/L)</th>
<th>Day 60 (U/L)</th>
<th>Day 90 (U/L)</th>
<th>Day 180 (U/L)</th>
<th>Day 270 (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>10,727</td>
<td>619</td>
<td>2257</td>
<td>1135</td>
<td>1553</td>
<td>2300</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>12,826</td>
<td>4795</td>
<td>910</td>
<td>2159</td>
<td>5070</td>
<td>2665</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>10,985</td>
<td>687</td>
<td>2061</td>
<td>2392</td>
<td>10,055</td>
<td>1295</td>
</tr>
</tbody>
</table>

9 Months: 82% Reduction in CK
## SUMMARY OF CLINICAL DATA AT 9 MONTHS
ALL SUBJECTS SHOWED IMPROVEMENT IN ALL FUNCTIONAL MEASURES

<table>
<thead>
<tr>
<th>Subject</th>
<th>Assessment</th>
<th>NSAD</th>
<th>Time to Rise (sec)</th>
<th>4 Stairs Up (sec)</th>
<th>100 m (sec)</th>
<th>10 m (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Baseline</td>
<td>40</td>
<td>5.0</td>
<td>2.4</td>
<td>49.3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>41</td>
<td>4.1</td>
<td>2.3</td>
<td>43.2</td>
<td>4.5</td>
</tr>
<tr>
<td>2</td>
<td>Baseline</td>
<td>48</td>
<td>1.5</td>
<td>1.6</td>
<td>59.3</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>54</td>
<td>1.2</td>
<td>1.3</td>
<td>48.4</td>
<td>3.2</td>
</tr>
<tr>
<td>3</td>
<td>Baseline</td>
<td>41</td>
<td>3.5</td>
<td>2.8</td>
<td>49.9</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>47</td>
<td>3.0</td>
<td>1.9</td>
<td>48.6</td>
<td>4.3</td>
</tr>
</tbody>
</table>
SUMMARY OF CLINICAL DATA AT 9 MONTHS
ALL SUBJECTS SHOWED IMPROVEMENT IN ALL FUNCTIONAL MEASURES

<table>
<thead>
<tr>
<th>Subject</th>
<th>Assessment</th>
<th>NSAD</th>
<th>Time to Rise (sec)</th>
<th>4 Stairs Up (sec)</th>
<th>100 m (sec)</th>
<th>10 m (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Baseline</td>
<td>40</td>
<td>5.0</td>
<td>2.4</td>
<td>49.3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>41</td>
<td>4.1</td>
<td>2.3</td>
<td>43.2</td>
<td>4.5</td>
</tr>
<tr>
<td>2</td>
<td>Baseline</td>
<td>48</td>
<td>1.5</td>
<td>1.6</td>
<td>59.3</td>
<td>3.4</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>54</td>
<td>1.2</td>
<td>1.3</td>
<td>48.4</td>
<td>3.2</td>
</tr>
<tr>
<td>3</td>
<td>Baseline</td>
<td>41</td>
<td>3.5</td>
<td>2.8</td>
<td>49.9</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Day 270</td>
<td>47</td>
<td>3.0</td>
<td>1.9</td>
<td>48.6</td>
<td>4.3</td>
</tr>
</tbody>
</table>
### BASELINE DEMOGRAPHICS OF AGE-MATCHED LGMD2E NATURAL HISTORY GROUP (4-15 YEARS)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>
AGE-MATCHED LGMD2E NATURAL HISTORY COHORT

Mean Change from Baseline in North Star Assessment for Limb Girdle Muscular Dystrophies (NSAD), Subjects with Baseline Ages 4 to 15

Mean (SD) Change from Baseline in NSAD

Duration of Follow-Up (Days)

Baseline 30 DAYS 60 DAYS 90 DAYS 180 DAYS 200 DAYS 270 DAYS 360 DAYS 450 DAYS

Natural History (n=5)
Mean Change from Baseline in North Star Assessment for Limb Girdle Muscular Dystrophies (NSAD), Subjects with Baseline Ages 4 to 15

Mean (SD) Change from Baseline in NSAD

Duration of Follow-Up (Days):
- Baseline
- 30 Days
- 60 Days
- 90 Days
- 180 Days
- 200 Days
- 270 Days
- 360 Days
- 450 Days

SRP-9003 (n=3)

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 $5 \times 10^{13}$ 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

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

AAVrh74.MHCK7.SGCB (SRP-9003)
### Sarepta’s Current Clinical Programs in LGMD

<table>
<thead>
<tr>
<th>Program</th>
<th>LGMD2E</th>
<th>LGMD2D</th>
<th>LGMD2B</th>
<th>LGMD2C</th>
<th>LGMD2L</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target Function</strong></td>
<td>Stabilizes DAPC, prevents muscle damage during contraction</td>
<td>Stabilizes DAPC, prevents muscle damage during contraction</td>
<td>Muscle membrane repair</td>
<td>Stabilizes DAPC, prevents muscle damage during contraction</td>
<td>Muscle membrane repair</td>
</tr>
<tr>
<td><strong>Vector</strong></td>
<td>AAVrh74</td>
<td>AAVrh74</td>
<td>AAVrh74</td>
<td>AAVrh74</td>
<td>AAVrh74</td>
</tr>
<tr>
<td><strong>Promoter</strong></td>
<td>MHCK7</td>
<td>tMCK</td>
<td>MHCK7</td>
<td>MHCK7</td>
<td>tMCK</td>
</tr>
<tr>
<td><strong>Full Length</strong></td>
<td>β-sarcoglycan</td>
<td>α-sarcoglycan</td>
<td>Dysferlin</td>
<td>γ-sarcoglycan</td>
<td>Anoctamin-5</td>
</tr>
</tbody>
</table>

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
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