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

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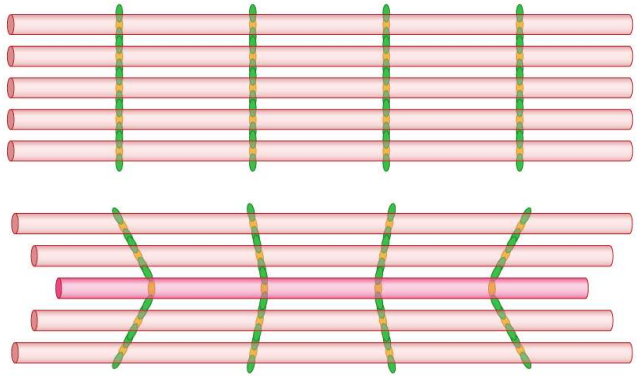
Disclosures

- Han Phan serves as principal investigator for Edgewise, Sarepta, Fibrogen, Capricor, Harmony and Scholar Rock. Other authors are employees of Edgewise and may own stock.
- EDG-5506 is investigational and not available in any territory.

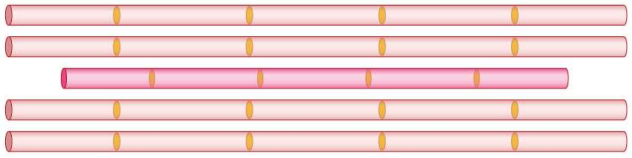
Modulation of Fast Myosin Protects against Contraction-Induced Muscle Damage

Dystrophin connects contractile proteins to the membrane and surrounding matrix

With dystrophin – fibers support each other



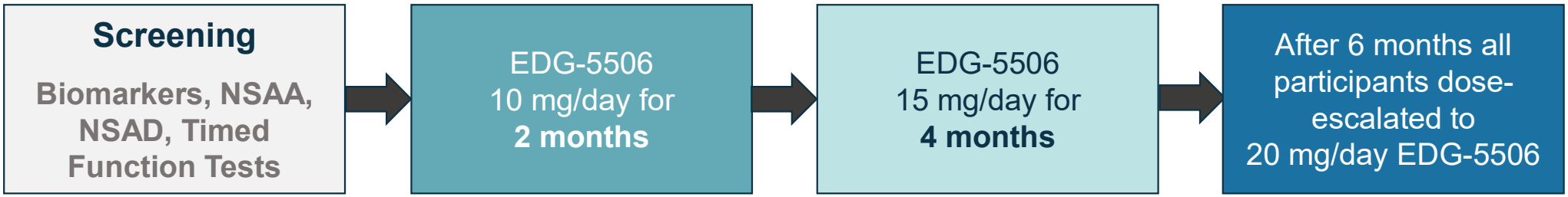
No dystrophin – fibers contract without support



- Fast muscle fibers are disproportionately injured in Duchenne and Becker muscular dystrophy (DMD, BMD)
- In animal models modulation of fast myosin contraction protects against contraction induced injury while preserving function
- EDG-5506 is a selective inhibitor of fast myosin in clinical development for BMD and DMD

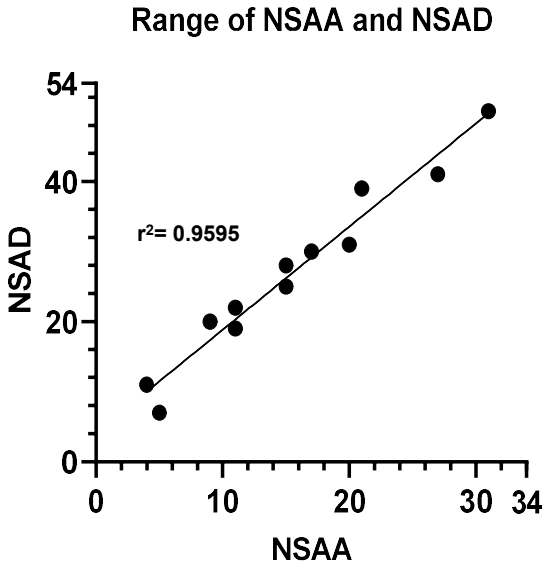
Study Design

- An open-label, single-center study of EDG-5506 to assess the safety and pharmacokinetics (PK) of EDG-5506 in adults with Becker muscular dystrophy (BMD)
- Primary objective: Safety and tolerability
- Key inclusion criteria
  - Participants who have completed Study EDG-5506-001 (Phase 1) OR
  - All of the following:
    - Ambulatory males aged 18 to 55 years with a documented dystrophin mutation with a BMD phenotype, not on corticosteroids (who could complete 100 m timed test)
- Enrollment: 12, off EDG-5506 > 3 months
- Duration up to 24 months



