Initial results from an open-label phase 1/2 study of BMN 351, an antisense oligonucleotide for exon 51 skip–amenable Duchenne muscular dystrophy

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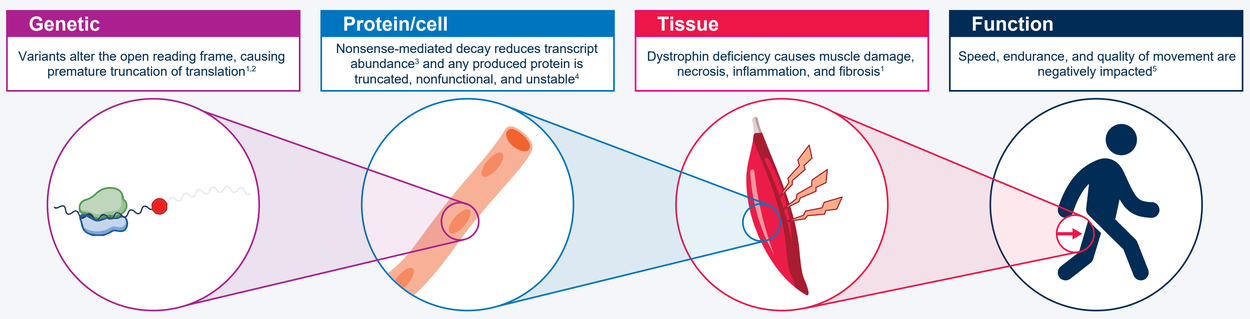
Introduction

- Duchenne muscular dystrophy (DMD) is a progressive and ultimately fatal neuromuscular disease caused by a deficiency in dystrophin, an essential protein in muscle fibers that enables motor function (**Figure 1**)[1]
- Antisense oligonucleotides (ASO) can be used to skip over the multi-exon deletions and restore the correct reading frame[1]

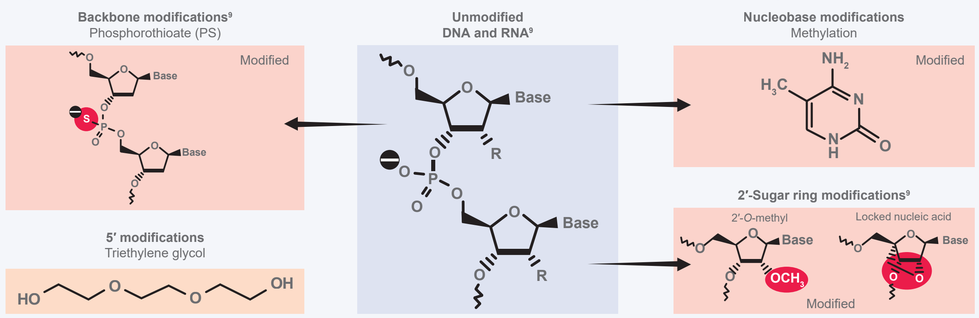
Figure 1. Without sufficient dystrophin, progressive muscle wasting leads to functional impairments



BMN 351 is an ASO that targets a novel, highly active splicing enhancer site to skip exon 51 and the flanking introns to restore the dystrophin open reading frame[6–8]

- The negatively charged 2′OMePS backbone of BMN 351 (**Figure 2**) produces an ASO with robust tissue penetration[6,7]
- BMN 351 includes additional structural modifications to reduce immunogenicity and improve the binding affinity and half-life of the ASO

Figure 2. Structural modifications of BMN 351 to improve safety and efficacy



The dystrophin protein produced with BMN 351 is expected to be near full-length and to retain most of its functionality, similar to naturally occurring forms of dystrophin produced in less severe forms of Becker muscular dystrophy

Interim results from 351-201

- A total of 14 boys with a mean (standard deviation) age of 7.2 (1.4) years have been enrolled in the 351-201 clinical trial and received BMN 351 treatment (**Table 1**)

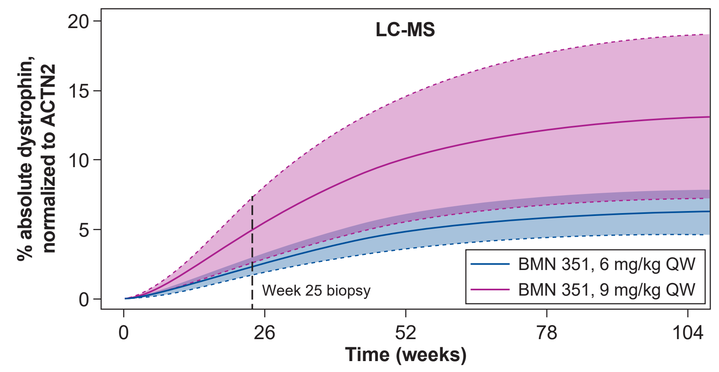
Table 1. Demographics and baseline characteristics of the enrolled population

