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CANYON Trial Results: Sevasemten, an Investigational Fast Skeletal Myosin Inhibitor, Reduced Muscle Damage Biomarkers and Stabilized Function in BMD

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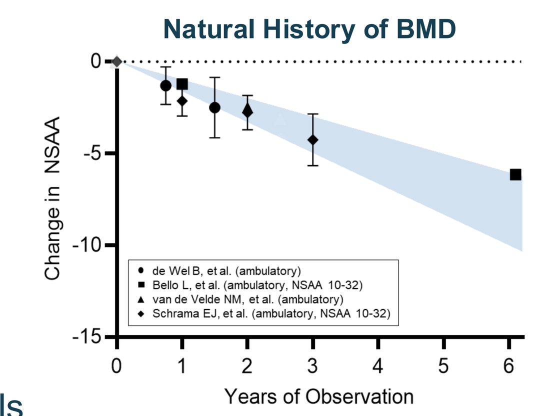
Background

Becker muscular dystrophy (BMD) is a serious, rare, neuromuscular disorder with no currently approved therapies.

Individuals with BMD experience contraction-induced muscle damage. Fast muscle fibers are disproportionately injured by contraction in BMD.



Multiple natural history studies in individuals with BMD demonstrate the North Star Ambulatory Assessment (NSAA) average score decline of 1.0 to 1.7 points annually.[1-5] Sevasemten is an investigational, novel, oral, fast skeletal myosin inhibitor designed to protect muscle against contraction-induced damage while preserving function.

Methods

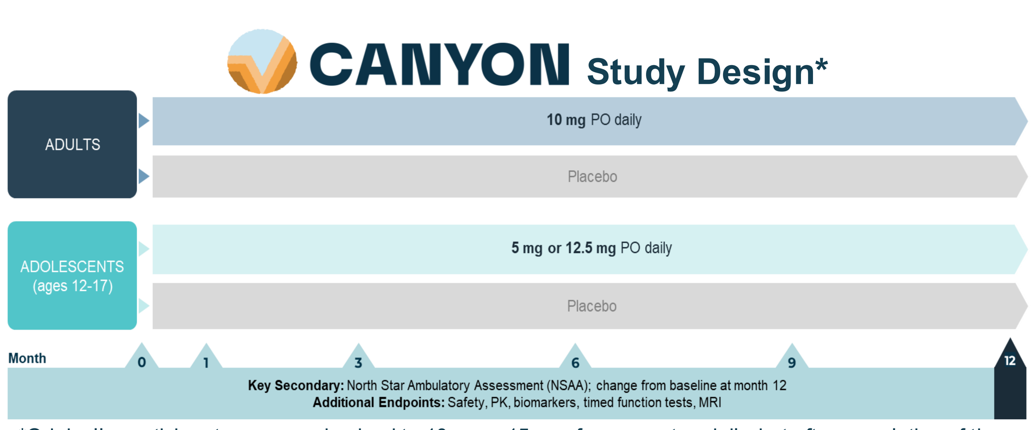
Study Design

The CANYON study (NCT05291091) is a Phase 2, double-blind, placebo-controlled study of sevasemten

- **Enrollment**: 40 adults and 29 adolescents with BMD
- **Primary endpoints:** safety, change from baseline in serum creatine kinase (CK) over 6-12 months for adults
- **Key secondary endpoint:** change from baseline in the NSAA total score in adults at month 12

Key Inclusion Criteria:

- Ambulatory males aged 12 to 50 years old
- Dystrophin mutation and a BMD phenotype
- Not on corticosteroids
- NSAA between 5-32 for adults, NSAA ≥5 for adolescents



*Originally, participants were randomized to 10mg or 15mg of sevasemten daily, but after completion of the ARCH trial, participants all received 10mg.