Baseline Characteristics: BMD Participants Had Significant Functional Impairment and Decreased Muscle Mass

Characteristic	BMD Participants (N=12)	Age Normative Values
Age (SD)	32.8 (8.1) years	
Functional Measures (median)		
10-meter walk/run	8.4 sec	< 4 sec
Rise from floor	6/12 could perform	< 3 sec
NSAA	15.5	
Serum Creatinine (mean, mg/dL)	0.44	0.92 - 1.16
Serum CK (mean, U/L)	1,390	<210
DXA % Lean Mass	54.9%	>75%



BMD patients had an NSAA range from 4-31

Source: Data on file

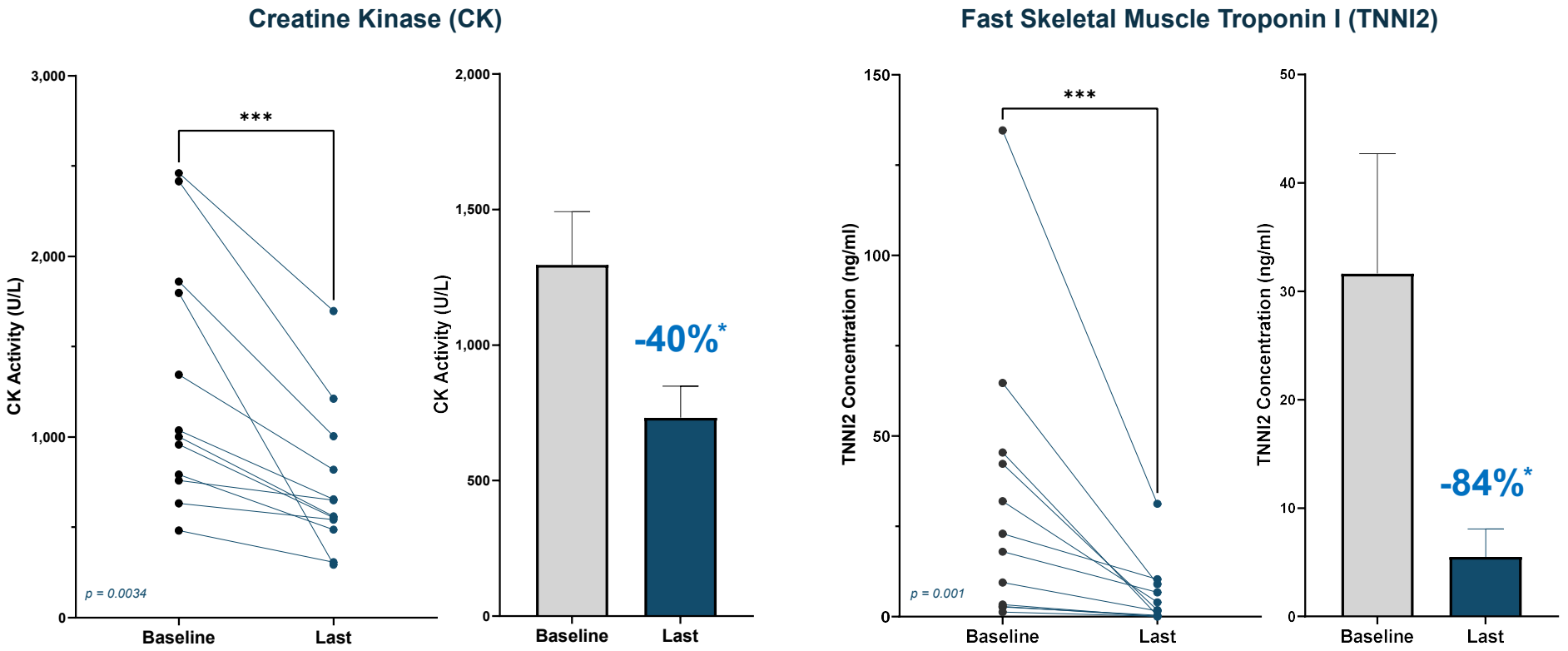
EDG-5506 Was Well-Tolerated: No Dose Reductions or Adjustments, No Treatment Discontinuations Due to AEs and No SAEs

