

Effects of Sevasemten (EDG-5506), a Fast Myosin Modulator, on Function and Biomarkers of Muscle Damage in Adults with Becker Muscular Dystrophy (Becker)

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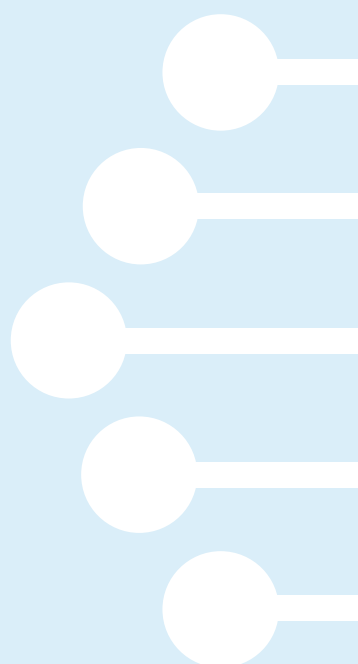
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Disclosures:

Joanne Donovan MD, PhD is Chief Medical Officer at Edgewise Therapeutics
Sevasemten (EDG-5506) is investigational and not approved in any territory.



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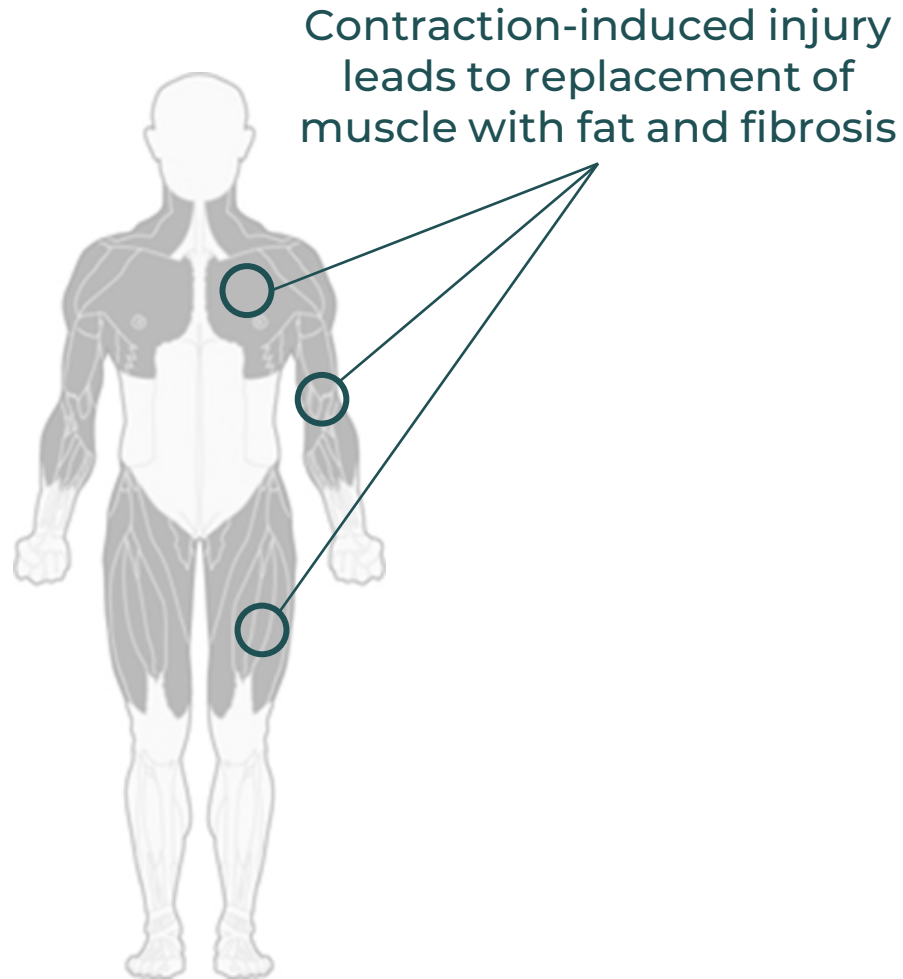
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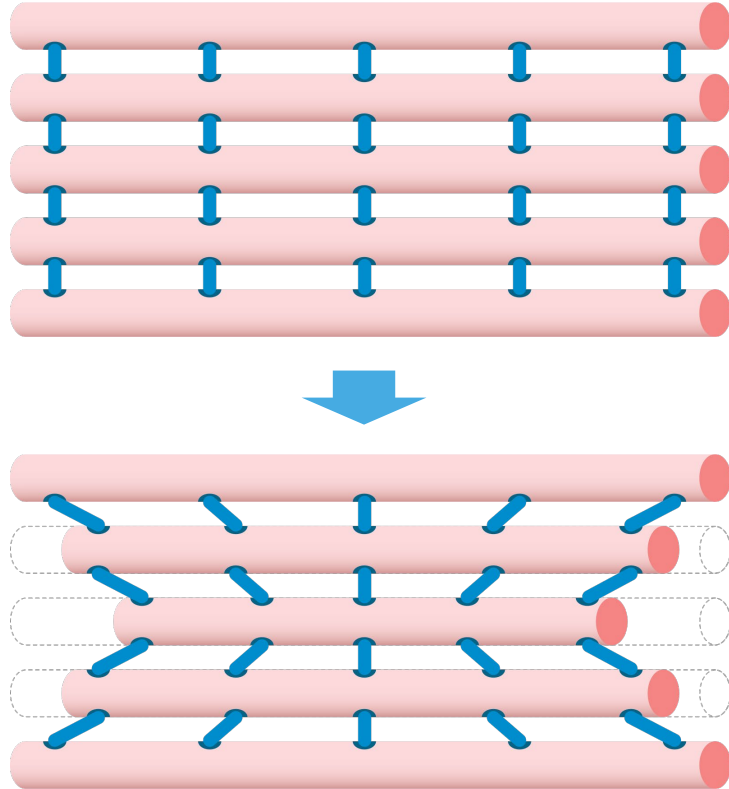
Becker is a severe, underappreciated condition with major unmet medical need and no standard of care