Baseline Characteristics

- Sevasemten group adults had more advanced disease
  - Sevasemten vs placebo difference in NSAA: -5.8 (p<0.04)
  - In 4SC: -0.12 (p<0.02)
- Adolescents were not in decline at baseline

Functional test	Adults Sevasemten (n=28)	Adults Placebo (n=12)	Adolescents Sevasemten (n=20)	Adolescents Placebo (n=9)
Mean total NSAA score, points (SD)	18.4 (7.66)	24.2 (8.19)	31.3 (2.53)	29.3 (6.34)
Mean 4SC velocity, 1/seconds (SD)	0.22 (0.128)	0.34 (0.173)	0.50 (0.113)	0.43 (0.161)
Mean RFF velocity, 1/seconds (SD)	0.14 (0.114)	0.21 (0.128)	0.36 (0.122)	0.31 (0.157)
Mean 10MWR velocity, meters/second (SD)	1.52 (0.731)	2.00 (0.884)	2.86 (0.506)	2.61 (0.692)
Mean 100MTT velocity, meters/second (SD)	1.50 (0.856)	1.78 (0.782)	3.01 (0.680)	2.57 (0.892)

Abbreviations: NSAA, North Star Ambulatory Assessment; 4SC velocity, 4-stair climb velocity; RFF, rise from floor; 10MWR, 10-minute walk/run; 100 MTT, 100-meter timed test

Safety

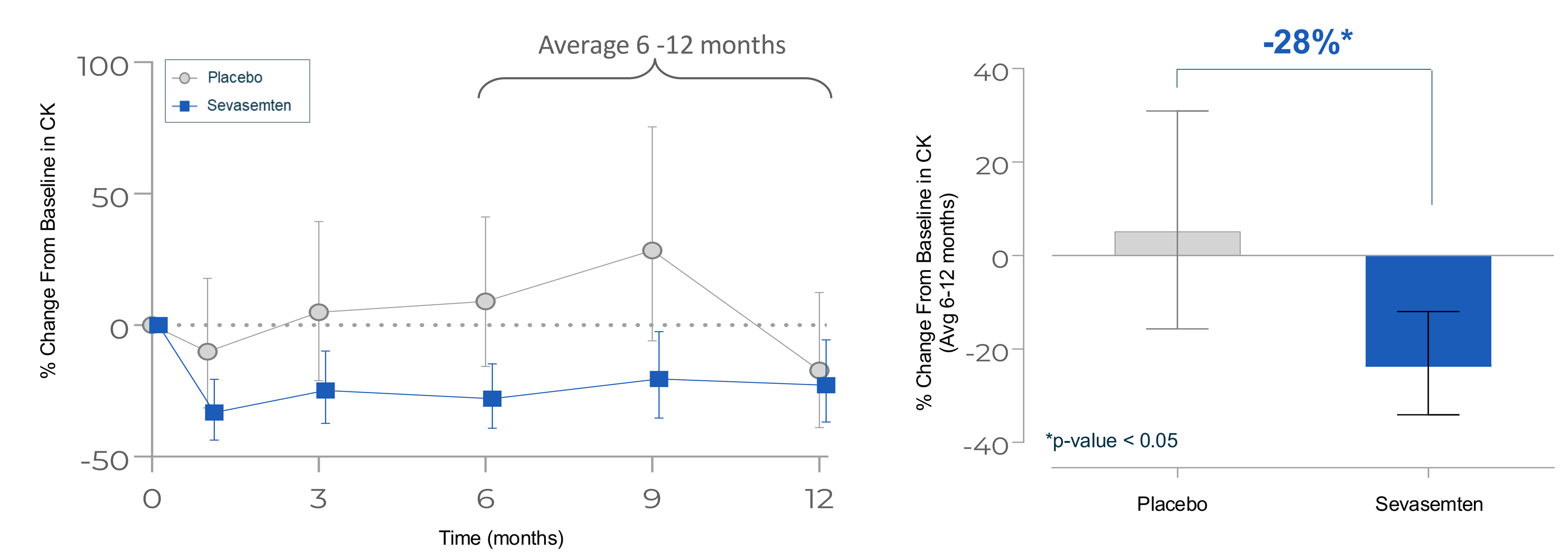
Sevasemten was found to be well-tolerated.

