Clinical Update: MOMENTUM Multiple-Ascending Dose Study of SRP-5051 for Duchenne Muscular Dystrophy

DOUG INGRAM
President and CEO

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Executive Vice President, R&D and Chief Medical Officer

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SAREPTA THERAPEUTICS

Welcome and Introduction

Doug Ingram
President and CEO

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 potential benefits of PPMO, including enhanced PMO tissue penetration leading to greater exon skipping and dystrophin production and more efficient dosing, potential market opportunities and expected timelines and milestones for SRP-5051 and other PPMOs, including having data from the 30 mg/kg arm in Q2 2021, commencing 40 mg/kg cohort in Q1 2021, commencing Part B of MOMENTUM study once MTD determined, and applying learnings to inform the development of PPMOs for other exons in Duchenne and other indications.

These forward-looking statements involve risks and uncertainties, many of which are beyond our control. Known risk factors include, among others: success in preclinical trials and clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful; 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 we utilize to assess particular safety or efficacy parameters may yield different statistical results, and even if we believe the data collected from clinical trials of our product candidates are positive, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities; if the actual number of patients suffering from DMD is smaller than estimated, our revenue and ability to achieve profitability may be adversely affected; 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, due to a variety of reasons, some of which may be outside of our control, including possible limitations of company 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 with respect to patents that cover our product candidates and the COVID-19 pandemic; and even if Sarepta's programs result in new commercialized products, Sarepta may not achieve the expected 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, 2019, 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 presentation. Sarepta does not undertake any obligation to publicly update its forward-looking statements based on events or circumstances after the date hereof.

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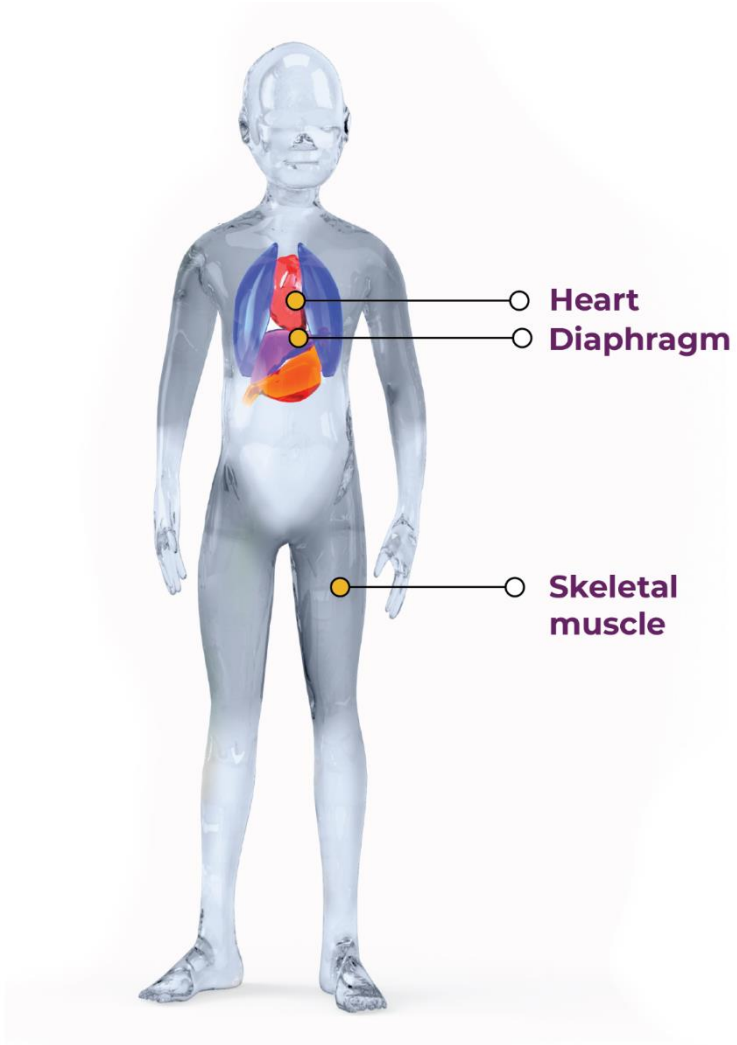
SAREPTA THERAPEUTICS

Duchenne Muscular Dystrophy (DMD)

DMD affects approximately 1 in 3,500-5,000 males worldwide[1]

- DMD is a rare, fatal neuromuscular genetic disease inherited in an X-linked recessive pattern[2]
- Muscle weakness becomes increasingly noticeable by age 3 to 5, and most patients use a wheelchair by the time they are 11[2]
- During adolescence, cardiac and respiratory muscle deterioration lead to serious, life-threatening complications[3]



1. National Institutes of Health. Genetics Home Reference. Duchenne and Becker muscular dystrophy. https://ghr.nlm.nih.gov/condition/duchenne-and-becker-muscular-dystrophy. Accessed Jan 2020.
2. Hoffman EP, Brown RH, et al. Dystrophin: the protein product of the Duchenne muscular dystrophy locus. Cell. 1987;51:919-928.
3. Passamano L, Taglia A, et al. Improvement of survival in Duchenne Muscular Dystrophy: retrospective analysis of 835 patients. Acta Myologica. 2012;31(1): 121-125.

Sarepta's Proprietary PMO Technology

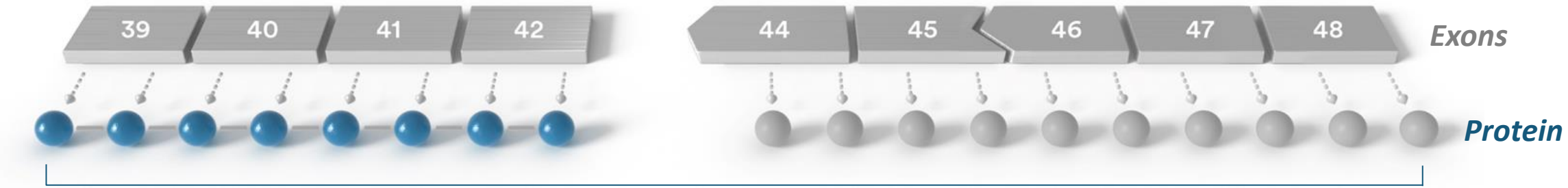
Phosphorodiamidate morpholino oligomer (PMO) technology

Specificity: Enhanced affinity for targeting pre-mRNA for precise binding to the selected RNA target

Stability: Highly resistant to degradation by enzymes

Versatility: Ability to rapidly design and construct drug candidates that are specific for human or pathogen RNA; and target specific tissues

Safety: Built upon a charge-neutral backbone, which may be reflected in tolerability



The PMO directs the splicing machinery to skip an exon when processing the pre-mRNA. As a result, the alternate mRNA allows for the production of a shortened, functional dystrophin protein.

Kole R, Lepper BJ. Discovery Medicine, Volume 14, Number 74, July 2012

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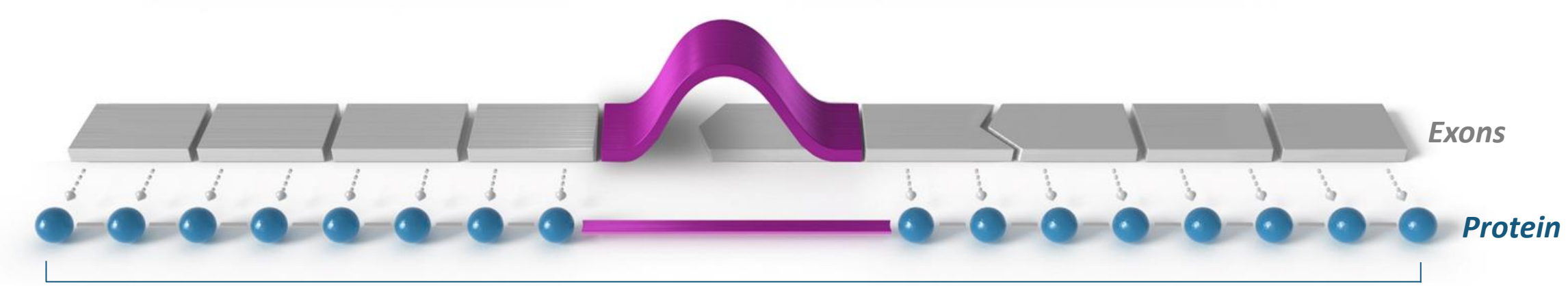