- Becker can lead to relentlessly progressive loss of motor function
- Individuals with Becker lose mobility, function and independence in the prime of their lives
- There is no approved therapy for Becker

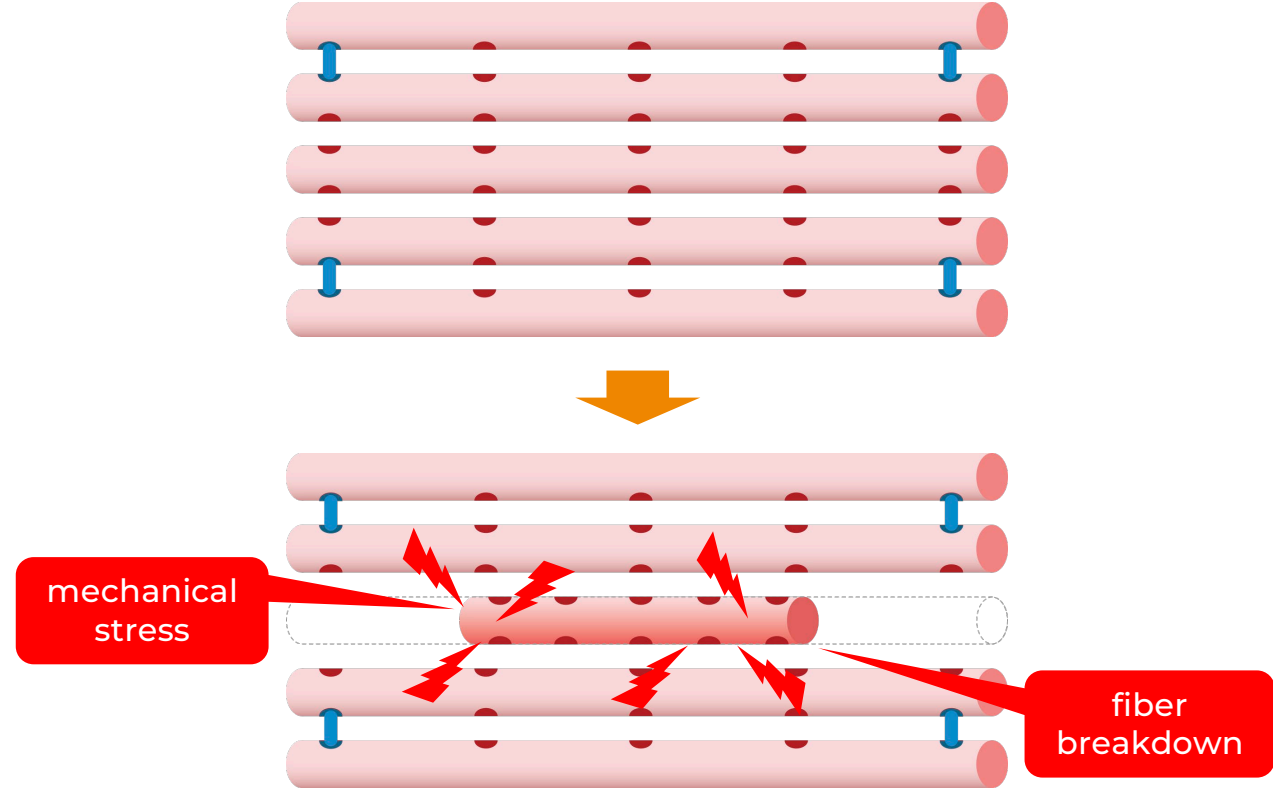
In Becker, fast muscle fibers are disproportionately injured by normal, everyday contractions

Healthy muscle contraction



Dystrophin connects contractile proteins to the membrane and surrounding matrix to protect against contraction-induced injury.