Mean (SD)	6 mg/kg/QW (n = 6)	9 mg/kg/QW (n = 6)	12 mg/kg/QW (n = 2)	Overall (N = 14)
Age at enrollment, years	7.2 (1.3)	7.3 (1.2)	7.0 (2.8)	7.2 (1.4)
Weight, kg	21.8 (4.0)	23.6 (1.5)	23.5 (7.1)	22.8 (3.4)
Height, cm	114.2 (6.9)	121.4 (3.6)	118.5 (16.3)	117.9 (7.5)
BMI, kg/m^2	16.7 (2.2)	16.0 (0.6)	16.5 (0.6)	16.4 (1.5)
NSAA total score, points	19.0 (7.2)	22.3 (3.2)	20.0 (8.5)	20.6 (5.6)
6-minute walk distance, m	373.1 (79.7)	371.6 (79.5)	365.1 (162.0)	371.3 (83.1)

BMI, body mass index; NSAA, North Star Ambulatory Assessment; QW, once weekly; SD, standard deviation.

- BMN 351 achieved dose-dependent dystrophin expression in the 6 and 9 mg/kg cohorts at the early 25-week biopsy
- By LC-MS, mean ± standard error of the % absolute dystrophin (normalized to alpha-actinin-2) was 2.40% ± 0.36% (n = 4; 6 mg/kg) and 5.01% ± 1.37% (n = 6; 9 mg/kg) at week 25 (**Figure 3**)
- The differentiated phosphorothioate chemistry of BMN 351 is anticipated to provide continued dystrophin accumulation at week 52 compared with week 25
- The safety profile to date is enabling study progression to the 12 mg/kg cohort (2 of 6 participants currently enrolled)

Figure 3. Observed and predicted dystrophin expression



Solid lines represent mean dystrophin (% of normal) and dashed lines represent 90% CI. Simulations are informed by observed dystrophin data from the 6 and 9 mg/kg QW cohorts and rely on model-based assumptions that include structural PK parameters (apparent volume [V] and elimination rate constant [Ke]) and PD modeled using an indirect response with production rate (Kin), degradation rate (Kout), and EC50; residual variability is incorporated via a proportional error model. The simulations are based on the best available data but do not account for all potential biological variables and should not be interpreted as a guarantee of clinical efficacy, safety, or actual patient outcomes.
ACTN2, alpha-actinin-2; CI, confidence interval; EC50, half-maximal effective concentration; LC-MS, immunoaffinity ultra-performance liquid chromatography coupled with tandem mass spectrometry; PD, pharmacodynamic; PK, pharmacokinetic; QW, once weekly.

Full results, including functional assessments, for the 6 and 9 mg/kg cohorts will be presented Wednesday, March 11, 2026 (in room Florida 4 at 12 PM)

BMN 351-201

A phase 1/2, open-label, dose-escalation study to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of multiple intravenous doses of BMN 351 in boys with Duchenne muscular dystrophy

