Edgewise THERAPEUTICS

4-Month Interim Results from the ARCH Open Label Study of EDG-5506 in BMD

Investor Call and Webcast

September 12, 2022

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Edgewise THERAPEUTICS

Opening Remarks

Kevin Koch, CEO

Edgewise THERAPEUTICS

Edgewise Therapeutics is a Clinical-Stage Company Focused on Advancing Innovative Treatments for Severe, Rare Muscle Disorders

- Developing EDG-5506 to become the **foundational therapy** for muscular dystrophies
- Leveraging our **discovery and development capabilities** to advance additional programs
- Plan to enhance portfolio from **internal research** and **external business development**
- **Experienced management team** with deep expertise in muscle physiology/rare diseases

Our vision is to improve the lives of patients and families suffering from rare muscle disorders

Our Precision Medicine Muscle Platform has Generated One Clinical Stage Program and Multiple Research Programs

Program	Target	Indications	Preclinical	Phase 1	Phase 2	Phase 3
EDG-5506 *Myosin ATPase*	Skeletal Muscle	BMD				
EDG-5506 *Myosin ATPase*	Skeletal Muscle	DMD				
EDG-5506 *Myosin ATPase*	Skeletal Muscle	LGMD, McArdle				
EDG-5506 *Myosin ATPase*	Skeletal Muscle	BMD	***ARCH OL Study Ongoing***			
EDG-002 *Undisclosed Target*	Cardiac Muscle	HFpEF, HCM				

Abbreviations: BMD, Becker muscular dystrophy; DMD, Duchenne muscular dystrophy; LGMD, limb-girdle muscular dystrophy; HFpEF, heart failure with preserved ejection fraction; HCM, hypertrophic cardiomyopathy; OL, open label

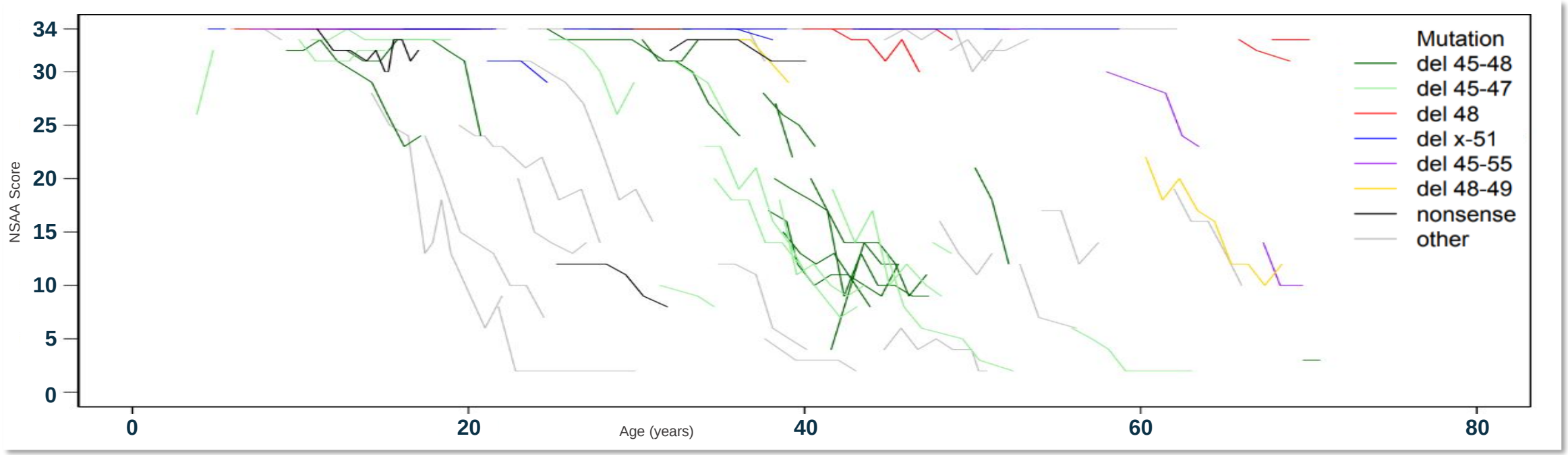
BMD and DMD Represent a Continuum of the Same Disease; Our Goal is to Treat Across the Spectrum, Regardless of Dystrophin Mutation