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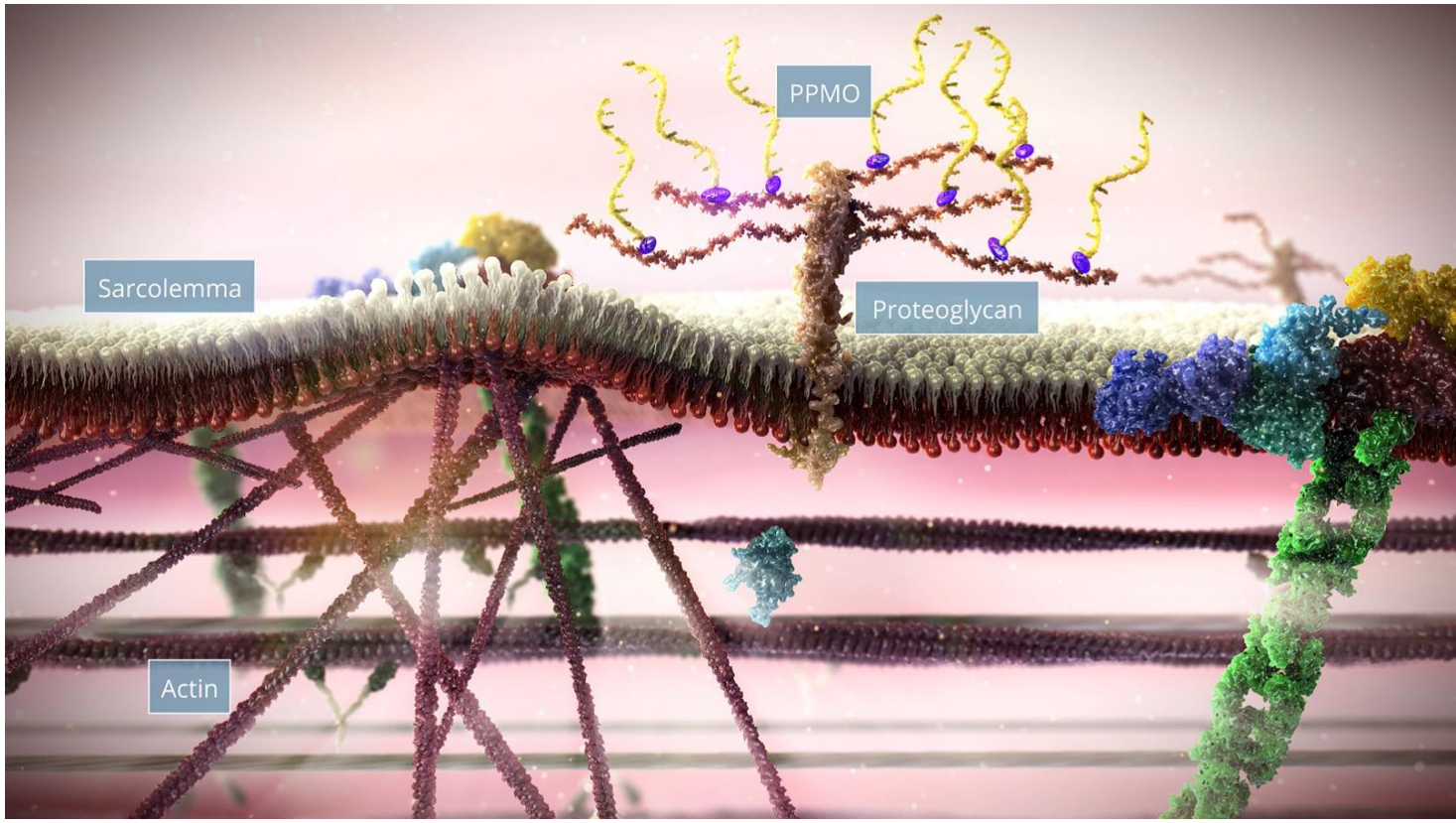
Peptide-conjugated PMO (PPMO): Next-generation Technology for Enhanced PMO Tissue Penetration Leading to Greater Exon Skipping and Dystrophin Production

Enhances PMO

- Conjugated peptide greatly increases cell penetration
- Could potentially lead to more efficient dosing and greater benefit for patients
- Non-clinical data demonstrates delivery of PPMOs to unique muscle types (e.g., heart)

Lead PPMO candidate: SRP-5051

- Designed to skip exon 51
- In clinical development to treat patients with DMD amenable to exon 51 skipping



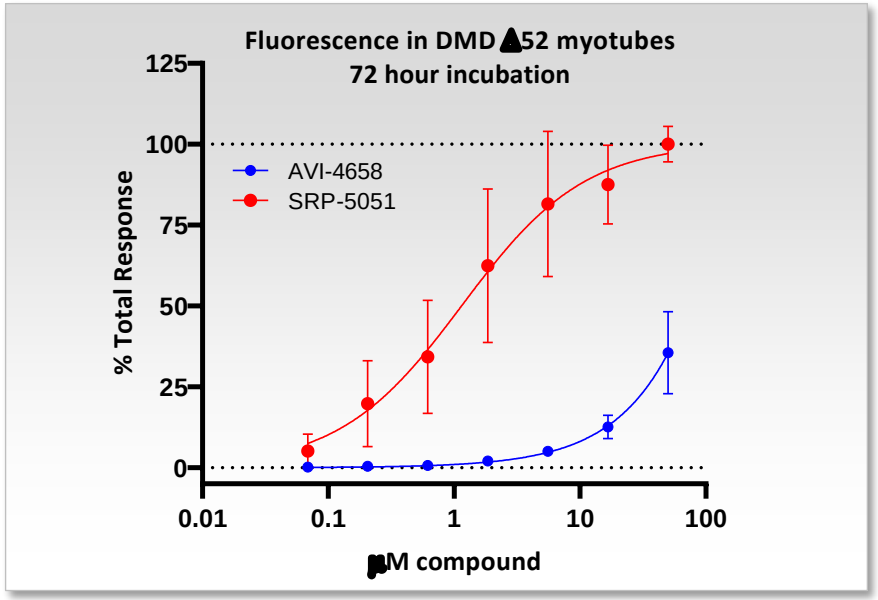
Pre-Clinical Data: SRP-5051

The Cell-Penetrating Peptide Drives Increased Cellular Uptake of SRP-5051 in Duchenne Patient Myotubes Compared to Eteplirsen (AVI-4658) and in a Concentration-dependent Manner

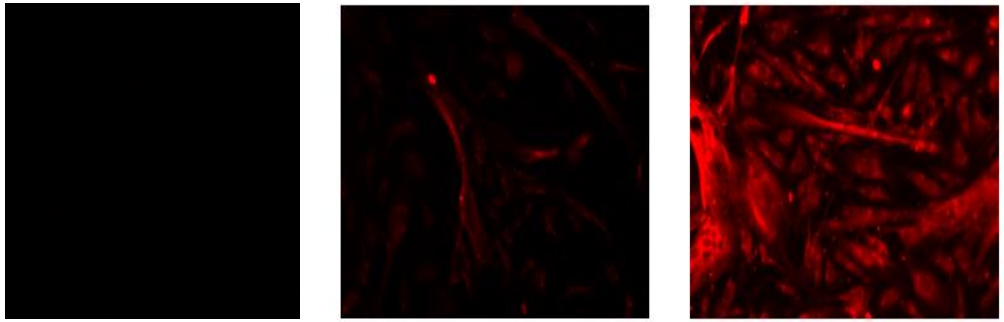
Experimental Design

- Immortalized myoblasts isolated from the paravertebral muscles of a 16-year-old DMD patient with a deletion in exon 52 amenable to exon 51 skipping were differentiated into myotubes and then treated with SRP-5051 or AVI-4658 for up to 72 hours.
- PMO was visualized using an anti-PMO antibody immunofluorescence assay.
- Uptake of SRP-5051 was complete within 2 hours (not shown).

Anti-PMO staining image analysis

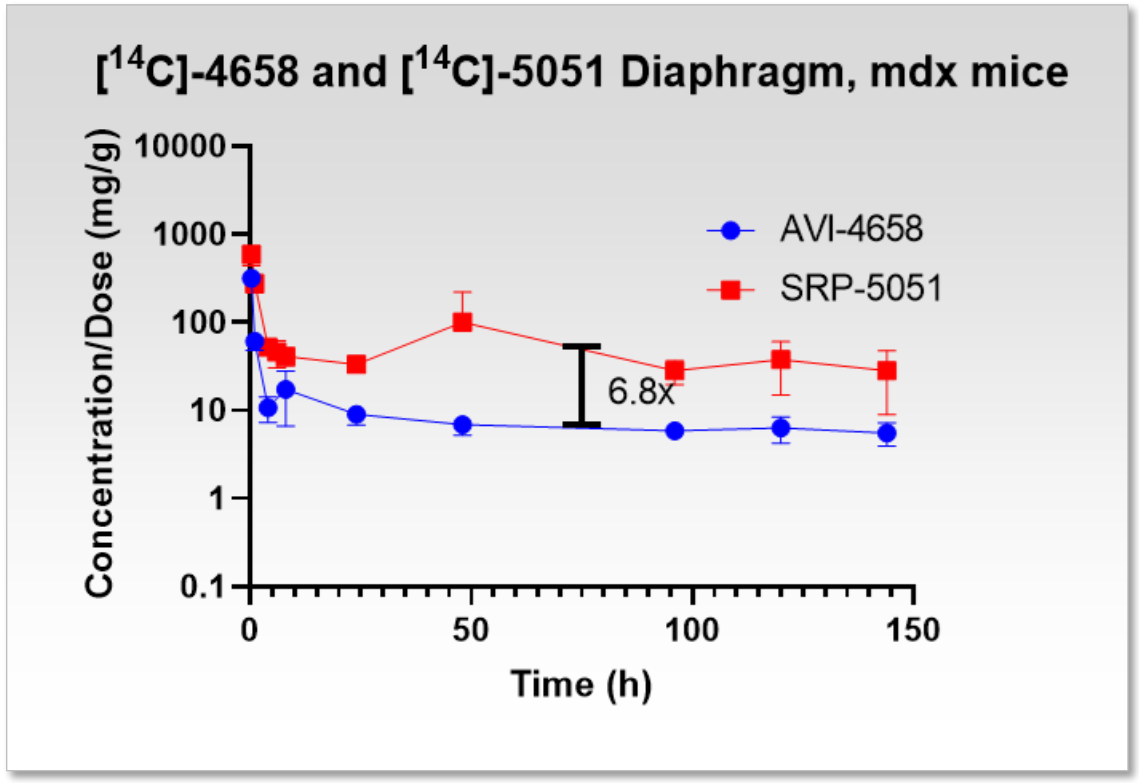


Localization of SRP-5051 and AVI-4658 (72 hrs)



