



## Sarepta Therapeutics Presents New Preclinical Data Demonstrating Robust Knockdown of Pathogenic DMPK RNA in the Nucleus with SRP-1003 in DM1 at 2026 Oligonucleotide Therapeutics Society Annual Meeting

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- **Correction of MBNL- dependent mis-splicing provides functional evidence that SRP-1003 is degrading disease-causing RNA within the nucleus.**
- **In a preclinical model, SRP-1003 reduced pathogenic DMPK mRNA in both the cytoplasm and nucleus in a dose-dependent manner, achieving up to approximately 80% knockdown in each compartment**
- **Nuclear target engagement supported by three independent methodologies, including compartment-fractionated ddPCR, RNA FISH, and RNAscope**
- **SRP-1003 remained detectable across multiple muscle groups for up to 16 weeks following a single intravenous dose**

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 14, 2026-- Sarepta Therapeutics, Inc. (NASDAQ:SRPT), the leader in precision genetic medicine for rare diseases, today presented new preclinical data at the 22nd Annual Meeting of the Oligonucleotide Therapeutics Society (OTS) demonstrating that SRP-1003, the company's investigational small interfering RNA (siRNA) program for the treatment of myotonic dystrophy type 1 (DM1), can directly reduce pathogenic DMPK transcripts within the nucleus, where the molecular drivers of DM1 pathology originate.

In the analysis, correction of muscleblind-like (MBNL)-dependent mis-splicing provide functional evidence of nuclear activity. Direct measurement of the nuclear and cytoplasmic transcripts pools further demonstrated the efficiency of that activity, with SRP-1003 producing comparable, dose-dependent DMPK in both compartments and achieving up to approximately 80% knockdown in each. The results were confirmed via three independent and complementary methods: RNA fluorescence *in situ* hybridization (FISH) foci quantification, compartment-fractionated ddPCR with purity controls, and *in situ* RNAscope in intact cells.

DM1 is caused by a CTG repeat expansion in the *DMPK* gene that leads to the buildup of toxic CUG-repeat RNA transcripts within the nucleus. This toxic RNA traps MBNL proteins and disrupts the normal processing, or splicing, of many other RNAs, leading to disease across multiple organ systems. Since both MBNL sequestration and pre-mRNA splicing occur in the nucleus, correcting MBNL mis-splicing is functional evidence that the therapy has reached and reduced the disease-causing RNA in the nucleus.

"For an siRNA approach to address the underlying biology of DM1, it must reduce the toxic DMPK in the nucleus," said Louise Rodino-Klapac, Ph.D., president, Research & Development and Technical Operations, Sarepta. "These results provide two complementary lines of evidence that SRP-1003 effectively and efficiently gets into the nucleus. We observed correction of MBNL-dependent mis-splicing, a functional readout that requires degradation of the nuclear transcript and measured comparable levels of DMPK knockdown in the nucleus and cytoplasm. Together with the reductions in toxic nuclear RNA foci across multiple models and methods, these data strengthen the biological rationale for SRP-1003 and support the continued advancement of the program in our ongoing Phase 1/2 clinical study, from which we expect to share results later this year."

Details from the SRP-1003 poster presentation:

### **P-066: Preclinical Evaluation of SRP-1003: An $\alpha v \beta 6$ Integrin-Targeting siRNA Platform for Targeted Knockdown of DMPK in Myotonic Dystrophy Type 1 (C. Greer, et al.)**

In DM1 patient-derived myotubes, compartment fractionated ddPCR directly measured DMPK mRNA in the nuclear and cytoplasmic transcript pools. SRP-1003 produced dose dependent reductions in both compartments, achieving up to approximately 80% knockdown in each, with nuclear knockdown comparable to cytoplasmic knockdown. Fractional purity was validated using established cytoplasmic and nuclear RNA controls, and DMPK knockdown was specific to SRP-1003 and was not observed with a scrambled siRNA control.