Spectrum of Severity Across Dystrophinopathies

Estimates Suggest there are 4,000-5,000 BMD Patients in the US With Similar Numbers in the EU and UK

~82% of BMD Patients Present with Progressive Disease with Measurable Annual Declines in NSAA

The Padova Cohort has One of the Most Comprehensively Characterized BMD Cohorts with Robust Longitudinal Data (N=76)



Predictive Value of Baseline NSAA Score – Adult BMD Progression

Baseline NSAA Score	Estimate of Yearly Change	Standard Error	P-value
All	-0.63	0.04	<0.0001
33-34	-0.03	0.01	ns
10-32	-1.22	0.07	<0.0001
<10	-0.01	0.05	ns

Reference: Presented by Luca Bello at MDA, March 2022

Topline 4-month Results from the ARCH Open Label Study

Joanne Donovan MD PhD, CMO

Edgewise THERAPEUTICS

ARCH: EDG-5506 Open Label Study Overview

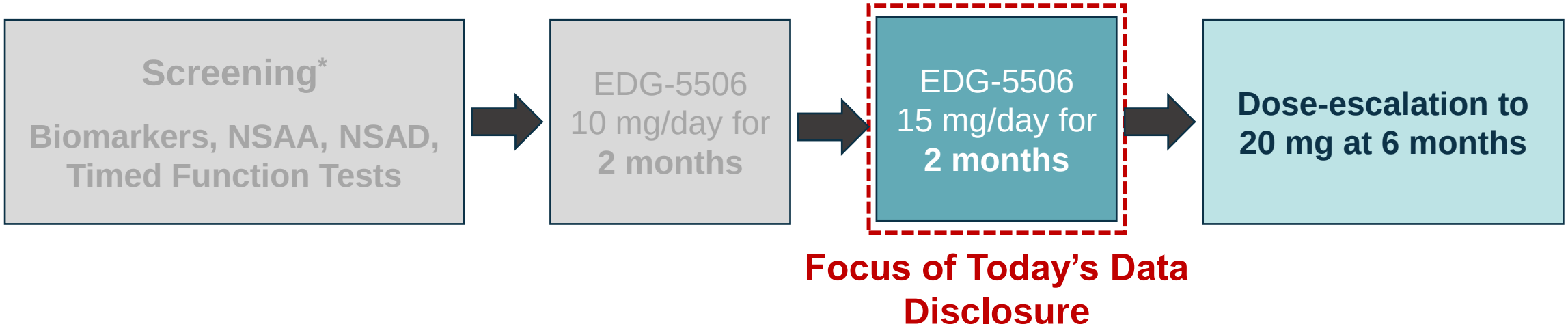
An open label, single-center study of EDG-5506 to assess the safety and pharmacokinetics (PK) of EDG-5506 in adults with Becker muscular dystrophy (BMD)

Trial Design

- Population: Ambulatory adults with BMD
  - Open to 7 participants from the Phase 1 study, with additional participants for a total of 12
  - Minimum of ~3 months between dosing in Phase 1 and open label study
  - **Unlike in the Phase 1 study, participants continued at typical daily activity levels**
- Single site (Atlanta GA)
- Duration: 1 year
- Dose: based on pharmacokinetic modeling
  - Tablets, dosed at night
  - **10 mg/day starting dose with planned dose escalation**
- Assessments include safety, tolerability, biomarkers, PK
  - Biomarkers: CK, myoglobin, fast/slow/cardiac troponin
  - SOMAscan
  - Functional measures at baseline, and continue to monitor for ≥1 year

ARCH 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)



* Interval between Phase 1 and open-label was ~3 months
Abbreviations: NSAA, North Star Ambulatory Assessment; NSAD, North Star Assessment for Limb Girdle Type Muscular Dystrophies