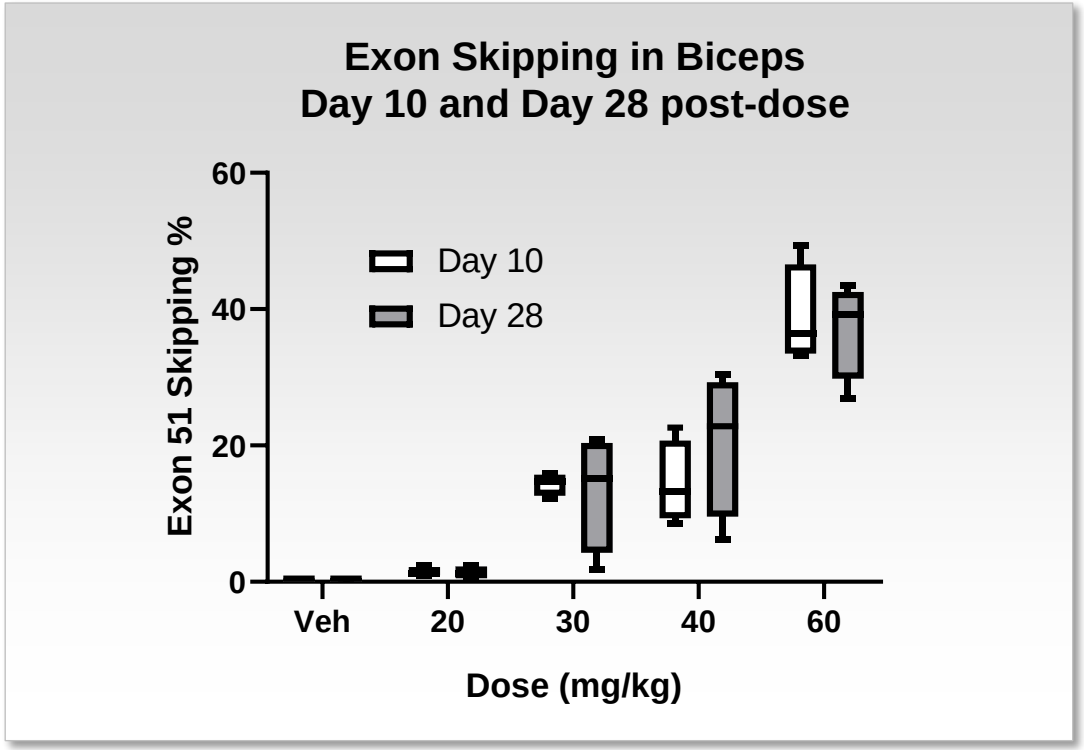
Untreated cells | Del52 16.7 μM AVI-4658 | Del52 16.7 μM SRP-5051

SRP-5051 Exhibits Higher Tissue Exposure Compared to Eteplirsen in the *mdx* Mouse Model



- SRP-5051 has a tissue half life of ~8 days
- SRP-5051 exhibits ~7X higher tissue exposure than Eteplirsen

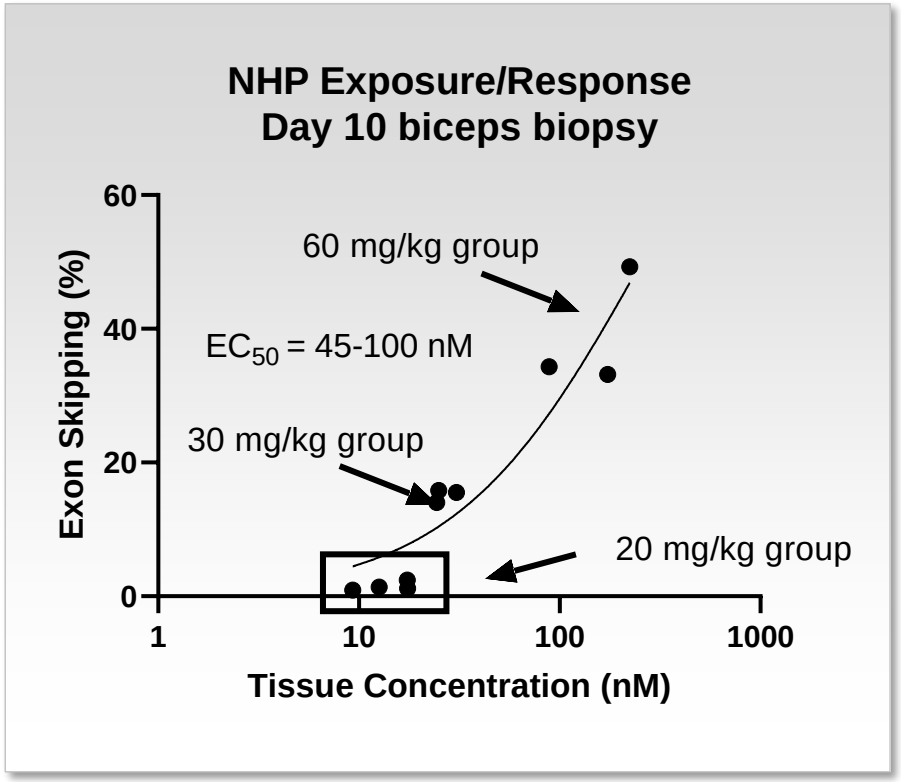
Single Dose SRP-5051 in NHP Exhibits a Dose-Dependent Increase In Exon Skipping that is Maintained for at Least 28 Days

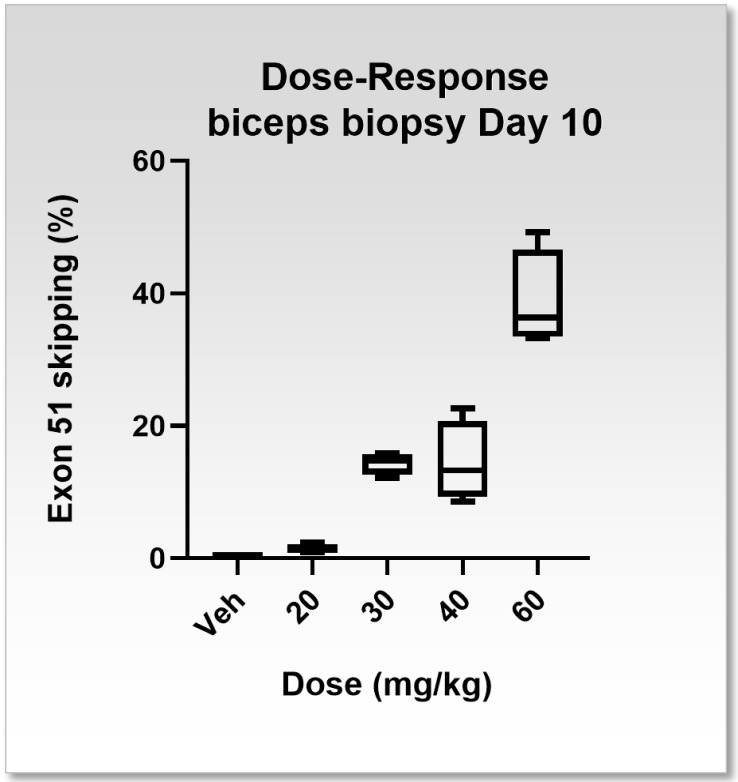


- NHP were infused for 1 hour with 20, 30, 40, or 60 mg/kg SRP-5051.
- Biceps biopsies were taken on days 10 and 28.
- Exon skipping was measured using ddPCR.

- **Prolonged pharmacodynamic effect of SRP-5051, to at least 28 days, supports monthly dosing**
- **Current NOAEL is 40 mg/kg, toxicology studies ongoing at higher doses**
- **No adverse findings at 60 mg/kg in ongoing 12-week once-monthly NHP study**
- **No adverse findings at 80 mg/kg in ongoing 16-week once-monthly juvenile rat study**

Increased Tissue Exposure with SRP-5051 Led to Higher Exon Skipping with a Steep Dose-response in NHP





- NHP were infused for 1 hour with 20, 30, 40, or 60 mg/kg SRP-5051.
- Biceps biopsies were taken on day 10. Exon skipping (ddPCR) and tissue concentrations were measured.