	Adults Sevasemten (n=28) n (%)	Adults Placebo (n=12) n (%)	Adolescents Sevasemten (n=20) n (%)	Adolescents Placebo (n=9) n (%)
Any TEAE in ≥5% of participants	26 (92.9%)	10 (83.3%)	19 (95%)	9 (100%)
Eye disorders				
Vision blurred	1 (3.6%)	2 (17%)	0 (0%)	0 (0%)
General disorders and administration site conditions				
Fatigue	5 (18%)	3 (25%)	3 (15%)	1 (11%)
Pyrexia	0 (0%)	0 (0%)	2 (10%)	2 (22%)
Infections and infestations				
COVID-19	6 (21%)	2 (17%)	0 (0%)	0 (0%)
Nasopharyngitis	6 (21%)	2 (17%)	5 (25%)	2 (22%)
Upper respiratory tract infection	5 (18%)	2 (17%)	4 (20%)	2 (22%)
Influenza	4 (14%)	1 (8%)	0 (0%)	0 (0%)
Sinusitis	0 (0%)	0 (0%)	4 (20%)	0 (0%)
Injury, poisoning and procedural complications				
Fall	8 (29%)	2 (17%)	4 (20%)	0 (0%)
Investigations				
Ejection fraction decreased	0 (0%)	2 (17%)	0 (0%)	0 (0%)
Musculoskeletal and connective tissue disorders				
Back pain	3 (11%)	0 (0%)	0 (0%)	0 (0%)
Nervous system disorders				
Headache	9 (32%)	2 (17%)	0 (0%)	0 (0%)
Dizziness	9 (32%)	0 (0%)	1 (5%)	2 (22%)
Somnolence	5 (18%)	1 (8%)	3 (15%)	0 (0%)
Migraine	3 (11%)	1 (8%)	0 (0%)	0 (0%)
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain	4 (14%)	0 (0%)	0 (0%)	0 (0%)
Cough	3 (11%)	0 (0%)	0 (0%)	0 (0%)
Sinus congestion	0 (0%)	0 (0%)	2 (10%)	2 (22%)
Upper respiratory tract congestion	0 (0%)	0 (0%)	1 (5%)	2 (22%)
Gastrointestinal disorders				
Diarrhea	0 (0%)	0 (0%)	2 (10%)	1 (11%)
Nausea	0 (0%)	0 (0%)	2 (10%)	1 (11%)
Vomiting	0 (0%)	0 (0%)	2 (10%)	1 (11%)

