Sarepta Therapeutics and Arrowhead Pharmaceuticals Licensing Deal

Strengthening Sarepta's leadership position as an enduring genetic medicine company for rare disease

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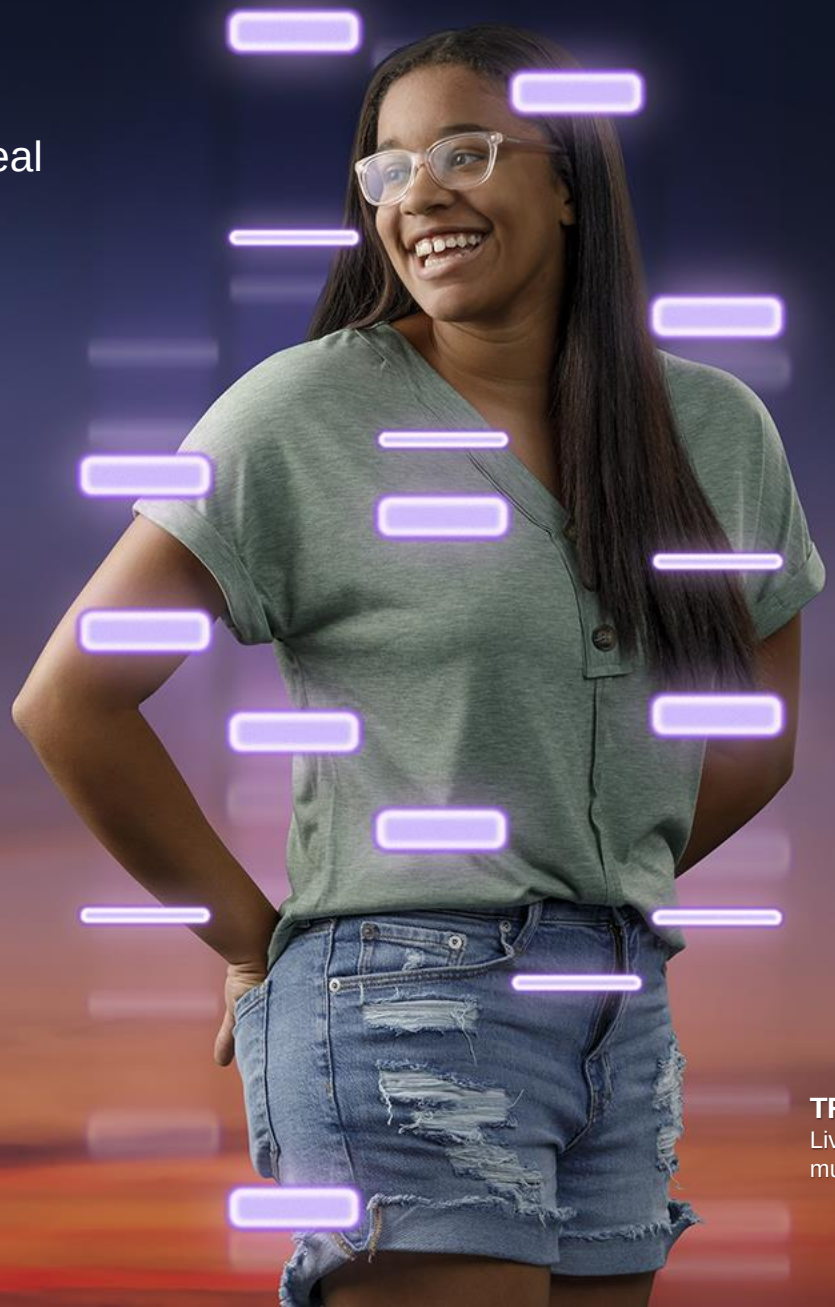
SAREPTA THERAPEUTICS



TRYNITY
Living with limb-girdle muscular dystrophy

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 our opportunities in the rare disease space; the potential benefits from the Arrowhead transaction, including future revenue opportunities; the closing of the Arrowhead transaction and equity investment; Sarepta’s payment of regulatory and sales milestones, and royalty payments to Arrowhead pursuant to the agreement; the expected targets of the clinical and pre-clinical programs licensed pursuant to the agreement; ongoing development of therapeutics against a broad range of skeletal muscle gene targets by Sarepta and Arrowhead; Arrowhead’s potentially best-in-class approach to siRNA and the potential benefits of its targeted RNAi Molecule (TRiM) platform; the expected timing of future data readouts and transitions of certain clinical trials; the amount and timing of repurchases under Sarepta’s share purchase program; and our current expectation that we do not anticipate other large transactions like the Arrowhead transaction.