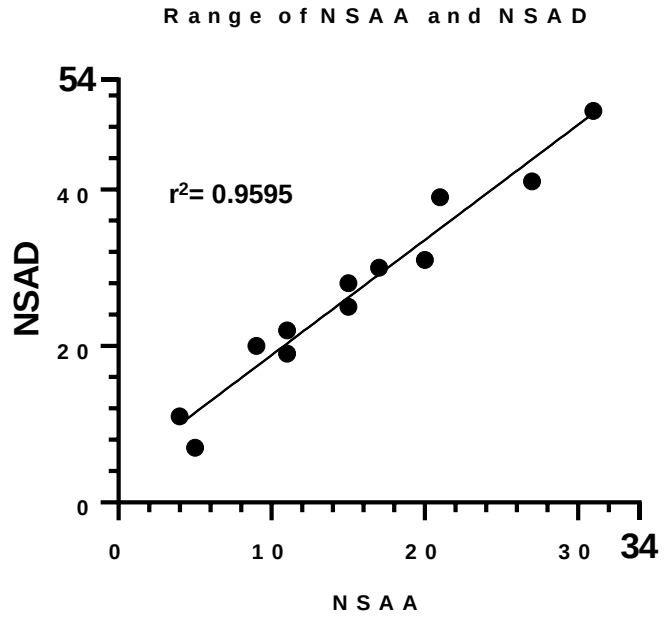
Summary of Observations at the 2 Month Time Point in the ARCH Open Label Study of EDG-5506 in BMD Patients

- EDG-5506 **continued to be well-tolerated**
- PK at 10 mg daily dosing led to **~61% of exposure** vs. Phase 1 two-week study dosed at 20 mg daily
- BMD patients treated with EDG-5506 **were more active** vs. baseline
- **CK and Fast Skeletal Muscle Troponin I showed a sustained decrease** through 2 months despite participants being at full daily activity levels
- These results supported **dose escalation to 15 mg/day**

Baseline Characteristics

BMD Patients in ARCH Have Significant Functional Impairment and Decreased Muscle Mass

Characteristic	BMD Participants (N=12)	Age Normative Values
Age	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
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 Continued to be Well Tolerated After Four Months Following Escalation to the 15 mg Dose

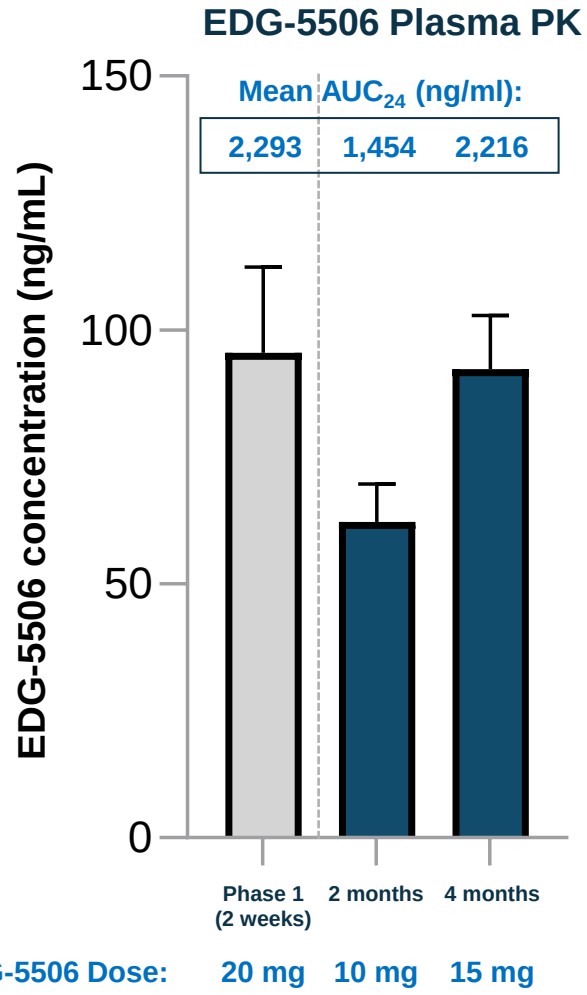
Treatment Emergent AEs	2-month (%); 10 mg EDG-5506	4-month (%); 15 mg EDG-5506	Total
Dizziness	2 (17%)	1 (8%)	3 (25%)
Somnolence	2 (17%)	1 (8%)	3 (25%)
Headache	-	3 (25%)	3 (25%)
Fall*	-	2 (17%)	2 (17%)
Gastroenteritis virus	1 (8%)	-	1 (8%)
Arthropod sting	-	1 (8%)	1 (8%)
Back pain	1 (8%)	-	1 (8%)
Concussion	-	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%)
TMJ syndrome	-	1 (8%)	1 (8%)
Toothache	1 (8%)	-	1 (8%)

