Long-Term Stabilization of Function in Becker: Sevasemten Prevented Functional Decline Up to 3.5 Years with MESA Open-Label Extension

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Conclusion

- NSAA scores of ARCH and CANYON trial participants treated with sevasemten remained stable after 3.5 years and 2 years, respectively.
- Using a predictive model based on individual participant characteristics, observed NSAA scores were consistently higher than scores predicted by the model.
- For CANYON participants initially on placebo, NSAA scores trended up during the 1 year after sevasemten initiation.
- No new safety concerns identified following longer duration dosing.
- Sevasemten continues to be investigated in Becker muscular dystrophy in the ongoing MESA trial and a pivotal cohort, GRAND CANYON (NCT05291091).

Background

Becker muscular dystrophy (BMD) is a serious, rare, neuromuscular disorder with no currently approved therapies. 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.[1-4]

Sevasemten is an investigational, novel, oral, fast skeletal myosin inhibitor designed to protect muscle against contraction-induced damage while preserving function. Sevasemten is currently being investigated in BMD and Duchenne muscular dystrophy.

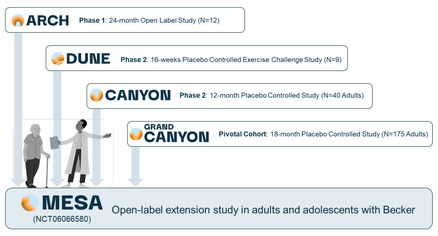
ARCH (NCT05160415) is a Phase 1b, open-label, single-center clinical trial of sevasemten in ambulatory adults with BMD. CANYON (NCT05291091) is a Phase 2, double-blind, multi-center, placebo-controlled study of sevasemten in ambulatory adults with BMD.[5,6]

Methods

MESA (NCT06066580) is an open-label extension evaluating long-term safety, tolerability, and efficacy in adults and adolescents with BMD previously enrolled in sevasemten clinical trials

- **Endpoints:** safety (primary), abnormal lab results (secondary)
- **Enrollment:** 52 participants with BMD from ARCH and CANYON

Study Design



This interim analysis includes ARCH and CANYON participants reaching ≥12 months of sevasemten treatment.

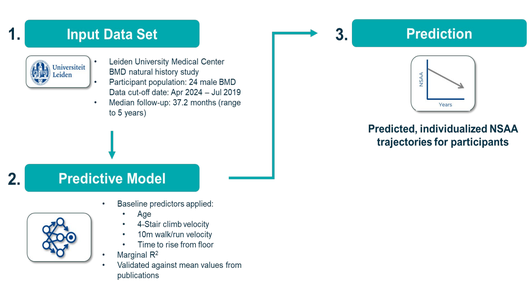
Baseline Characteristics

	ARCH	CANYON	
Functional test	**Sevasemten (n=12)**	**Initially Sevasemten (n=28)**	**Initially Placebo (n=12)**
Mean total NSAA score, points (SD)	15.1 (8.4)	18.4 (7.7)	23.1 (8.3)
Mean 4SC velocity, 1/seconds (SD)	0.19 (0.16)	0.22 (0.13)	0.32 (0.16)
Mean RFF velocity, 1/seconds (SD)*	0.16 (0.20)	0.14 (0.11)	0.21 (0.14)
Mean 10MWR velocity, meters/second (SD)	1.15 (0.52)	1.52 (0.73)	1.86 (0.75)
Mean 100MTT velocity, meters/second (SD)	1.08 (0.50)	1.50 (0.86)	1.65 (0.60)

*At baseline, 5 ARCH and 11 CANYON participants (9 Initially Sevasemten, 2 Initially Placebo) were unable to rise from floor
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

Predictive Model Development and Validation

- Predictive model based on BMD natural history data developed
- Generates the predictive change for NSAA based on time and each individual participant's baseline characteristics
- Validated against published baseline profiles and NSAA changes at 12 months from Bello L, et al. 2016[1] and at 9 and 18 months from De Wel B, et al. 2024.[3,7]