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 such risks and uncertainties could materially and adversely affect our business, results of operations and trading price. Potential known risk factors include, among others, the following: 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; 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 data for our different programs, including gene therapy-based product candidates, may not be sufficient for obtaining regulatory approval; the expected benefits and opportunities related to our agreements with our strategic partners may not be realized or may take longer to realize than expected due to a variety of reasons, including any inability of the parties to perform their commitments and obligations under the agreements, challenges and uncertainties inherent in product research and development and manufacturing limitations; our dependence on our manufacturers to fulfill our needs for our clinical trials and commercial supply, including any failure 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 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, 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, 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 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.

A transformative moment for Sarepta

Doug Ingram, President & CEO

Deal elevates Sarepta to an enduring, fully integrated genetic medicines company

Strength of Elevidys launch enables this transaction; deal represents strategic deployment of capital

- Strengthens Sarepta's leadership position in genetic medicine
- Leverages Sarepta's successful track record in developing and commercializing neuromuscular therapies
- Addresses large markets with unmet patient need
- Advances competitively differentiated best-in-class therapies
- Generates multiple, near-term clinical data readouts and robust revenue opportunity
- Strengthens business model and employs strategic allocation of capital

Drives value and growth for near-, mid- and long-term

Deal adds meaningfully to Sarepta's pipeline with 13 programs in muscle, pulmonary and CNS

4 CLINICAL PROGRAMS

- **Muscle**
  - **ARO-DUX4:** Facioscapulohumeral muscular dystrophy type 1 **(FSHD1)**
  - **ARO-DM1:** Myotonic dystrophy type 1 **(DM1)**
- **Pulmonary**
  - **ARO-MMP7:** Idiopathic Pulmonary Fibrosis **(IPF)**
- **Central nervous system (CNS)**
  - **ARO-ATXN2:** Spinocerebellar ataxia type 2 **(SCA2)**

3 PRECLINICAL PROGRAMS

- **CNS**
  - **ARO-ATXN1:** Spinocerebellar ataxia type 1 **(SCA1)**
  - **ARO-ATXN3:** Spinocerebellar ataxia type 3 **(SCA3)**
  - **ARO-HTT:** Huntington's Disease **(HD)**

Leveraging Arrowhead's next-generation blood brain barrier crossing TRiM platform

Up to 6 DISCOVERY TARGETS

- **Skeletal muscle**
- **Cardiac muscle**
- **CNS**

Leveraging Arrowhead's next-generation targeting ligands for muscle, cardiomyocytes and CNS

Agreement terms

Sarepta fully funded the deal with cash on hand

- Sarepta will pay Arrowhead upfront fees of $500 million, make an equity investment of $325 million at a 35% premium and an additional $250 million paid over five years
- Arrowhead has potential to receive an additional $300 million in near-term clinical trial enrollment-related milestone payments
- Arrowhead will be responsible for Phase 1/2 trials currently underway
- Clinical-stage programs will transition to Sarepta no later than the completion of current trials
- Sarepta to receive investigational treatments that leverage Arrowhead's Targeted RNAi Molecule (TRiM™) platform
- Arrowhead to transition preclinical assets to Sarepta upon completion of IND-enabling activities

Strengthened investor profile

- Robust revenue trajectory and profitability
- Strong cash position
- Multiple on-market therapies
- Leading-edge competitive science
- Strong intellectual property (IP) position
- Deep, advancing pipeline
- Multiple shots on goal
- Near and mid-term momentum; multiple catalysts
- Competitive business model to drive value appreciation