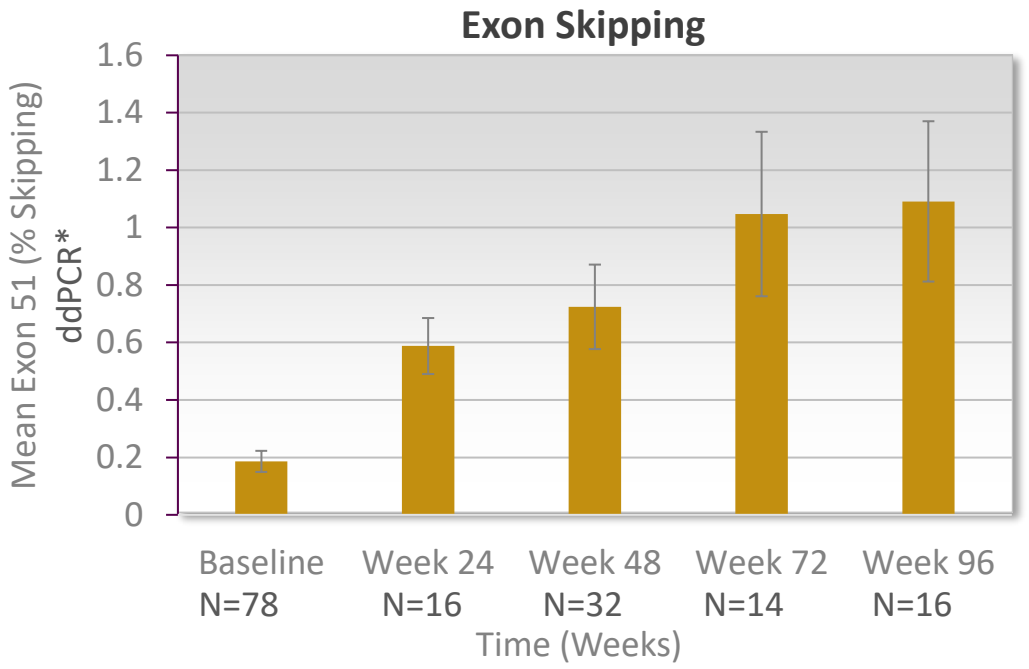
Increasing the dose from 20 to 30 mg/kg in NHP increased exon skipping ~10-fold

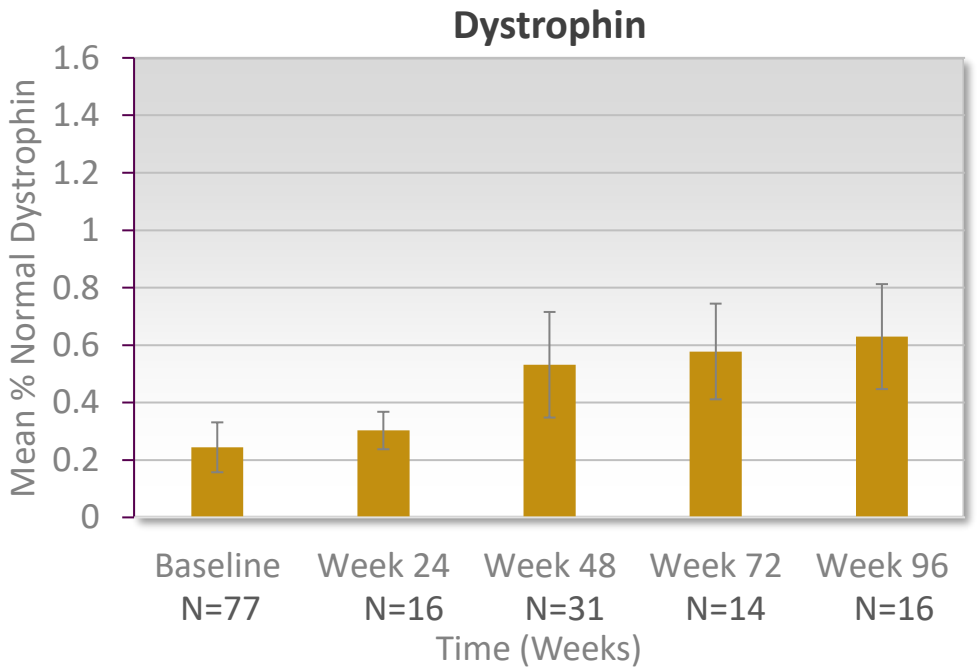
Pre-Clinical Summary

- Adding CPP increases muscle tissue uptake of PMO
- Prolonged PD effects of SRP-5051 support once-monthly dosing
- Current NOAEL 40mg/kg
- No adverse safety findings at 60 mg/kg in ongoing NHP toxicology study or 80 mg/kg in ongoing juvenile rat toxicology study
- Increased tissue exposure with SRP-5051 led to higher exon skipping with a steep dose-response

Clinical Update: PPMO SRP-5051 MOMENTUM Multiple-Ascending Dose Study

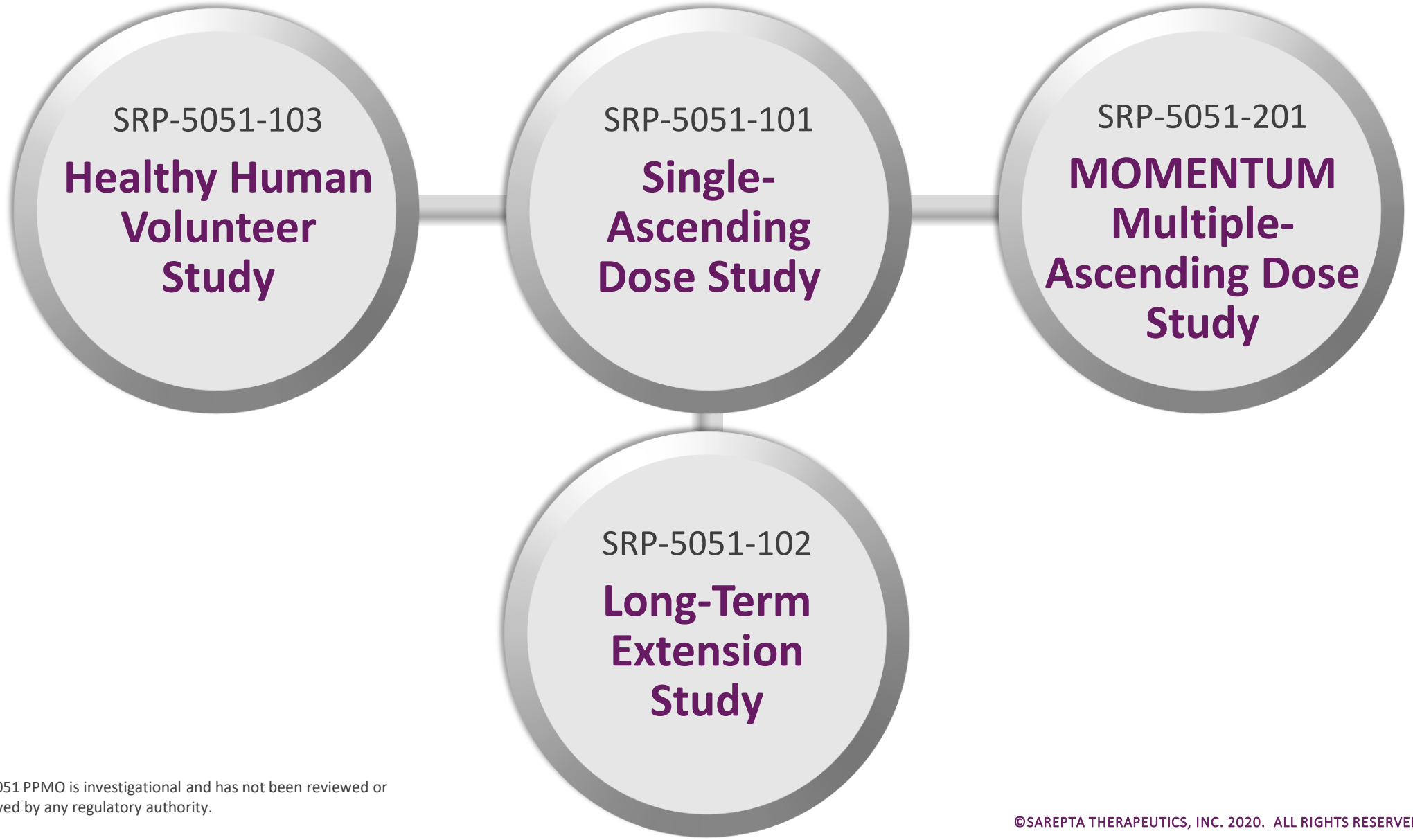
Strong Evidence that Exon Skipping and Dystrophin Increase Over Time, as Seen in PROMOVI with Eteplirsen