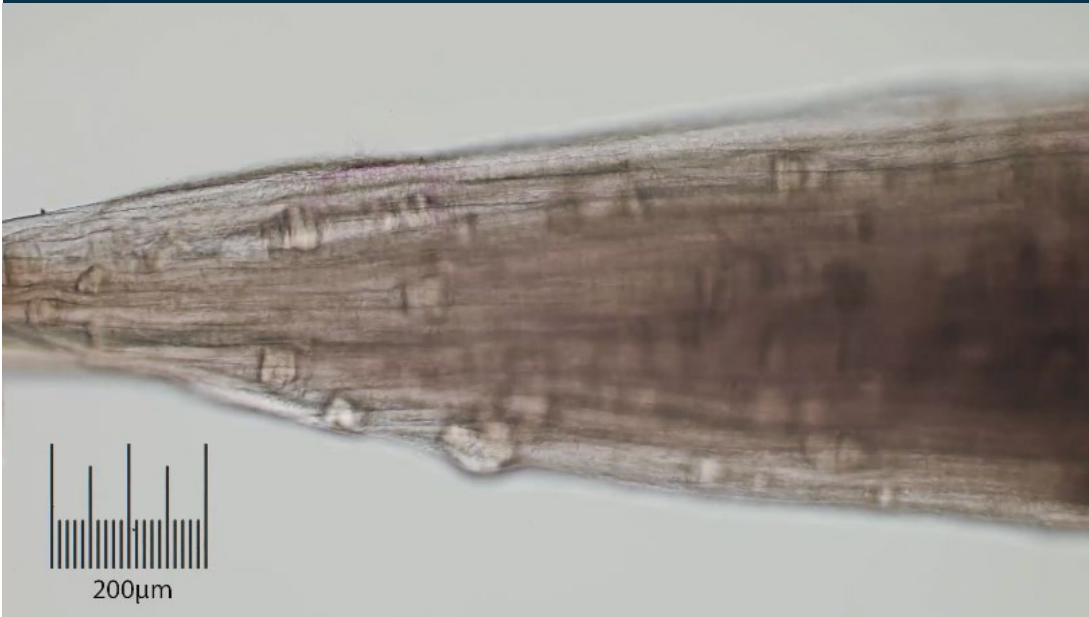
Becker muscle contraction



Contraction-induced muscle injuries occur in the absence of full-length dystrophin.

Sevasemten targets fast myosin to protect dystrophic muscle against contraction-induced injury in *mdx* mouse models

Contracting at 100% without sevasemten



In *mdx* mouse muscle, even a few contractions cause visible injury

Contracting at 85% with sevasemten

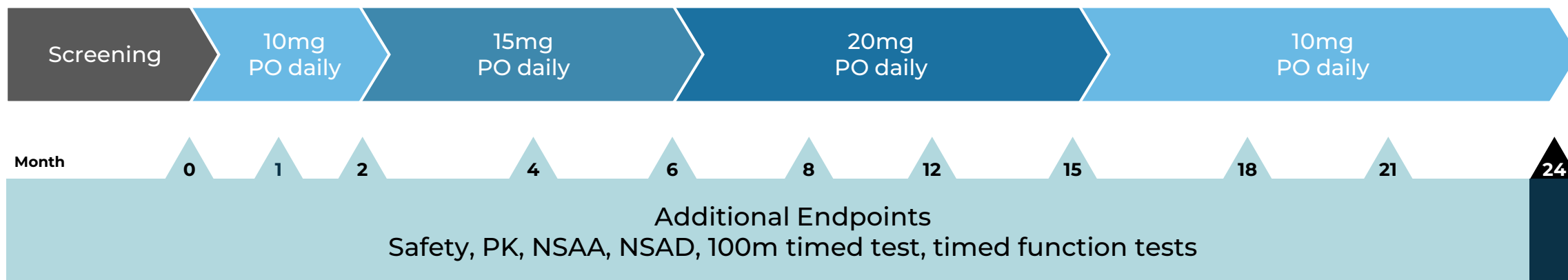


By minimally decreasing contraction while preserving function, contraction-induced injury is prevented

Both videos have been sped up 3x
Reference: Russell AJ, et al. J Clin Invest. 2023.