Abbreviations: TEAE, treatment emergent adverse event

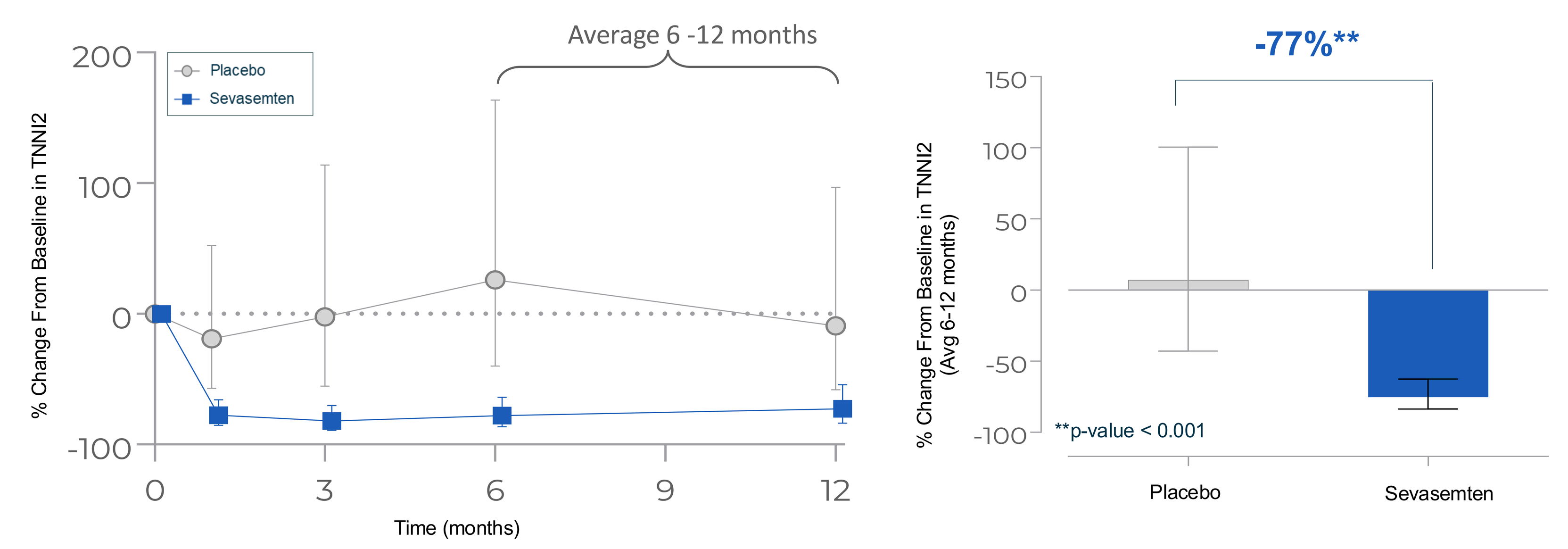
Results

The CANYON trial met its primary endpoint of change from baseline in CK.



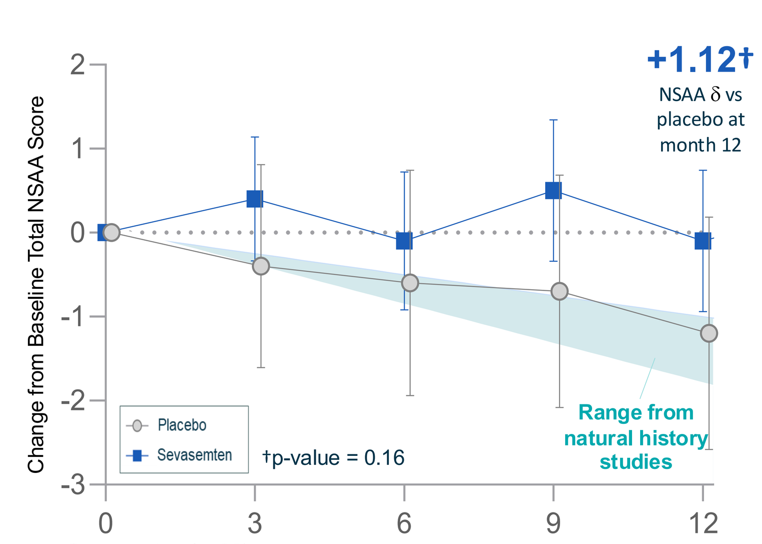
Error bars are 95% CI. CK values are log-transformed. LS (least squares), means, LS mean differences and CIs were back-transformed to percent scale.

Fast skeletal troponin I (TNNI2) decreased in the sevasemten group compared to placebo, averaged over months 6 through 12.