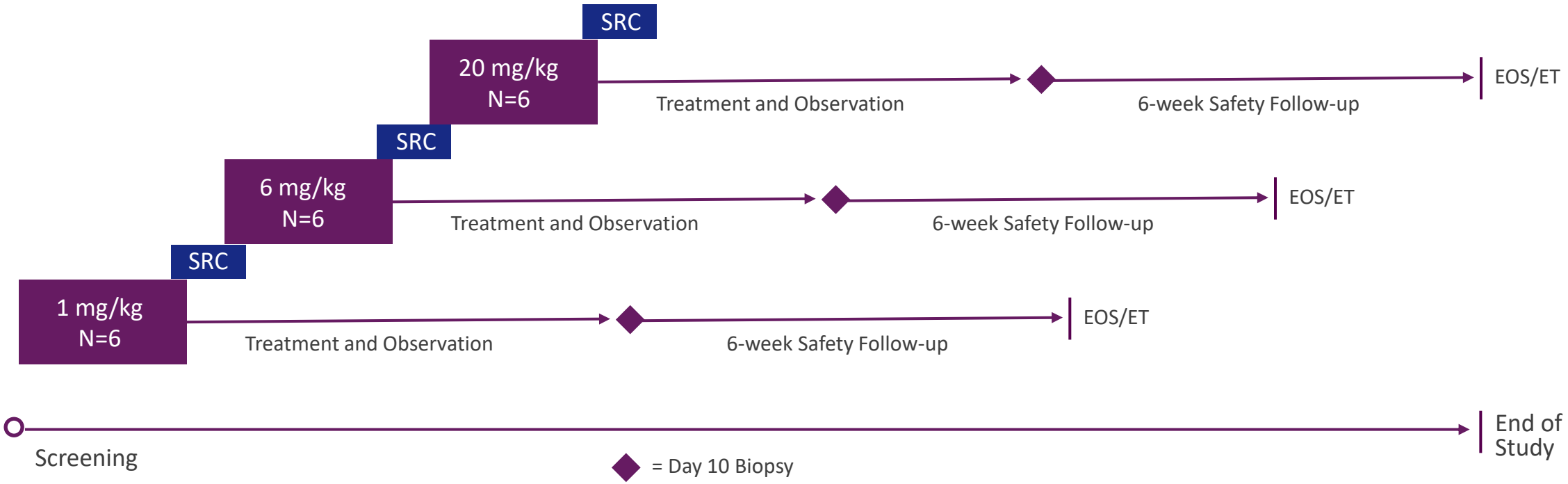
**A quantitative ddPCR assay was used to measure % exon skipping, providing precise and accurate measurements*

SRP-5051 Clinical Development Plan



SRP-5051 PPMO is investigational and has not been reviewed or approved by any regulatory authority.

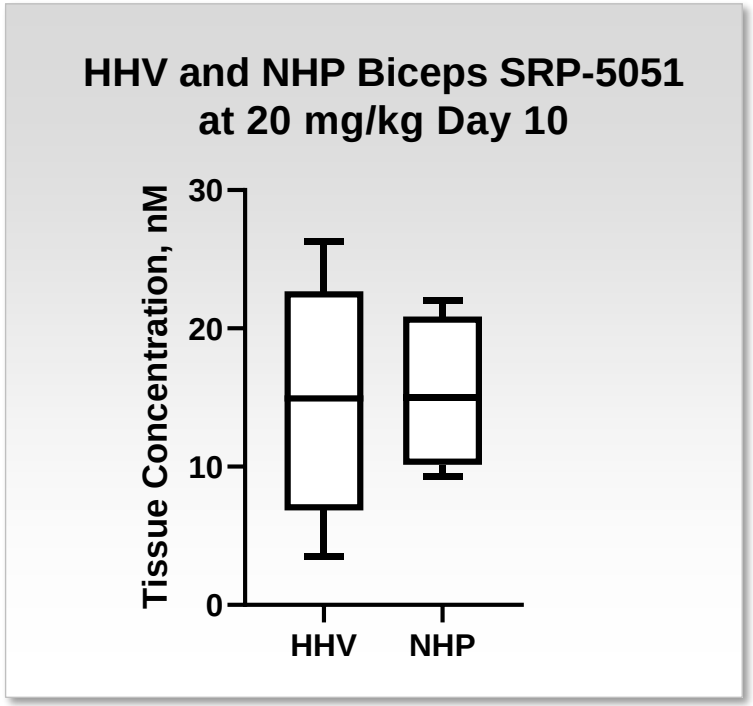
SRP-5051-103 Healthy Human Volunteer (HHV) Study



EOS = End of Study; ET=Early Termination; SRC=Safety Review Committee

SRP-5051 PPMO is investigational and has not been reviewed or approved by any regulatory authority.

Concentrations of SRP-5051 in Muscle Biopsies from the Single-Ascending Dose HHV and Single Dose NHP Studies were Comparable



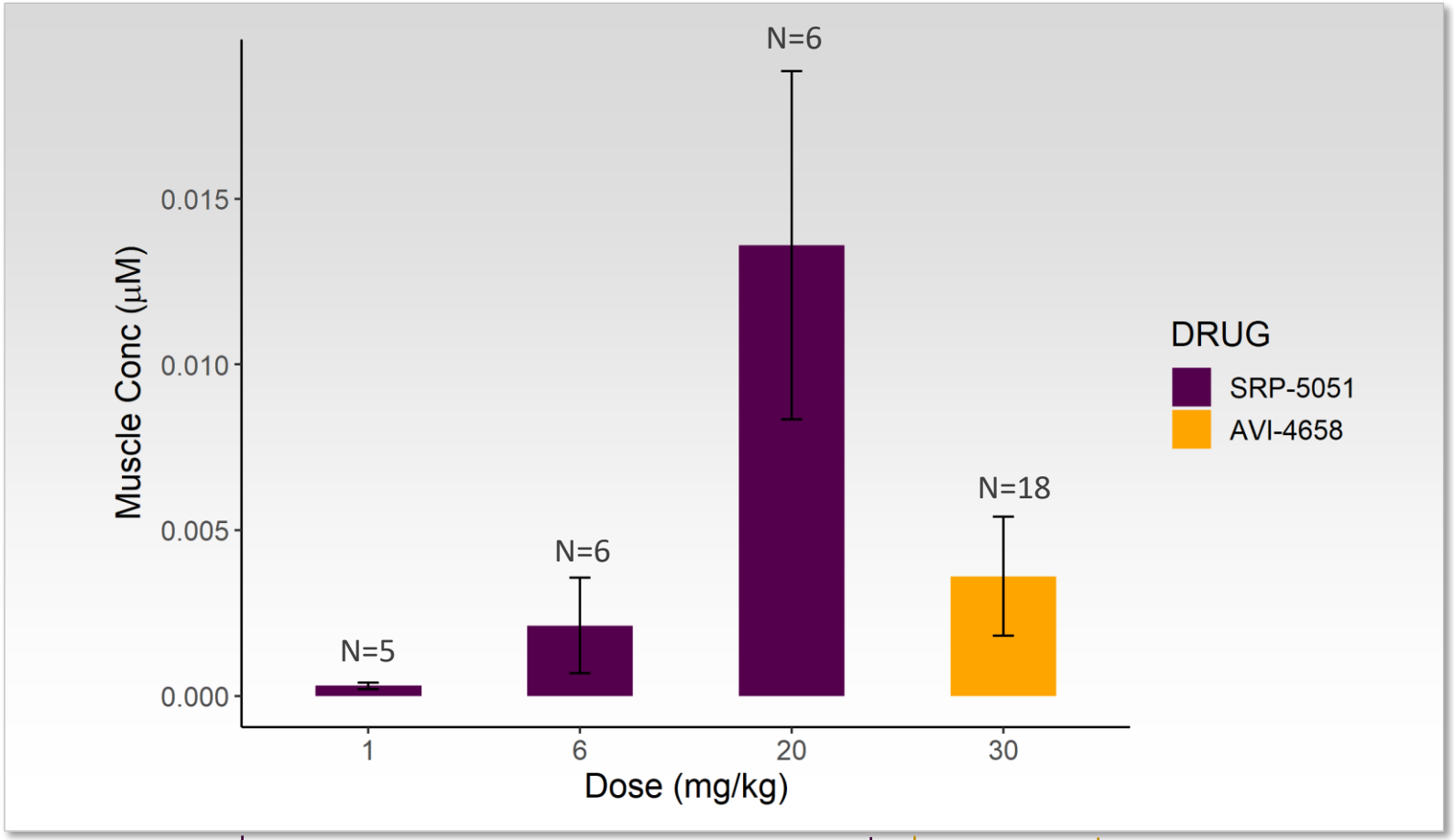
HHV			NHP		
Mean (nM)	SD	N	Mean (nM)	SD	N
15.4	8.6	12	15.3	5.6	4

As a result, Sarepta has adopted the 1:1 weight-based scaling method using NHP data to:

1) predict human exposure and the maximum recommended safe dose (MRSD),
2) calculate safety margins based on no-observed-adverse-effect levels (NOAELs), and
3) predict PD and efficacious dose ranges