- Primary objective: Safety and tolerability at 24 months
- Key inclusion criteria: Ambulatory males aged 18 to 55 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, who could complete 100-m timed test
- Patients enrolled: 12

Study design - 24 months



CHARACTERISTIC	BECKER PARTICIPANTS (n=12)	AGE NORMATIVE VALUES
Age (SD)	33 (8) years	–
Functional Measures (median)		
<i>10-meter walk/run</i>	8.4 sec	< 4 sec
<i>Rise from floor</i>	6/12 could perform	< 3 sec
<i>NSAA</i>	15.5 (range 4-31)	–
Serum Creatinine (mean, mg/dL)	0.44	0.92 - 1.16
Serum CK (mean, U/L)	1,390	<210
DXA % Lean Mass	55%	>75%

Adults with similar baseline NSAA scores expected to decrease by 1.2 points per year^{2,3}

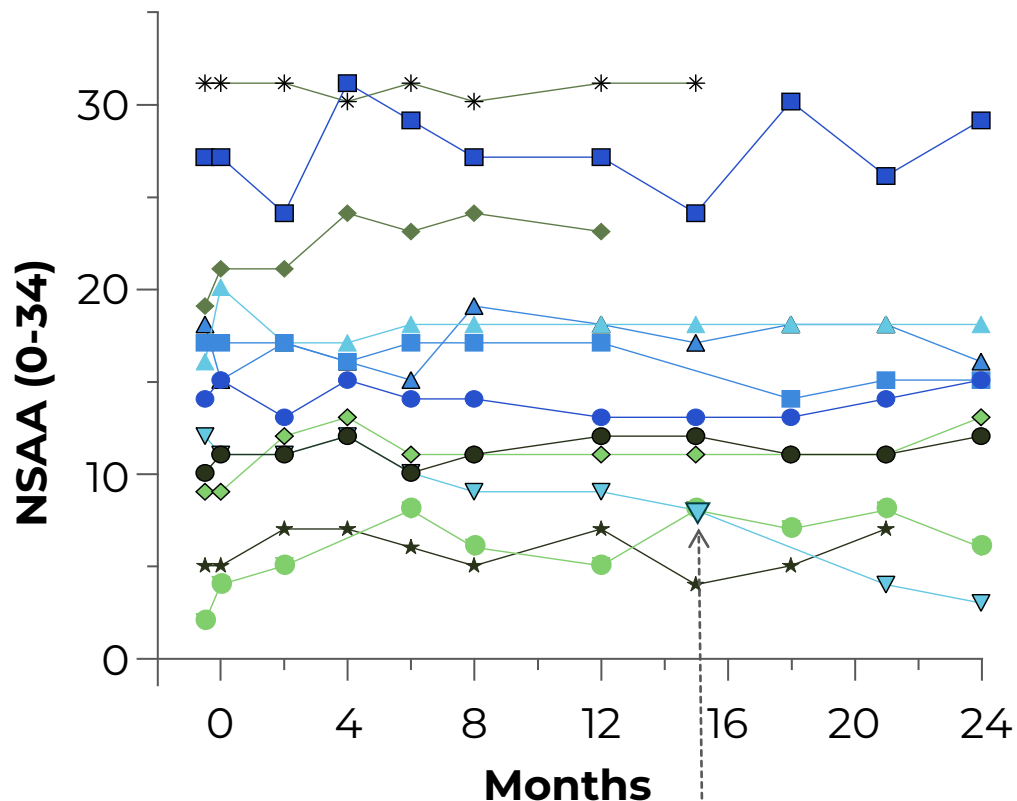
Abbreviations: DXA, dual energy x-ray absorptiometry
 Reference: 1. Data on file 2. Bello L, et al. Sci Rep. 2016. 3. Van de Velde NM, et al. Neurology. 2021.

Treatment Emergent AE (seen in >1 subject)	After One Year	After Two Years
COVID-19	4	5
Fall*	3	4
Dizziness	4	4
Arthralgia	4	4
Nasopharyngitis	3	3
URI	3	3
Procedural pain	2	3
Headache	3	3
Somnolence	3	3
GERD	2	3
Influenza	2	3
Sinusitis	2	2

- No dose reductions or adjustments
- No treatment discontinuations due to AEs
- No SAE
- Withdrawals:
 - 3 (2 of whom are planning to enroll in separate open-label extensions)