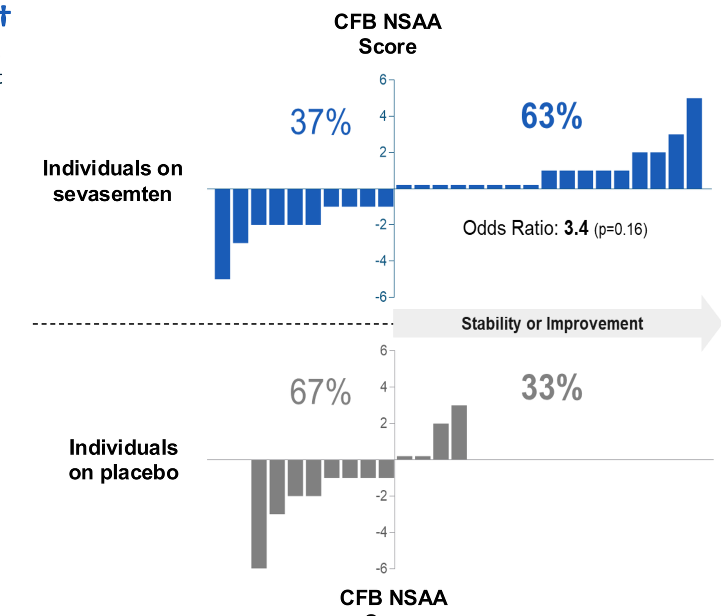
Error bars are 95% CI. TNNI2 values were log-transformed. LS means, LS mean differences and CIs were back-transformed to percent scale.

NSAA remained stable over time in the sevasemten treatment group.



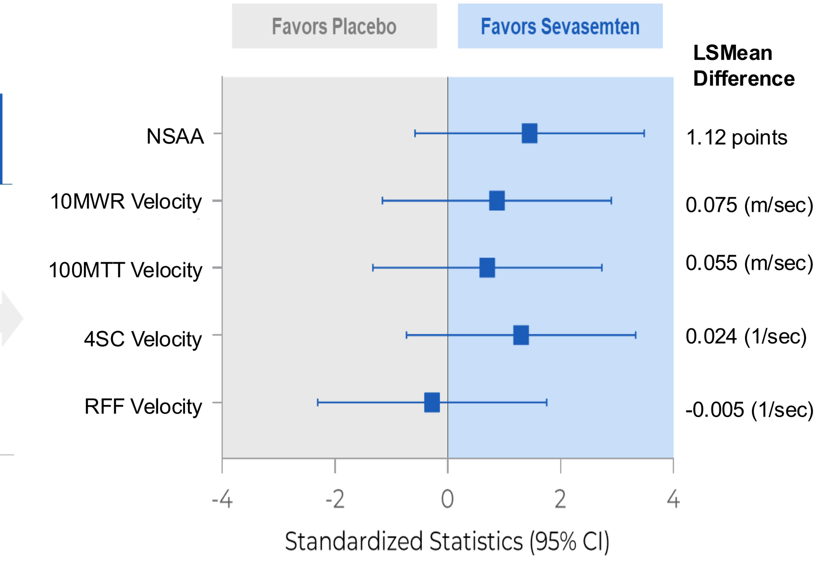
LS Means and 95% CI shown for Safety Population
Range of point estimates from natural history studies shown[1-5].

63% of participants* treated with sevasemten showed stable or improved function after 12 months.