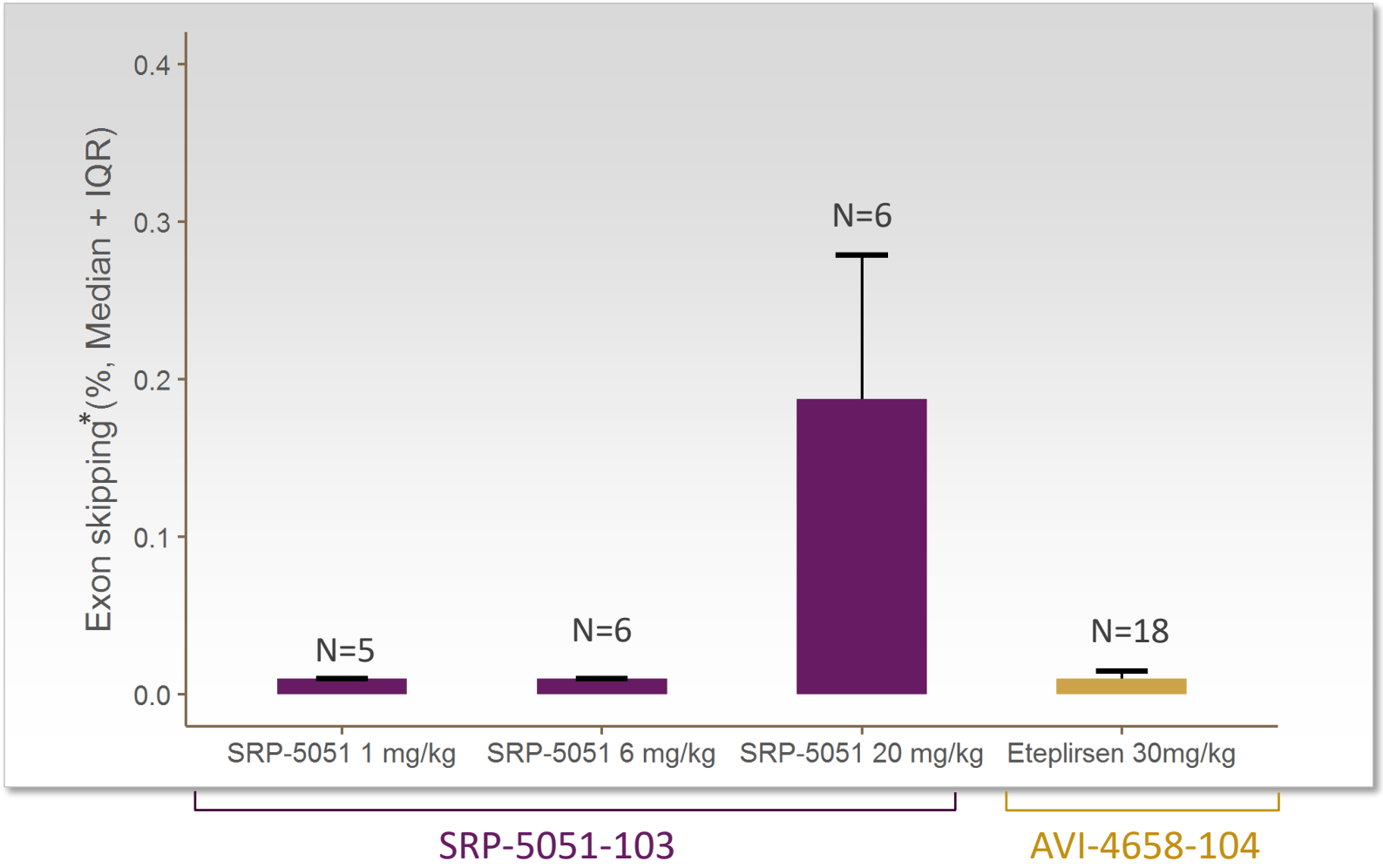
SRP-5051-103: SRP-5051 Drove Higher Muscle Concentration Compared to Eteplirsen in Healthy Subjects after a Single Dose

~3.8x greater muscle drug concentration of 20 mg/kg SRP-5051 compared to eteplirsen



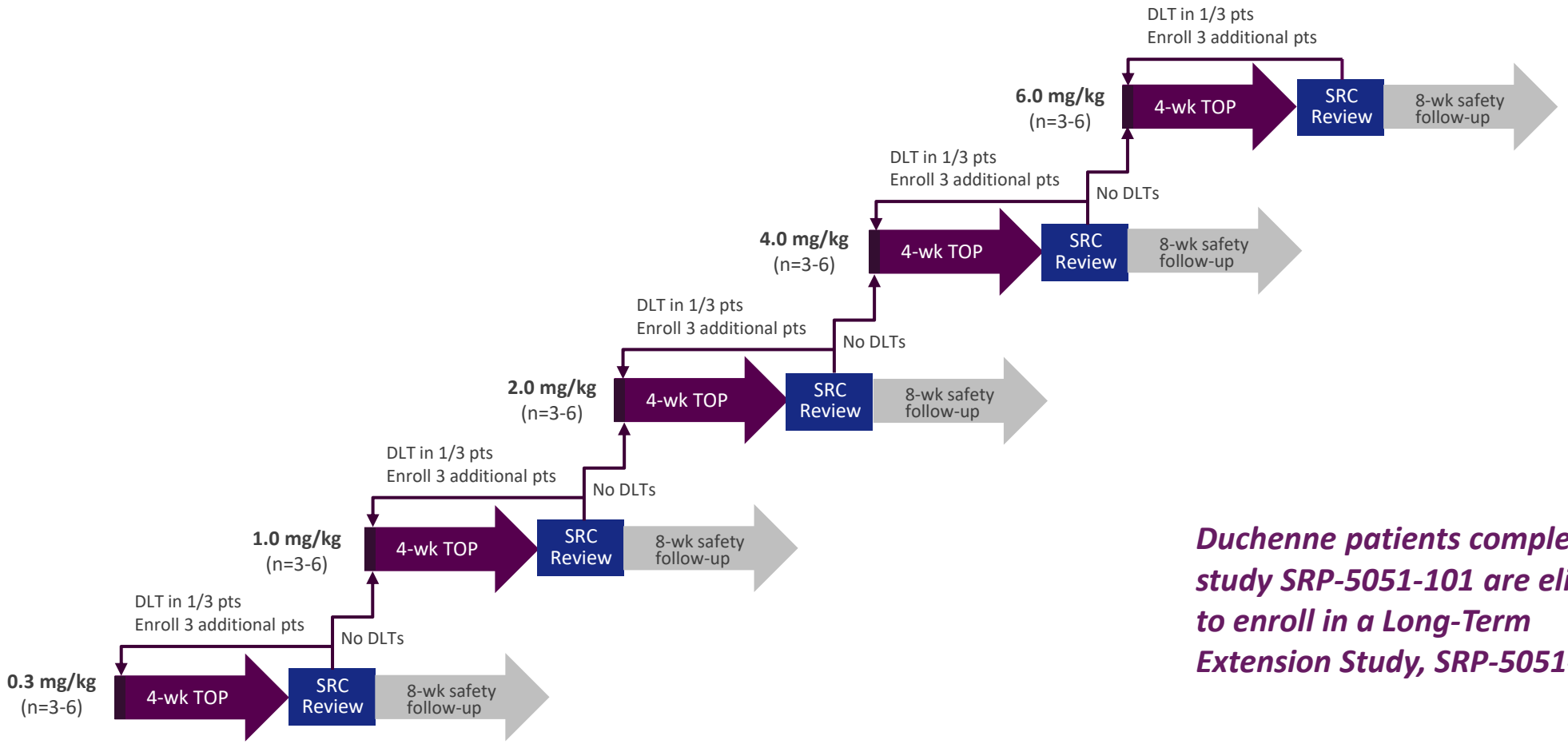
*AVI-4658-104 is a study of eteplirsen in healthy subjects.

SRP-5051-103: SRP-5051 Drove Higher Exon Skipping Compared to Eteplirsen in Healthy Subjects After a Single Dose



*Exon skipping measured by ddPCR.

SRP-5051-101 Single Ascending Dose Study

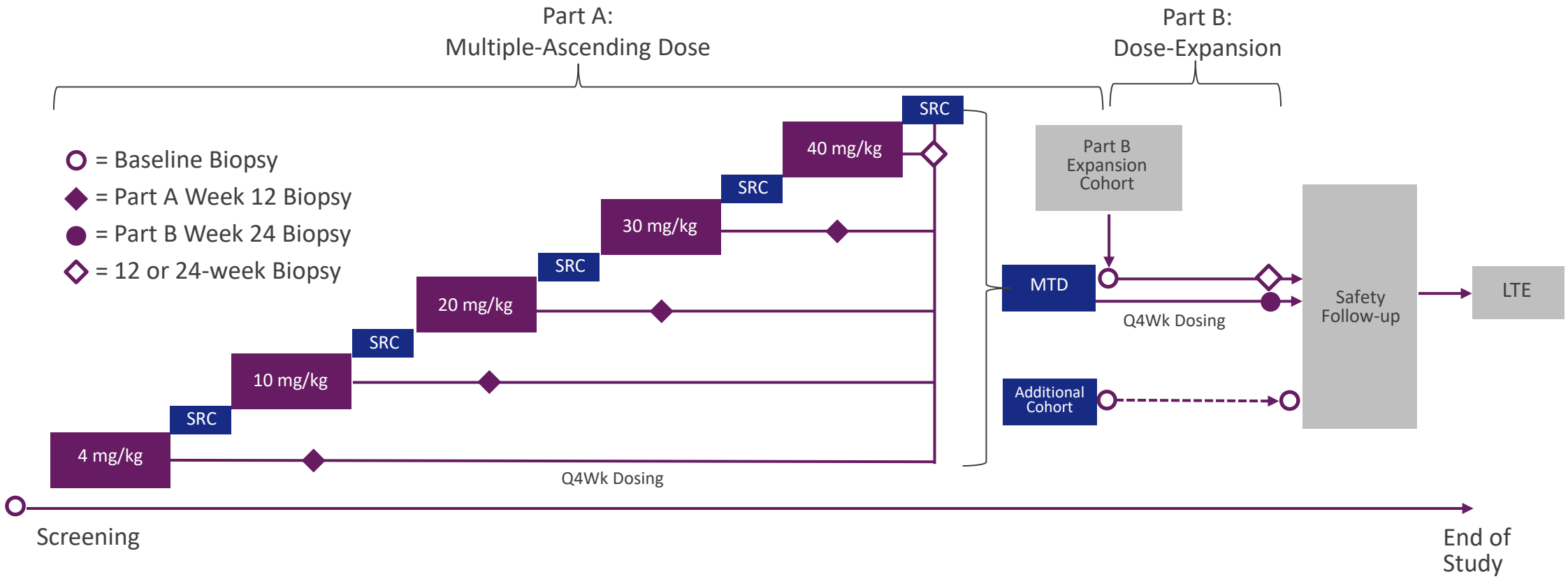


Duchenne patients completing study SRP-5051-101 are eligible to enroll in a Long-Term Extension Study, SRP-5051-102.