Treatment Emergent AEs	10 mg EDG-5506 2 months N (%)	15 mg EDG-5506 4 months N (%)	EDG-5506 6 months N (%)
Dizziness	2 (17%)	1 (8%)	3 (25%)
Somnolence	2 (17%)	1 (8%)	3 (25%)
Headache	-	3 (25%)	3 (25%)
Fall*	-	2 (17%)	2 (17%)
Gastroenteritis virus	1 (8%)	-	1 (8%)
Arthropod sting	-	1 (8%)	1 (8%)
Back pain	1 (8%)	-	1 (8%)
Concussion	-	1 (8%)	1 (8%)
Euphoric mood	-	1 (8%)	1 (8%)
Flushing	1 (8%)	-	1 (8%)
Hiccups	-	1 (8%)	1 (8%)
Nasopharyngitis	1 (8%)	-	1 (8%)
Procedural pain	1 (8%)	-	1 (8%)
Road traffic accident	-	1 (8%)	1 (8%)
Seasonal allergy	-	1 (8%)	1 (8%)
Sinusitis	-	1 (8%)	1 (8%)
Testicular adenoma (benign)		1 (8%)	1 (8%)
TMJ syndrome	-	1 (8%)	1 (8%)
Toothache	1 (8%)	-	1 (8%)

* Unassociated with other AEs and typical of falls observed in BMD patients

Source: Data on file

After 6 Months, EDG-5506 Led to a Sustained Decrease in Biomarkers of Muscle Damage