Safety

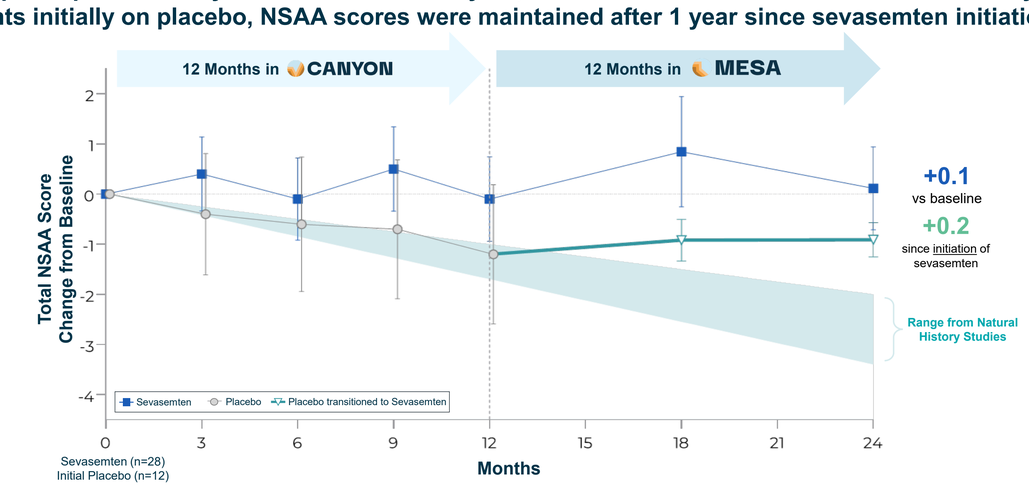
No new safety concerns found

Adverse Events*	N (%) Total N=52
Fall	9 (17%)
Arthralgia	6 (12%)
Dizziness	6 (12%)
Headache	6 (12%)
COVID-19	4 (8%)
Fatigue	4 (8%)
Migraine	4 (8%)
Viral Upper Respiratory Tract Infection	4 (8%)
Contusion	3 (6%)
Upper Respiratory Tract Infection	3 (6%)

*Common (≥5%) treatment emergent adverse events occurring in MESA for the ARCH and CANYON adult participants

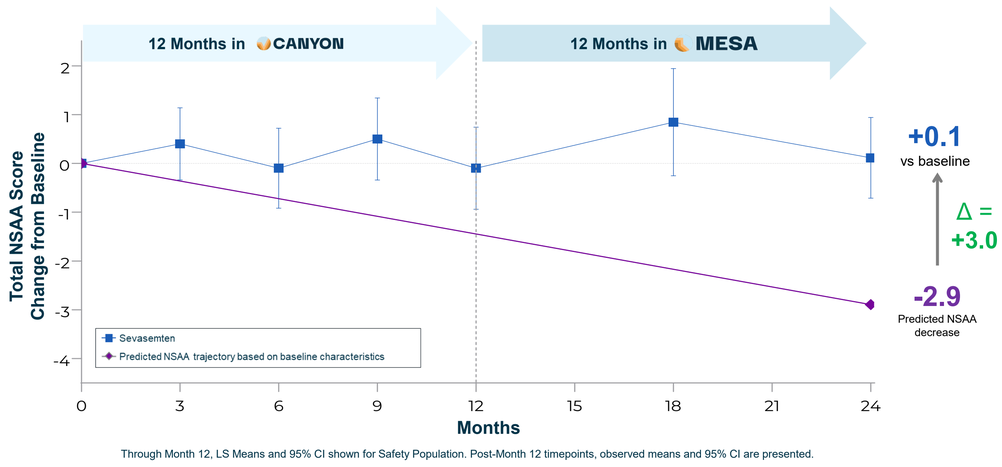
Results

For CANYON participants initially on sevasemten for 1 year, NSAA scores continued to be stable over 2 years. For participants initially on placebo, NSAA scores were maintained after 1 year since sevasemten initiation.