DLT=dose-limiting toxicity; SRC=Safety Review Committee; TOP=Treatment and Observation Period

ClinicalTrials.gov Identifier: NCT03375255.
SRP-5051 PPMO is investigational and has not been reviewed or approved by any regulatory authority.

SRP-5051-201 MOMENTUM: Multiple-Ascending Dose Study of Once Monthly SRP-5051 in Duchenne Patients



ClinicalTrials.gov Identifier: NCT04004065.
SRP-5051 PPMO is investigational and has not been reviewed or approved by any regulatory authority.

SRP-5051-201 MOMENTUM PART A: Designed to Assess Safety and PK/PD of Multiple Doses of SRP-5051 in Plasma and Muscle of Duchenne Patients

- **Primary Outcome Measure**
  - Safety
- **Secondary Outcome Measures Including:**
  - PK plasma concentration of SRP-5051
  - Change from baseline at 12 weeks:
    - Muscle concentration of SRP-5051
    - Muscle exon-skipping measured by ddPCR
    - Muscle dystrophin protein measured by western blot adjusted for muscle content
- **Inclusion criteria**
  - Confirmed DMD mutation amenable to exon 51-skipping
  - Stable dose of oral corticosteroids for at least 12 weeks prior to study drug administration, or no corticosteroids for at least 12 weeks prior to study drug administration.
  - Part A accepts ambulatory and non-ambulatory patients ages 7 to 21 years

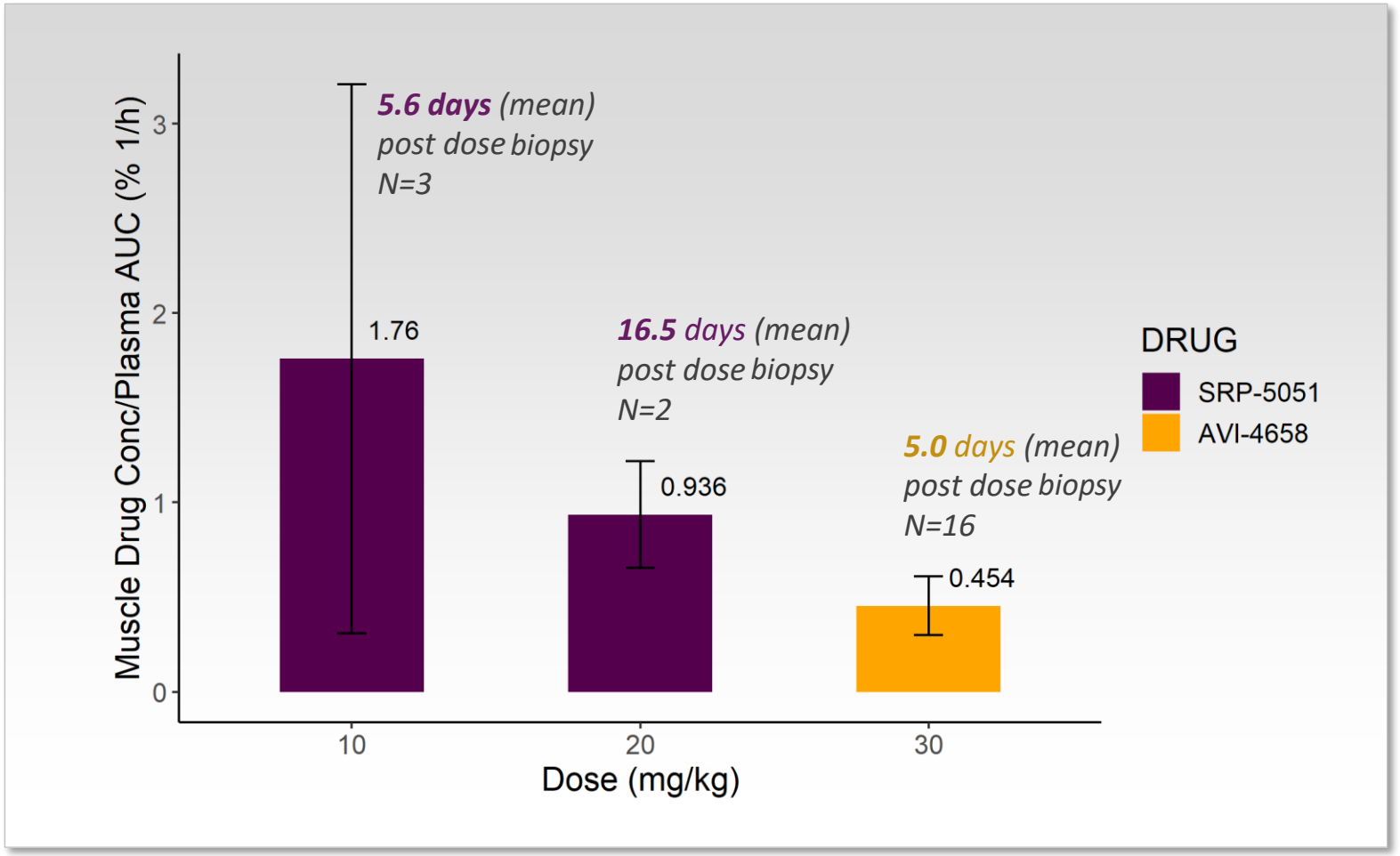
ClinicalTrials.gov Identifier: NCT04004065.
SRP-5051 PPMO is investigational and has not been reviewed or approved by any regulatory authority.

SRP-5051-201 MOMENTUM: Patient Demographics at Baseline

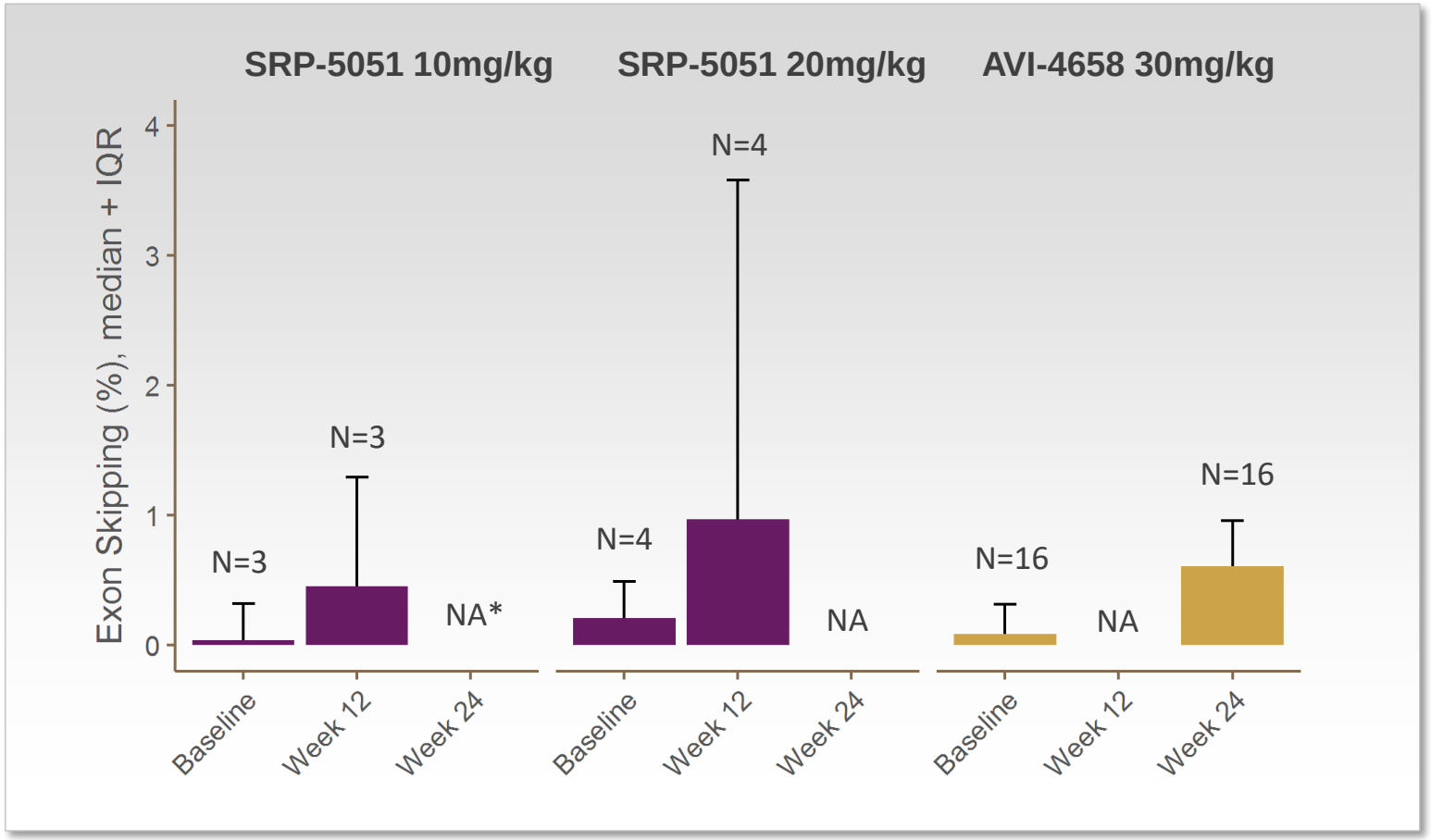
DRUG/DOSE	N	MEAN AGE (YEARS)	AMBULATORY (A/N)	MEAN WEIGHT (KG)	BIOPSIES at 12 WEEKS (A/N)	MEAN CUMULATIVE DOSE (MG) PER PATIENT
SRP-5051 ***4 mg/kg/month X4***	3	11.7	1A+2N	62.1	1A (needle) 2N (1 needle, 1 open)	810.6 (12 weeks)
SRP-5051 ***10 mg/kg/month X4***	3	13.3	2A+1N	44.3	2A (2 open) 1N (1 open)	1795.7 (12 weeks)
SRP-5051 ***20 mg/kg/month X4***	5	9.8	4A+1N	32.2	3A (1 open, 2 needle) 1A (missing) 1N (1 open)	2118.0 (12 weeks)