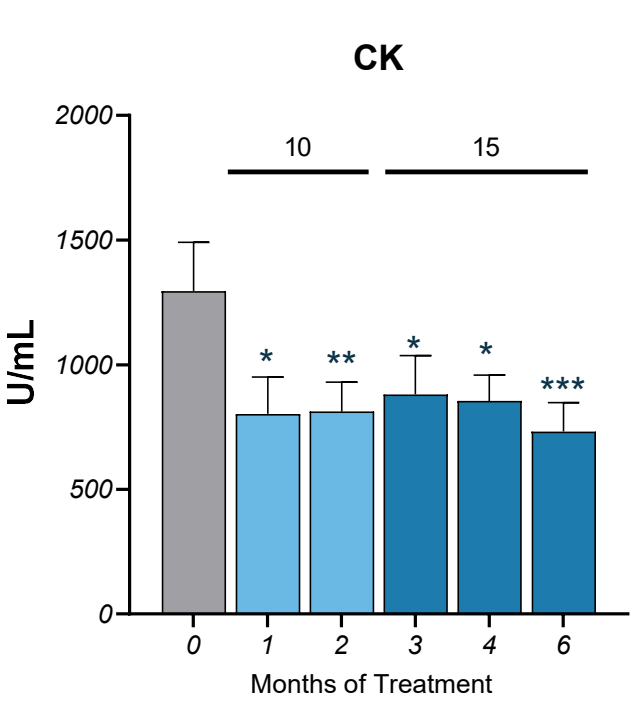


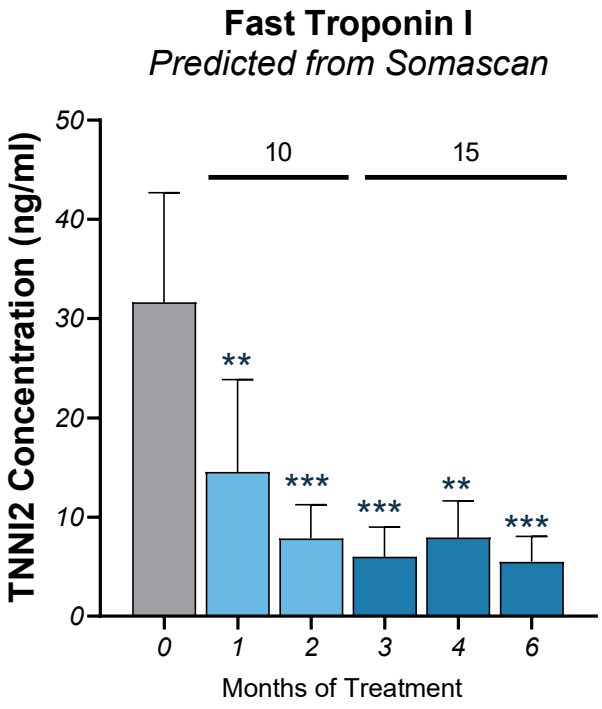
Individuals with the Highest Baseline Values Show Greatest Biomarker Effect, Suggesting Protection Against Activity-Induced Damage

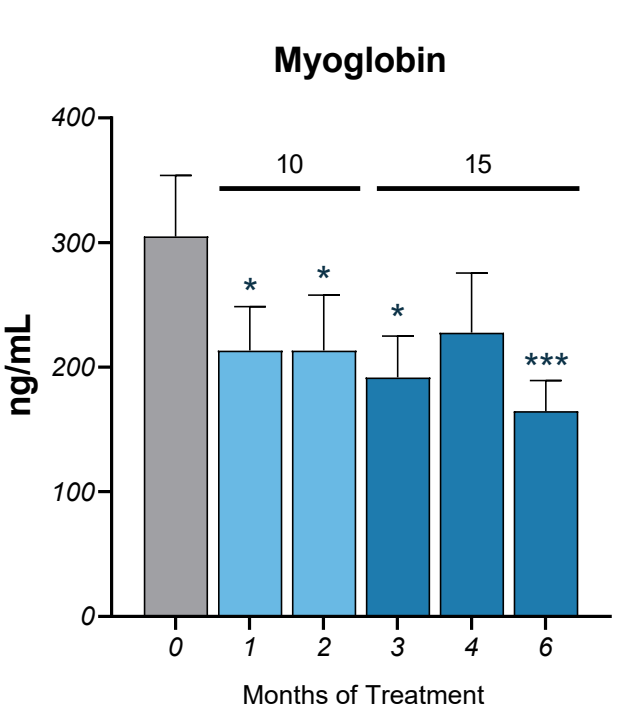
* % difference from mean baseline shown; Means + SEM
Source: Data on file