SRP-1003 also reduced toxic nuclear RNA foci in patient-derived myotubes, as demonstrated by RNA fluorescence *in situ* hybridization (RNA FISH). In the DMSXL mouse model of DM1, treatment reduced nuclear RNA foci in skeletal muscle, diaphragm, and myocardium and was associated with significant reductions in both human and mouse DMPK mRNA.

In a second DM1 mouse model expressing a pathogenic human DMPK transgene, an SRP-1003 surrogate siRNA reduced pathogenic human DMPK RNA in the nucleus and produced dose-dependent correction of MBNL-dependent mis-splicing as assessed by RNA sequencing.

This splicing correction is an important functional readout of nuclear activity: because the trapped MBNL proteins and the affected splicing machinery are located in the nucleus, the observed correction indicates that the disease-causing nuclear RNA was degraded rather than only in the cytoplasm.

In separate pharmacokinetic studies, SRP-1003 demonstrated sustained exposure across multiple upper and lower body muscle groups for up to 16 weeks following a single intravenous dose in preclinical models.

### **About DM1 and SRP-1003**

Myotonic dystrophy type 1 (DM1) is the most common form of adult-onset muscular dystrophy and is caused by a repeat expansion in the *DMPK* gene. DM1 is a progressive, multisystem disorder that affects skeletal and smooth muscle, as well as the heart, respiratory system, eye, endocrine, gastrointestinal, and central nervous systems. The disease is commonly associated with muscle weakness, daytime sleepiness, breathing difficulties,

and cardiac conduction abnormalities. There is currently no cure for DM1, and no disease modifying treatments are available.

SRP-1003 is an investigational siRNA treatment for DM1 and is designed to target and knockdown, or silence, the *DMPK* mRNA in target cells. SRP-1003 is currently being studied in a first-in-human, Phase 1/2, single ascending dose (SAD)/multiple ascending dose (MAD), randomized, placebo-controlled clinical trial (Study SRP-1003-101) that is being conducted in individuals with DM1 aged 18 to 65.

#### **About Sarepta Therapeutics**

Sarepta is on an urgent mission: engineer precision genetic medicine for rare diseases that devastate lives and cut futures short. We hold a leadership position in Duchenne muscular dystrophy (Duchenne) and are building a robust portfolio of programs across muscle, central nervous system, and cardiac diseases. For more information, please visit [www.sarepta.com](http://www.sarepta.com) or follow us on [LinkedIn](#), [X](#), [Instagram](#) and [Facebook](#).

#### **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](http://www.sarepta.com). We encourage investors and potential investors to consult our website regularly for important information about us.

#### **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 related to our priorities, technologies and research and development programs; the potential benefits of SRP-1003; and our plan to share data later this year from our Phase 1/2 trial.*

*These forward-looking statements involve risks and uncertainties, many of which are beyond Sarepta's control. Known risk factors include, among others: success in preclinical and clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful, and the results of future research may not be consistent with past positive results; differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials; pre-clinical and clinical data are often susceptible to varying interpretations and analyses, and the different methodologies, assumptions and applications we utilize to assess particular safety or efficacy parameters may yield different statistical results; even if we believe data collected from clinical trials of our product candidates are promising, these data may not be sufficient to support approval, including that FDA or foreign regulatory authorities could interpret these data in different ways from us; we rely on third parties, including in some cases our strategic partners, to conduct some aspects of our early-stage research and pre-clinical and clinical development, and accordingly, the inadequate performance by or loss of any of these third parties could affect the development and commercialization of our product candidate development, including delayed timelines; certain programs may never advance in the clinic or may be discontinued for a number of reasons, including regulators imposing a clinical hold and us suspending or terminating clinical research or trials; our product candidates may cause undesirable side effects, result in new safety signals or have other properties that could delay or prevent regulatory approval of product candidates; we may not be able to execute on our business plans, including meeting expected or planned regulatory milestones and timelines, clinical development plans, and bringing products to markets for various reasons including possible limitations of 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 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) 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, except as required by law.*

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