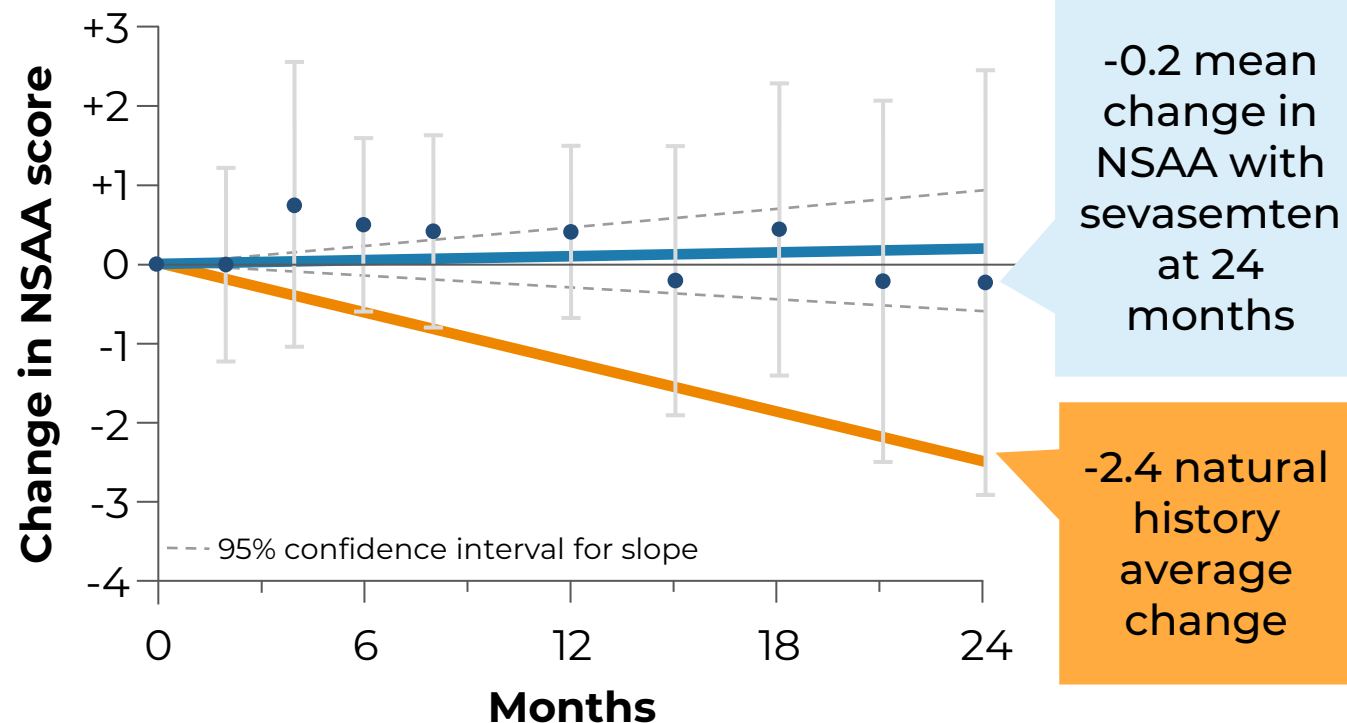
*Falls are typical for Becker patients and are not related to dizziness
 AEs, adverse events; SAE, serious adverse events
 Reference: Data on File