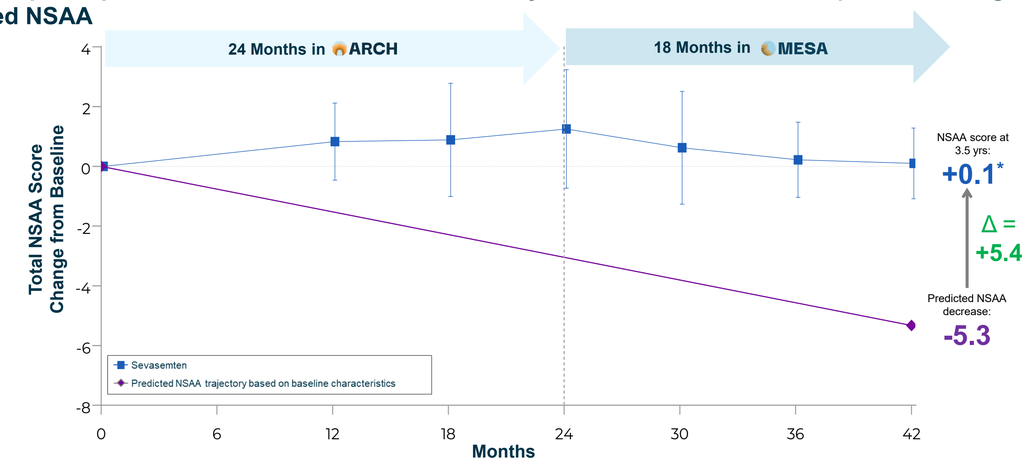
Through Month 12, LS Means and 95% CI shown for Safety Population. Post-Month 12 timepoints, observed means and 95% CI are presented.

NSAA of CANYON participants also demonstrated a positive difference in NSAA vs. predicted NSAA scores over 2 years



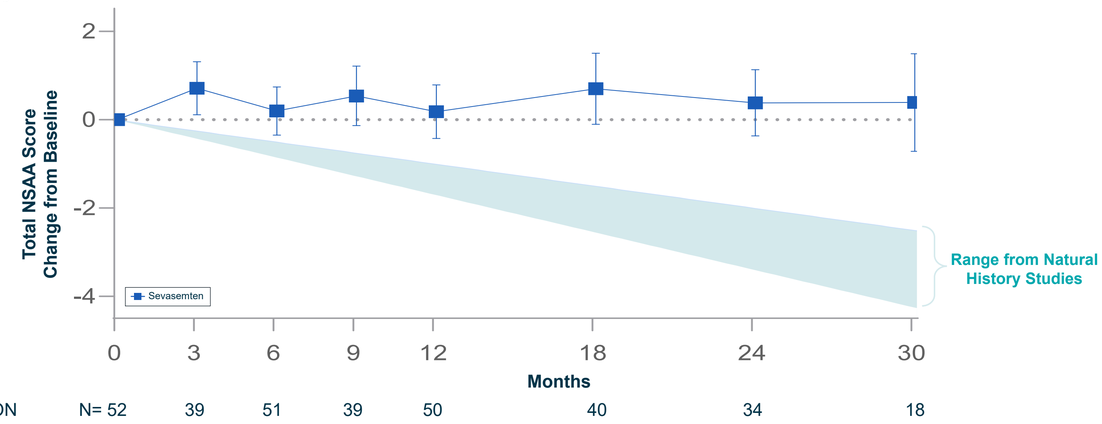
Through Month 12, LS Means and 95% CI shown for Safety Population. Post-Month 12 timepoints, observed means and 95% CI are presented.

NSAA of ARCH participants continued to be stable after 3.5 years on sevasemten, with positive divergence from predicted NSAA



*Subject with meniscal tear at month 15 excluded from subsequent NSAA measures. Means and 95% CI shown for Safety Population; Natural history comparators not available for time points earlier than 12 months.

Overall, NSAA scores of ARCH and CANYON adults remained stable after 2.5 years vs. a range of published natural history estimates



Observed Means and 95% CI shown for safety population

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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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