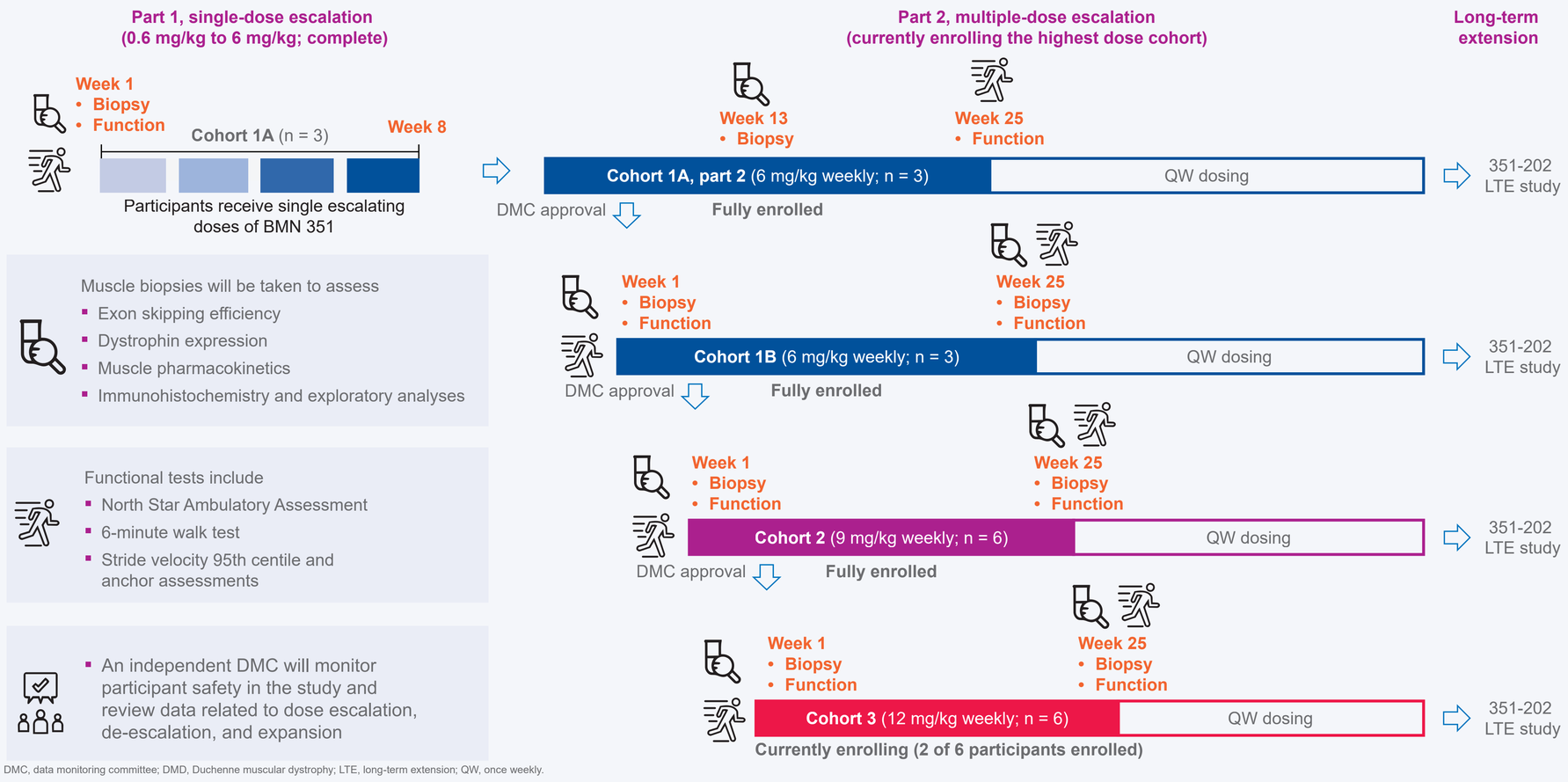
Study population: Boys with DMD who are amenable to exon 51 skipping

Number of participants: Up to 18

Primary objective: To assess the safety and tolerability of BMN 351 at different dose levels in boys with DMD

Secondary objective: To evaluate the plasma and urine pharmacokinetics and muscle concentration of BMN 351

Other objectives: Exon skipping and dystrophin expression; functional assessments



Muscle biopsies will be taken to assess
- Exon skipping efficiency
- Dystrophin expression
- Muscle pharmacokinetics
- Immunohistochemistry and exploratory analyses

Functional tests include
- North Star Ambulatory Assessment
- 6-minute walk test
- Stride velocity 95th centile and anchor assessments

- An independent DMC will monitor participant safety in the study and review data related to dose escalation, de-escalation, and expansion

Key eligibility criteria

- Boys age 4–10 years and ambulatory
- Clinical diagnosis of DMD resulting from a documented dystrophin variant in the dystrophin gene amenable to exon 51 skipping
- On a stable dose of oral corticosteroids for at least 12 weeks prior to baseline; must remain on a consistent dose/dose regimen throughout the study (except for modifications to accommodate changes in weight)
- No current or history of liver or renal disease
- Prior treatment with an approved exon skipping therapy is allowed, but a 12-week washout period will be required
- No prior treatment with any gene therapy for the treatment of DMD
- No known hypersensitivity to any oligonucleotide
- Previous investigational treatment must be discontinued 3 months prior to first dose

Key study features

- BMN 351 given via intravenous infusion every week, with the potential for at-home dosing being considered in a future protocol amendment
- Safety assessments include physical examination, vital signs, electrocardiogram, echocardiogram, and clinical laboratory tests
- Ongoing review of safety data by an independent data monitoring committee
- Two muscle biopsies are required per participant
- Opportunity for long-term extension study for continued dosing
- Participant burden minimized through home health assessments
- Education and support provided to participants and families

351-201 is currently recruiting in Spain, the United Kingdom, the Netherlands, Italy, and Türkiye

DMC, data monitoring committee; DMD, Duchenne muscular dystrophy; LTE, long-term extension; QW, once weekly.

References

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Disclosures

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BMN 351-related posters presented at MDA 2026

The BMN 351 development story

Transcriptional biomarkers of muscle composition in mouse modles, humans, and with BMN 351 treatment

Validity of proxy-completed DMD-QOL

Request a copy of the BMN 351 clinical data

Presented at the Muscular Dystrophy Association (MDA) Clinical & Scientific Conference: March 8–11, 2026; Orlando, Florida, USA