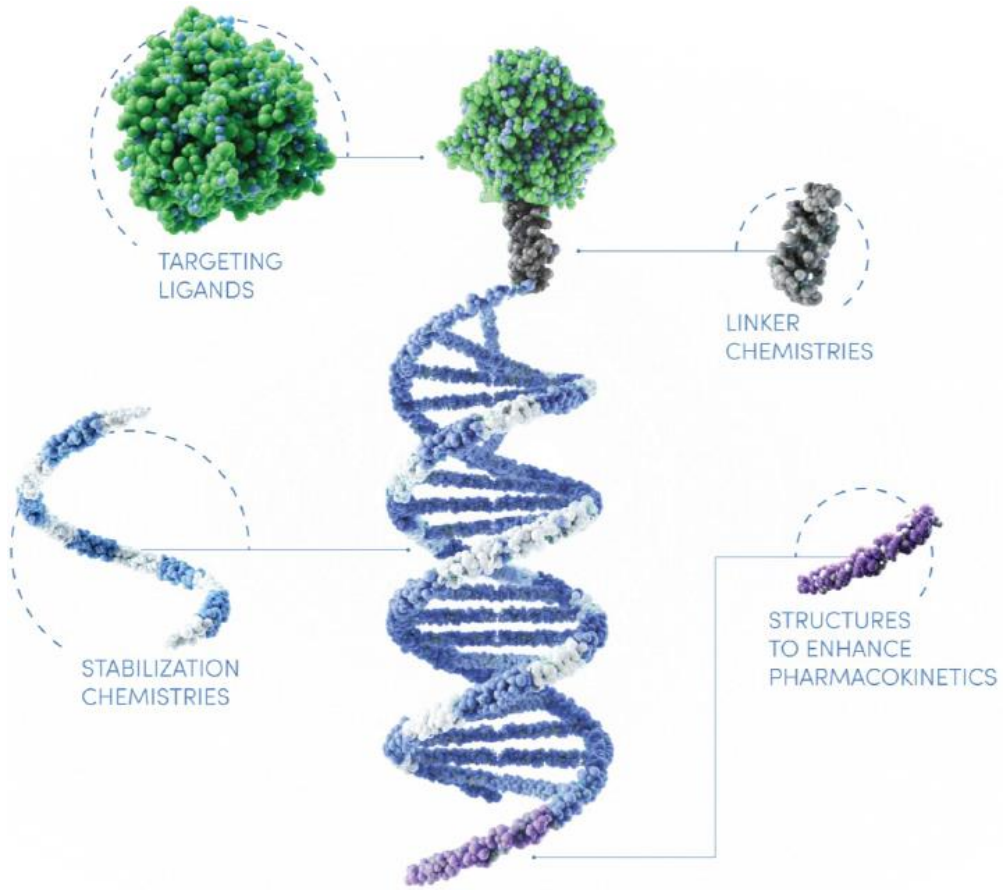
The Science and Pipeline Programs

Louise Rodino-Klapac, PhD
Executive Vice President, Head of R&D, Chief Scientific Officer

Targeted RNAi Molecule (TRiM™) platform capable of deep and durable target gene knockdown

Introduced by Arrowhead in 2017, brought >10 assets to clinic and treated thousands of patients

Delivery
Tissue-specific ligands (peptide, small molecule, Ab) to deliver siRNA to Liver, CNS, Muscle, Lung, Heart etc.



Linker
Provide stability/orientation. Program/Tissue-specific linker is selected to optimize activity, safety, and CMC complexity

siRNA Chemistry
Established and experimental chemical modifications to optimize potency, duration, and target specificity

PK/PD Structures
Certain programs have novel features to enhance PK/PD (e.g., lipid for skeletal muscle)

ARO-DUX4: Facioscapulohumeral muscular dystrophy type 1 (FSHD1)

siRNA therapy in development to treat FSHD1, with a differentiated profile based on data generated to date

FSHD: Rare, progressive, genetic muscle disease

- Autosomal dominant disease associated with the failure to maintain complete epigenetic suppression of DUX4 expression in differentiated skeletal muscle, leading to overexpression of DUX4, which is myotoxic and can lead to muscle degeneration
- Caused by changes in a region of chromosome 4 called D4Z4 that result in the abnormal activation of the DUX4 gene
- 2 types of FSHD: FSHD type1 and FSHD type 2; both present generally the same and are identified by their genetic cause[1]
- Disease presents as muscle weakness that progressively spreads from the face into other areas (scapular girdle muscles, upper limb muscles, pelvic girdle muscles, abdominal muscles and leg muscles)
- ~50% of FSHD patients will progress to becoming dependent on a wheelchair after ~20 years
- ~50% of FSHD patients have moderate to extreme levels of mobility restrictions
- Average age of diagnosis is 20-years-old[2]

Prevalence: ~13K diagnosed patients (U.S.); FSHD type 2 represent a minority of patients (~2 to 5% of the diagnosed prevalent population)

About ARO-DUX4

Scientific Approach:
Designed to reduce the production of human double homeobox 4 (DUX4) protein in skeletal muscle

Development Status:
Phase 1/2

Study Objective:
Dose-escalating study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of ARO-DUX4 in participants with FSHD1

1. *https://www.mda.org/sites/default/files/2024/07/Facioscapulohumeral-Muscular-Dystrophy-FSHD-Fact-Sheet.pdf*
2. https://www.mda.org/disease/facioscapulohumeral-muscular-dystrophy/signs-and-symptoms

ARO-DM1: Myotonic dystrophy type 1 (DM1)

Best-in-class RNA profile based on non-clinical data; differentiated efficacy, safety and dosing

Myotonic Dystrophy (DM): *Form of muscular dystrophy that affects muscles and other organs throughout the body*[1]

- There are two types of DM: DM1 is caused by mutations in the DMPK gene and is generally more severe than DM2[1]
- Pathogenesis of DM1 is driven by an expanded CUG trinucleotide repeat in the 3'-untranslated region of myotonic dystrophy protein kinase (DMPK) transcripts
- The abnormal transcripts cause mis-regulated splicing, known as spliceopathy, for certain messenger RNAs which are directly linked to the clinical manifestations of DM1
- DM1 impacts the respiratory muscle and significant breathing problems can result;[3] as DM1 progresses, the heart can develop an abnormal rhythm and weaken[1]
- Life expectancy is shortened[2]

Prevalence: ~30K diagnosed DM1 patients (U.S.)