NSAA responses



NOTE: ▽ patient had meniscal tear and surgery after month 15

NSAA change

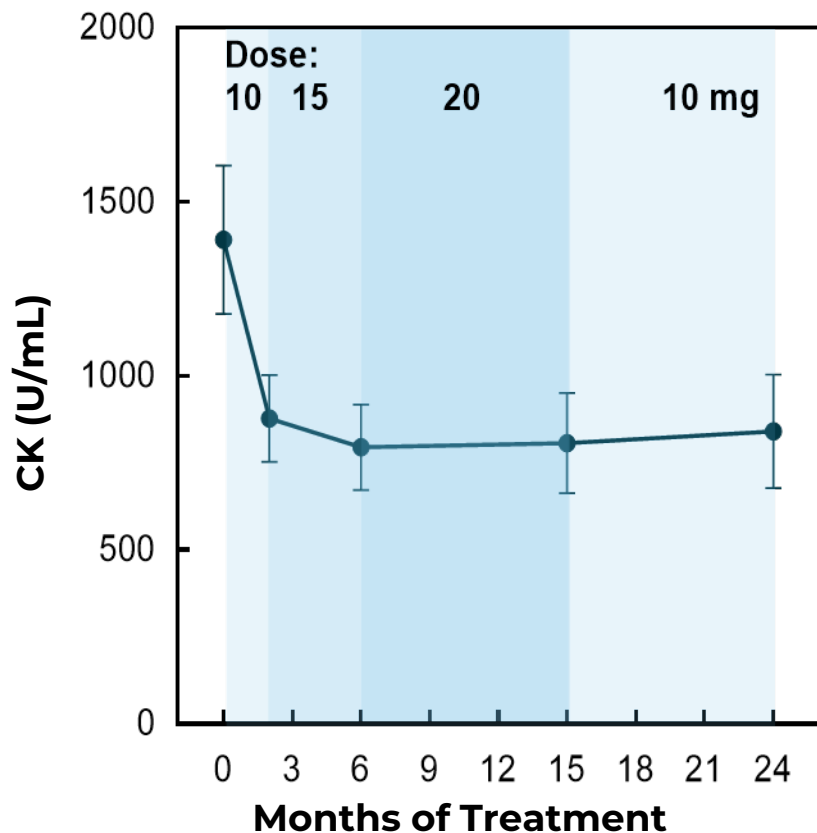


-0.2 mean change in NSAA with sevasepten at 24 months

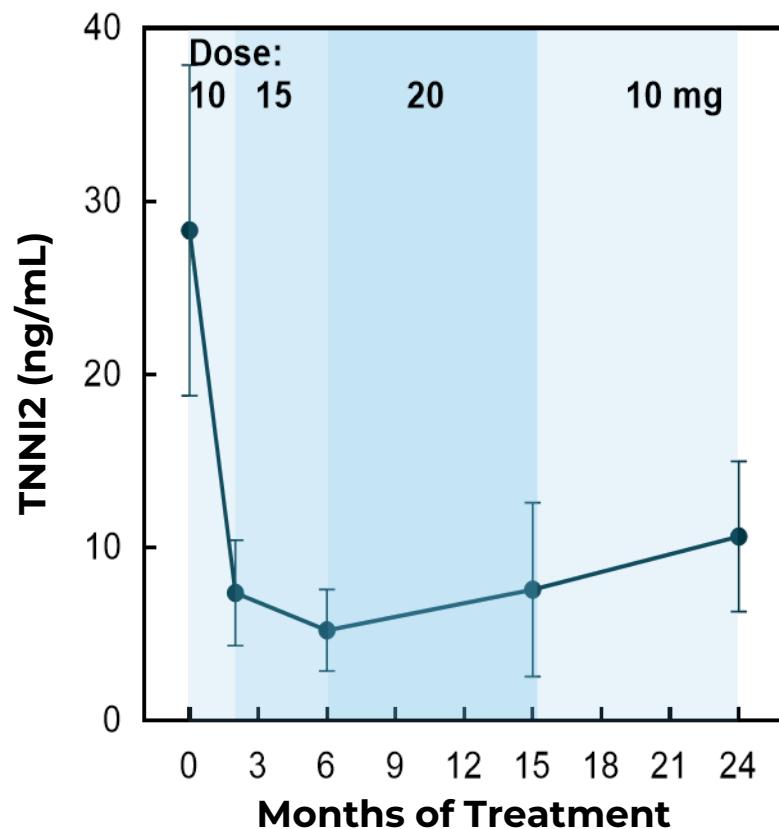
-2.4 natural history average change

*All data through 24m, including patient recovering from meniscus surgery
 Natural history based on data presented by Bello at MDA (2022) and van de Velde NM et. al., Neurology, 2021
 Mean ± 95% confidence intervals
 Abbreviations: NSAA, North Star Ambulatory Assessment

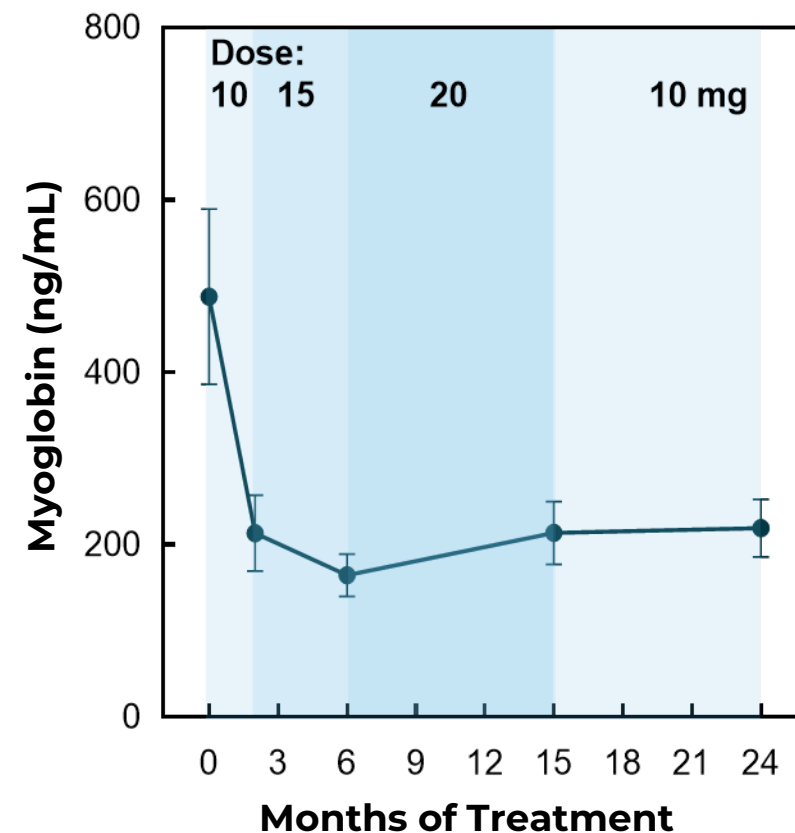
Creatine Kinase (CK)