DRUG/DOSE	N	MEAN AGE (YEARS)	AMBULATORY (A/N)	MEAN WEIGHT (KG)	BIOPSIES at 24 WEEKS (A/N)	MEAN CUMULATIVE DOSE (MG) PER PATIENT
AVI-4658 ***30 mg/kg/week X25*** (from PROMOVI)	16	9.6	16A	32.4	16A (16 open)	24903.1 (24 weeks)

SRP-5051-201 MOMENTUM: 10 mg/kg and 20 mg/kg Once Monthly of SRP-5051 Resulted in Higher Muscle Concentration at 12 Weeks vs. 30 mg/kg Once Weekly of Eteplirsen at 24 Weeks in DMD Patients



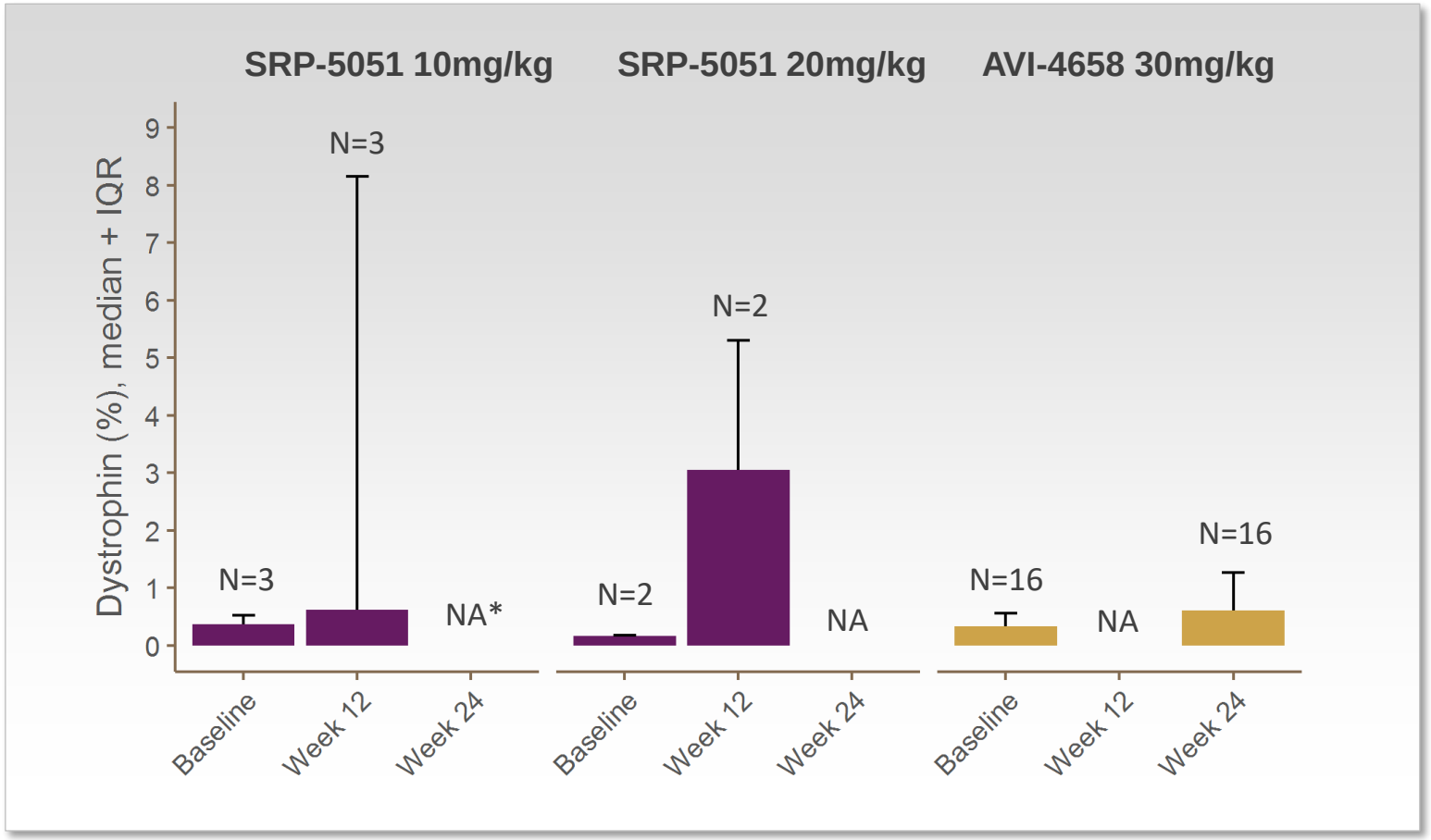
SRP-5051-201 MOMENTUM: SRP-5051 Drove Dose-dependent Exon Skipping at 12 Weeks vs. Baseline & vs. Eteplirsen at 24 Weeks



Ratio of Median SRP-5051 12 week vs. Eteplirsen 24 week	5051-201 10 mg/kg 12 week	5051-201 20 mg/kg 12 week
Exon skipping	0.7	1.6

*NA = Not Applicable, data not collected at these time points

SRP-5051-201 MOMENTUM: SRP-5051 Drove Dose-dependent Increases of Dystrophin at 12 Weeks vs. Baseline & vs. Eteplirsen at 24 Weeks



Ratio of Median SRP-5051 12 week vs. Eteplirsen 24 week	5051-201 10 mg/kg 12 week	5051-201 20 mg/kg 12 week
Adjusted Dystrophin	1.0	4.9

*NA = Not Applicable, data not collected at these time points

SRP-5051-201 MOMENTUM: Safety Experience

- Incidence of TEAEs across the cohorts does not suggest dose-dependency
- Incidence of TEAs reported is similar across all dosed cohorts
- No renal signals observed

4 mg/kg cohort

- 2 patients with treatment-emergent AE (TEAE), none of which were related to study drug
- 1 serious TEAE observed
- No TEAE lead to drug discontinuation

10 mg/kg cohort

- 3 patients with treatment-emergent AE (TEAE), all of which were related to study drug
- No serious TEAE observed
- No TEAE lead to drug discontinuation

20 mg/kg cohort

- 3 patients with treatment-emergent AE (TEAE), none of which were related to study drug
- No serious TEAE observed
- No TEAE lead to drug discontinuation

SRP-5051-201 MOMENTUM: Conclusions

- Safe and well-tolerated with no clinical or laboratory-based safety signals
- Human proof of concept for cell penetrating peptide
- Consistently higher tissue exposure, exon-skipping and dystrophin observed with 20 mg/kg SRP-5051 at 12 weeks compared to 30 mg/kg eteplirsen at 24 weeks
  - These increased levels were observed with fewer doses (4 vs 25) and less cumulative drug exposure (~10 times less)
- Nonclinical findings predict significantly greater changes as we continue to dose escalate in SRP-5051-201
  - Pre-clinical toxicology data support dosing higher than 40 mg/kg

Next Steps for SRP-5051 Development and Other PPMOs

- Continue dose escalation to find maximum tolerated dose (MTD)
  - Enrollment in 30 mg/kg cohort is complete and all patients have begun dosing
  - 40 mg/kg cohort expected to commence in Q1 2021
- Once MTD determined, commence Part B of MOMENTUM study
- Apply learnings from clinical studies of SRP-5051 to inform the development of PPMOs for other exons in Duchenne and other indications

Question and Answer