*** p<0.001

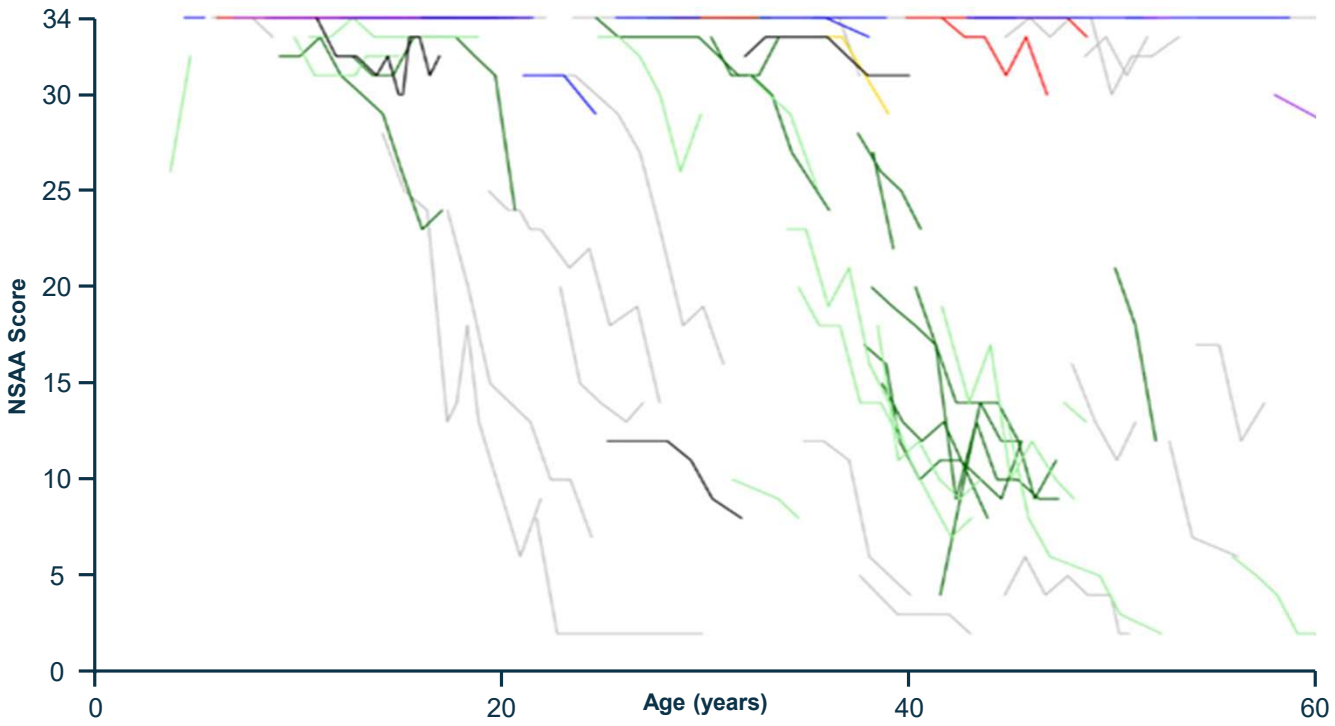
Biomarkers Show Near-Maximal Decrease at 10 mg Dose







Natural History of BMD: Longitudinal Changes in NSAA



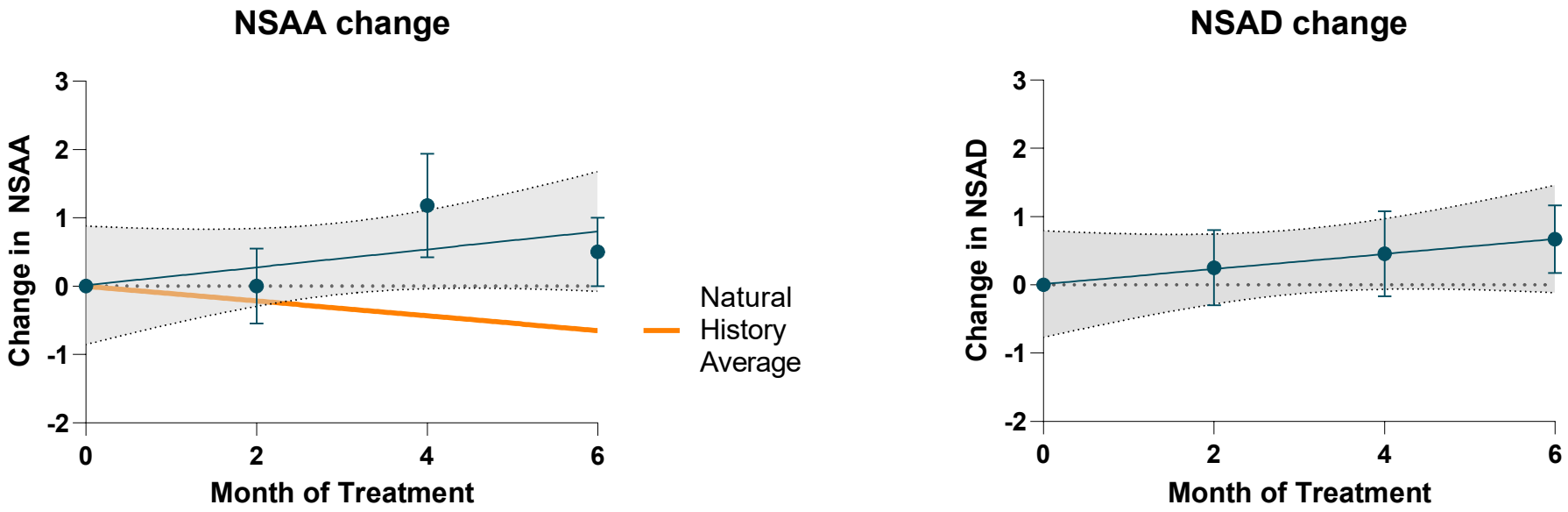
- In the most comprehensive natural history study to date over ~5 years, **NSAA decline was consistent in BMD patients who are already progressing, i.e., NSAA ≤ 32** (Bello, 2016, 2022)
- BMD individuals with a baseline NSAA score of 10-32 exhibit an estimated yearly NSAA decline of **-1.22 points**
- This is similar to data showing a **2.5 points NSAA decrease over 2 years** in unselected ambulatory BMD patients (van de Velde, 2021)