About ARO-DM1

Scientific Approach:

- Designed to target and suppress DMPK in skeletal muscle
- Silencing the aberrantly transcribed DMPK mRNA using ARO-DM1 may halt CUGexp-related spliceopathies in patients with DM1 and improve muscle strength and function

Development Status:

Phase 1/2

Study Objective:

Double-blinded, placebo-controlled, dose-escalating study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple ascending doses of ARO-DM1 compared to placebo in male and female subjects with DM1

1. *https://www.mda.org/disease/myotonic-dystrophy*
2. *https://www.ncbi.nlm.nih.gov/books/NBK1165/*
3. *https://www.myotonic.org/what-dm/how-dm-affects-your-body/respiratory-system*

ARO-ATXN2: Spinocerebellar ataxia type 2 (SCA2)

Poised to be first disease-modifying therapy; therapies in development for SCA1 and SCA3

SCA: *Progressive neurodegenerative disease*

- In SCA, the nerve fibers carrying messages to and from the brain are affected, resulting in degeneration of the cerebellum (the coordination center of the brain)[1]
- SCA2 is caused by mutations in the ATXN2 gene[2]
- There are more than 40 types of SCA[4]
- Patients with SCA generally need a wheelchair 10 to 20 years after diagnosis[1]
- Typical age of SCA2 onset is 20 to 30 years; as SCA2 progresses, loss of balance, difficulty walking, difficulty swallowing and slurred speech are common[3]

Prevalence:

- SCA2: ~2,000 diagnosed patients (U.S.)
- SCA1: ~1,400 diagnosed patients (U.S.)
- SCA3: ~3,200 diagnosed patients (U.S.)

About ARO-ATXN2: Designed to target the ataxin-2 protein (ATXN2) in the CNS

Development Status: Expected to begin Phase 1/2 clinical study for SCA2 by the end of 2024

1. https://www.ninds.nih.gov/health-information/disorders/spinocerebellar-ataxias-including-machado-joseph-disease
2. https://medlineplus.gov/genetics/condition/spinocerebellar-ataxia-type-2/#causes
3. https://www.ataxia.org/sca-2/
4. https://my.clevelandclinic.org/health/diseases/24077-spinocerebellar-ataxia

ARO-MMP7: Idiopathic Pulmonary Fibrosis (IPF)

ARO-MMP7 designed to inhibit fibrotic development by silencing MMP7

Idiopathic Pulmonary Fibrosis (IPF): Chronic, progressive, and irreversible condition of the lungs

- Cause is relatively unknown, the risk for IPF is higher amongst smokers or have a family history of IPF. Risk increases with age, most often impacting people over age 50.[1]
- The most common symptoms of IPF are shortness of breath and dry cough that get worse over time; complications of IPF include pulmonary hypertension and respiratory failure[1]
- There is a high unmet need with few options to slow the progression of the disease
- Death ~5 years from diagnosis[2]

Prevalence: ~60K diagnosed patients (U.S.)

About ARO-MMP7

Scientific Approach:
Designed to reduce expression of matrix metalloproteinase 7 (MMP7) in pulmonary epithelial cells

Development Status:
Phase 1/2

Study Objective:
Single ascending dose and multiple ascending dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARO-MMP7 healthy volunteers and patients with IPF

1. https://www.nhlbi.nih.gov/health/idiopathic-pulmonary-fibrosis/causes
2. https://pmc.ncbi.nlm.nih.gov/articles/PMC9779053/

Bolstering pipeline with 3 preclinical programs and up to 6 discovery targets in muscle (skeletal and cardiac) or CNS

PRECLINICAL PROGRAMS

- Preclinical CNS leverages TfR1-binding for optimal CNS delivery
- Differentiated approach via subcutaneous delivery reaches across the blood brain barrier

ARO-HTT for Huntington's Disease

ARO-ATXN1 for Spinocerebellar ataxia type 1 (SCA1)

ARO-ATXN3 for Spinocerebellar ataxia type 3 (SCA3)

DISCOVERY TARGETS

- Up to 6 targets in muscle (skeletal and cardiac) or CNS
- Sarepta and Arrowhead will work together exclusively to develop therapies for skeletal muscle diseases

Summary

Louise Rodino-Klapac, PhD

Executive Vice President, Head of R&D, Chief Scientific Officer

Closing Remarks

Doug Ingram, President & CEO

Q&A

Dragging tomorrow into today

#DraggingTomorrowIntoToday