Fast skeletal muscle troponin I (TNNI2)

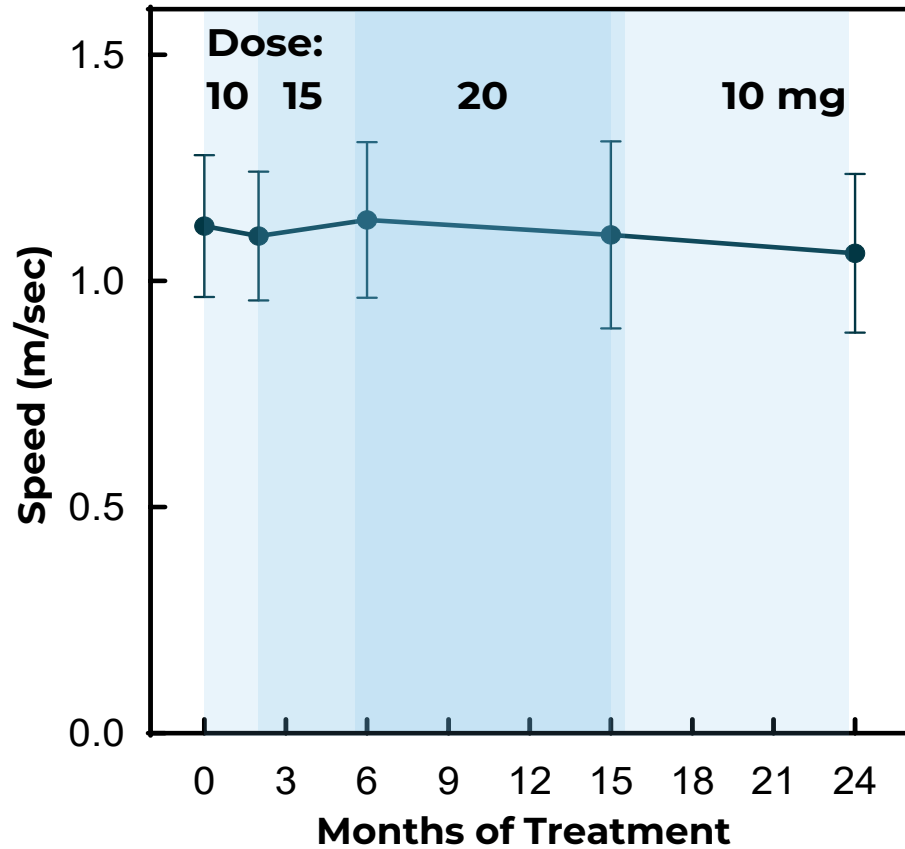


Myoglobin

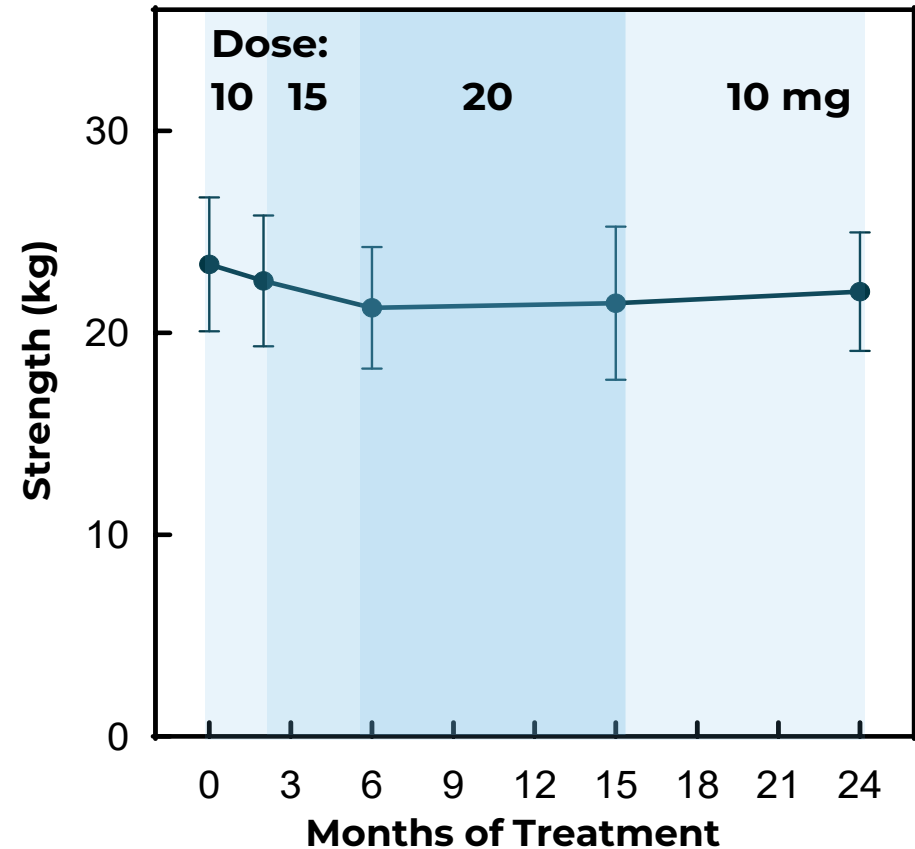


All participants
 Mean ± SEM
 Reference: Data on File

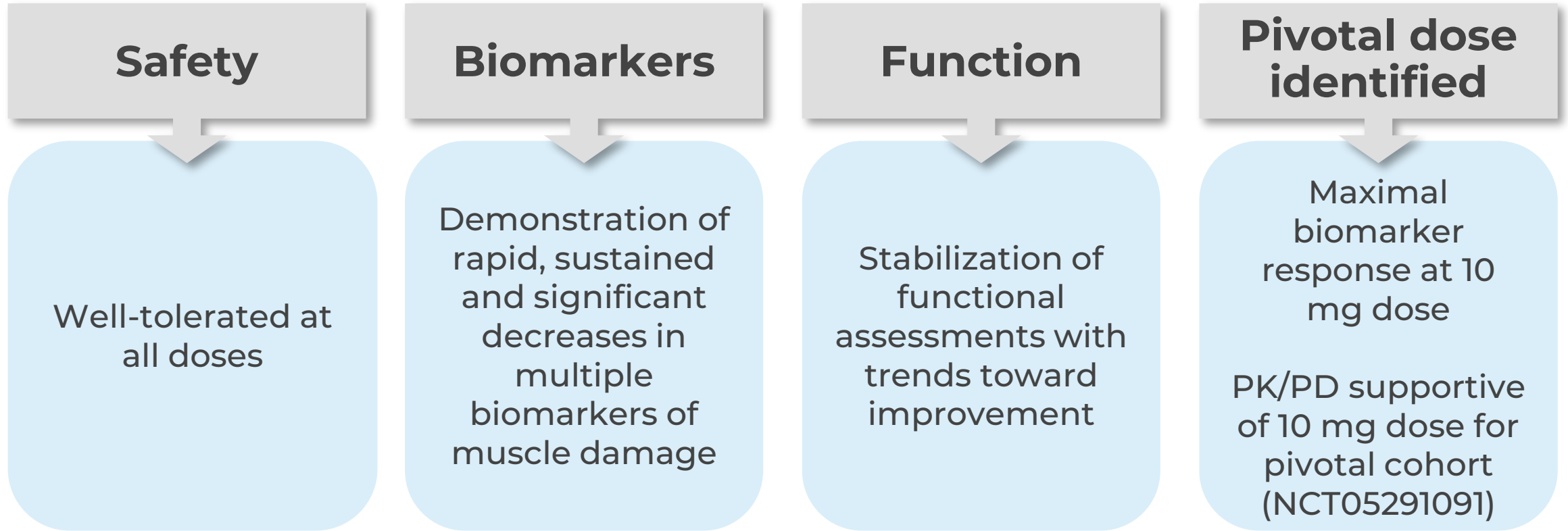
100-Meter Timed Test Velocity



Maximum Grip Strength



All participants
Mean \pm SEM
Reference: Data on File



Overall, the ARCH trial identified key factors for the design of a potentially registrational trial

An 18-month long trial to evaluate the effect of sevasekten on efficacy and safety in individuals living with Becker

Key inclusion criteria:

- ✓ Male, ages 18-50
- ✓ Mutation in *DMD* gene with Becker phenotype
- ✓ Ambulatory with NSAA between 5-32



NOW ENROLLING:

Anticipated to enroll 120 adult males diagnosed with Becker Muscular Dystrophy in the US and Europe



Acknowledgements

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