Baseline NSAA Score	Estimate of Yearly Change	Standard Error	P-value
10-32	-1.22	0.07	<0.0001

Source: Data presented by Luca Bello at MDA (2022); van de Velde NM *et. al., Neurology*, 2021

With EDG-5506 NSAA and NSAD Trended Toward Improvement Relative to Natural History

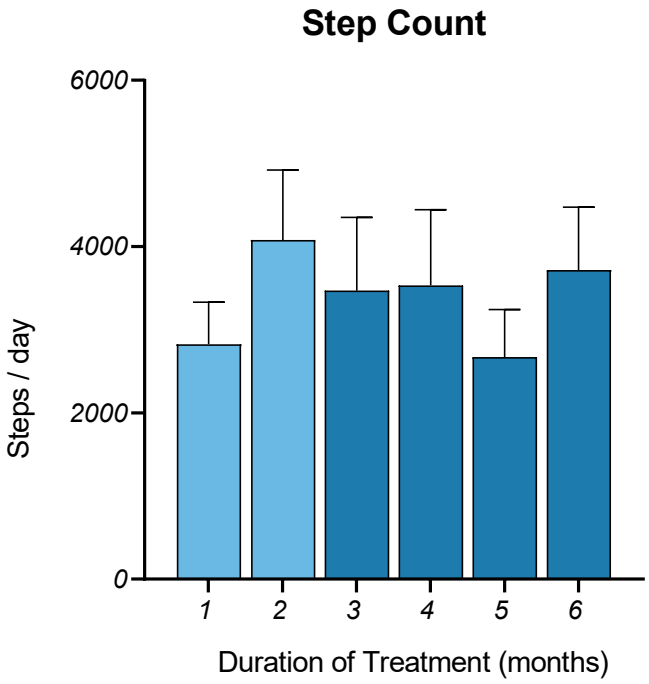
NSAA and NSAD are Integrated Measures of Function