*Data not available for one sevasemten-treated participant

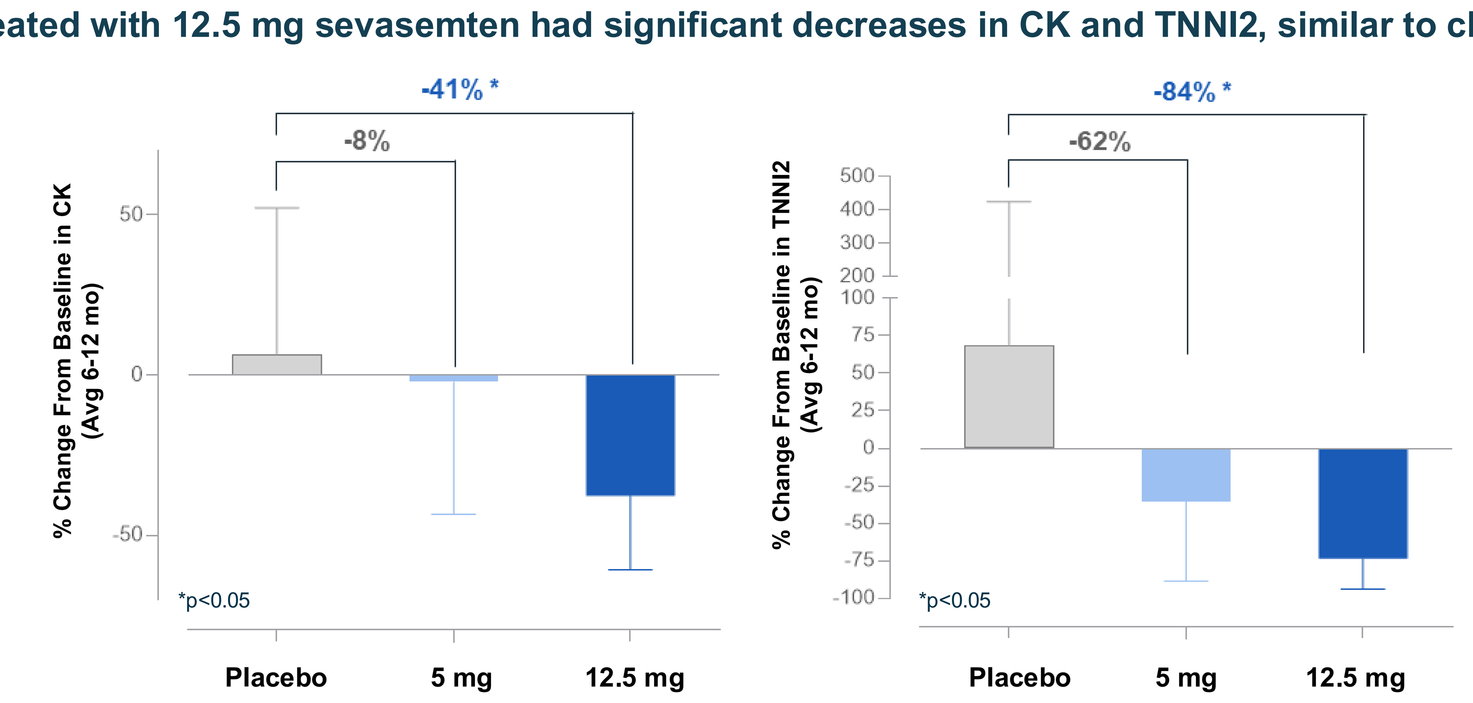
Trends in other functional measures favored sevasemten treatment arm.



Note: At baseline, 9 sevasemten and 1 placebo treated participants were unable to rise from floor. At month 12, 9 sevasemten and 2 placebo treated participants were unable to rise from the floor. LSM differences and CIs were standardized by dividing by the SE. LSM differences presented on the right of the figure are on original scale (without SE adjustment)

Abbreviations: 10MWR, 10-minute walk/run; 100 MTT, 100-meter timed test; 4SC velocity, 4-stair climb velocity; CFB, change from baseline; NSAA, North Star Ambulatory Assessment; RFF, rise from floor

Adolescents treated with 12.5 mg sevasemten had significant decreases in CK and TNNI2, similar to changes in adults.



CK and TNNI2 values were log-transformed. LS means, LS mean differences and CIs were back-transformed to percent scale.
Abbreviations: CK, creatine kinase; mo, months; TNNI2, fast skeletal troponin I2

Conclusions

- Sevasemten was **well-tolerated** in adults and adolescents.
- **The primary endpoint was achieved** in adults, with **a significant decrease in CK** for sevasemten versus placebo. An additional biomarker of muscle damage, TNNI2, significantly decreased from baseline versus placebo.
- **NSAA was stabilized** in adults, with trends toward improvement compared with placebo. Decreases in placebo-treated participants were consistent with natural history.
- **Significant decreases in CK and TNNI2** were seen in adolescents with 12.5 mg sevasemten, similar to observations in adults.
- A global pivotal cohort of adults in BMD, GRAND CANYON (NCT05291091), is fully enrolled with results expected in Q4 2026.

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Disclosures:
Sevasemten is an investigational agent that is not approved for use by any regulatory authority in any territory.
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