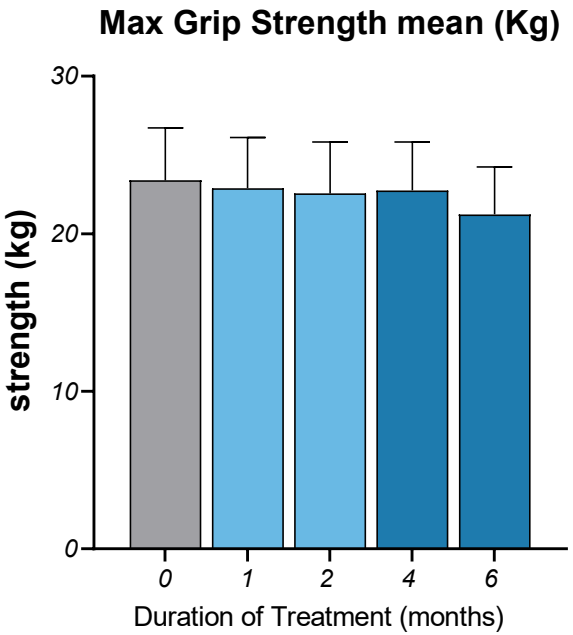


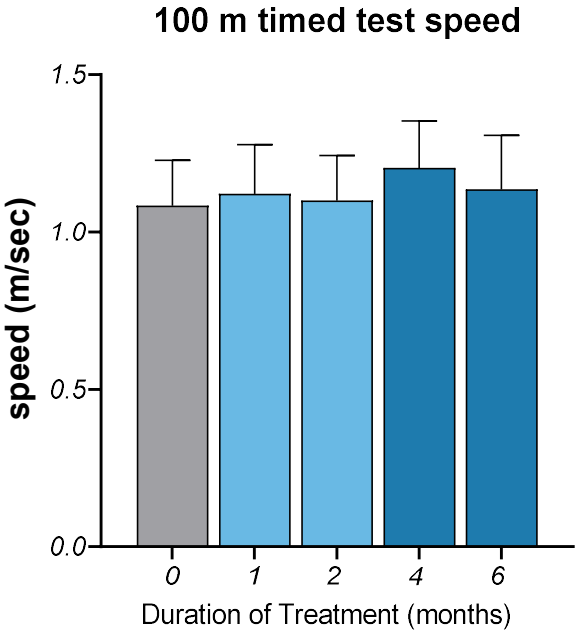
Dashed lines show 95% CI on the linear regression

Means ± SEM; Source: data on file
Natural history based on data presented by Luca Bello at MDA (2022) and van de Velde NM *et. al., Neurology*, 2021

Additional Functional Measures Show Stability



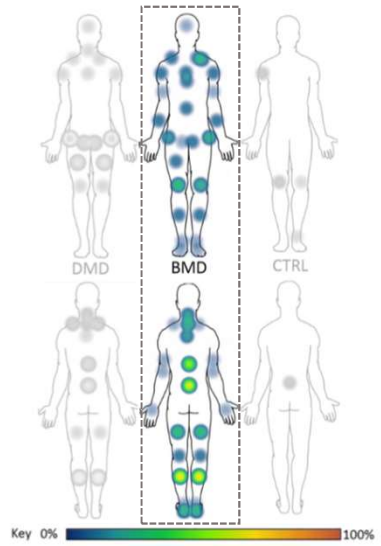




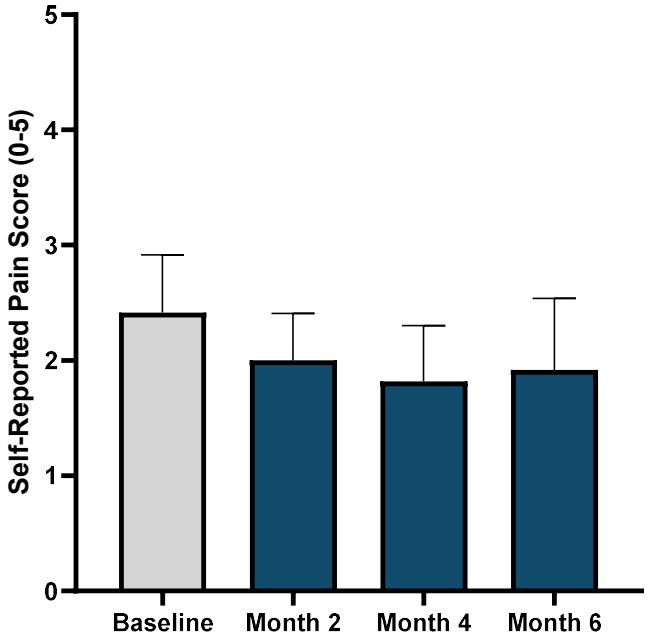
Means + SEM; Source: Data on file

Self-Reported Pain Scores Also Trended Better Following 6 Months of EDG-5506 Dosing

BMD Individuals Report More Diffuse Pain, Focus on Spine And Calves



References: Jacques MF, *et. al.*, 2019, *PLOS ONE*



- While the ARCH study is not placebo controlled, a positive trend in self-reported pain scores was observed after 6 months of EDG-5506 dosing
- Additionally, other patient-reported outcomes, such as mental health, fatigue and sleep, also trended better

Means + SEM; Source: Data on file

Conclusions

- **EDG-5506 was well-tolerated**
- **Rapid and sustained decreases in multiple biomarkers of muscle injury**
- **Trends toward functional benefit in NSAA compared with expected decreases based on natural history data**
- **Results support Phase 2 trials in BMD and DMD, currently recruiting (NCT05291091 and NCT05540860)**

Acknowledgements

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