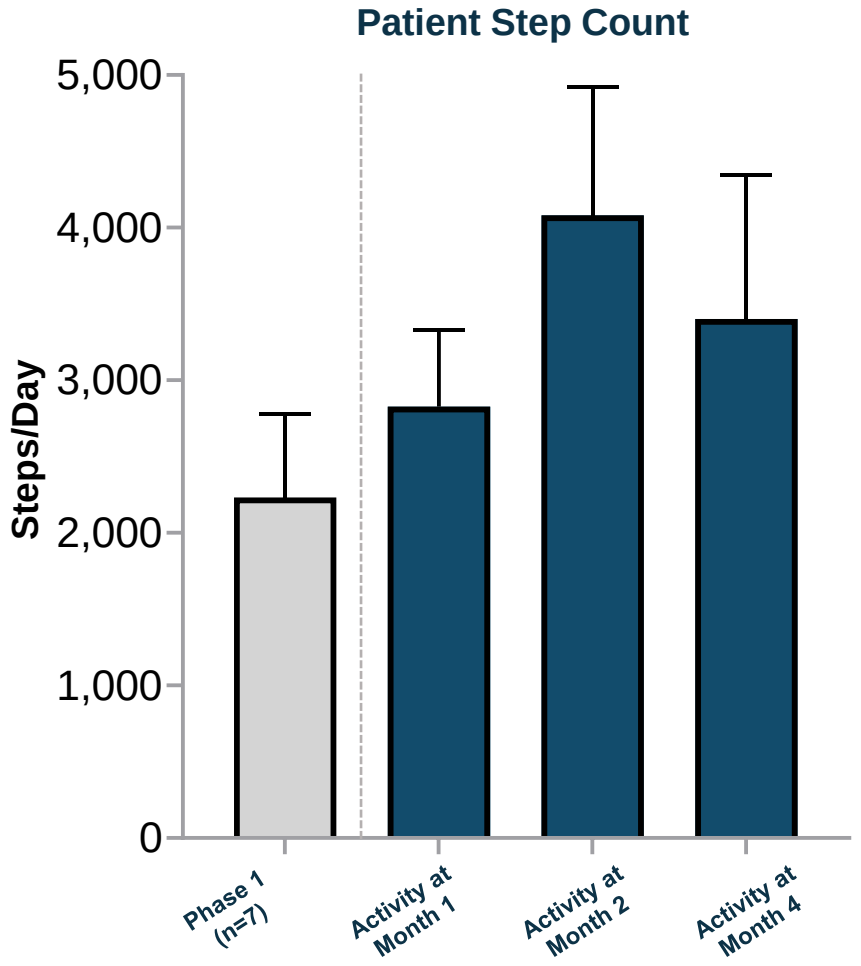
* Unassociated with other AEs and typical of falls observed in BMD patients

- There were no dose reductions or adjustments
- No patient discontinued treatment due to AEs
- All eligible patients are now on a 20 mg dose of EDG-5506

Source: Data on file

Target Plasma PK Achieved After Increasing Dose to 15 mg/day; BMD Patients Showed Continued Activity After 4 Months of Dosing

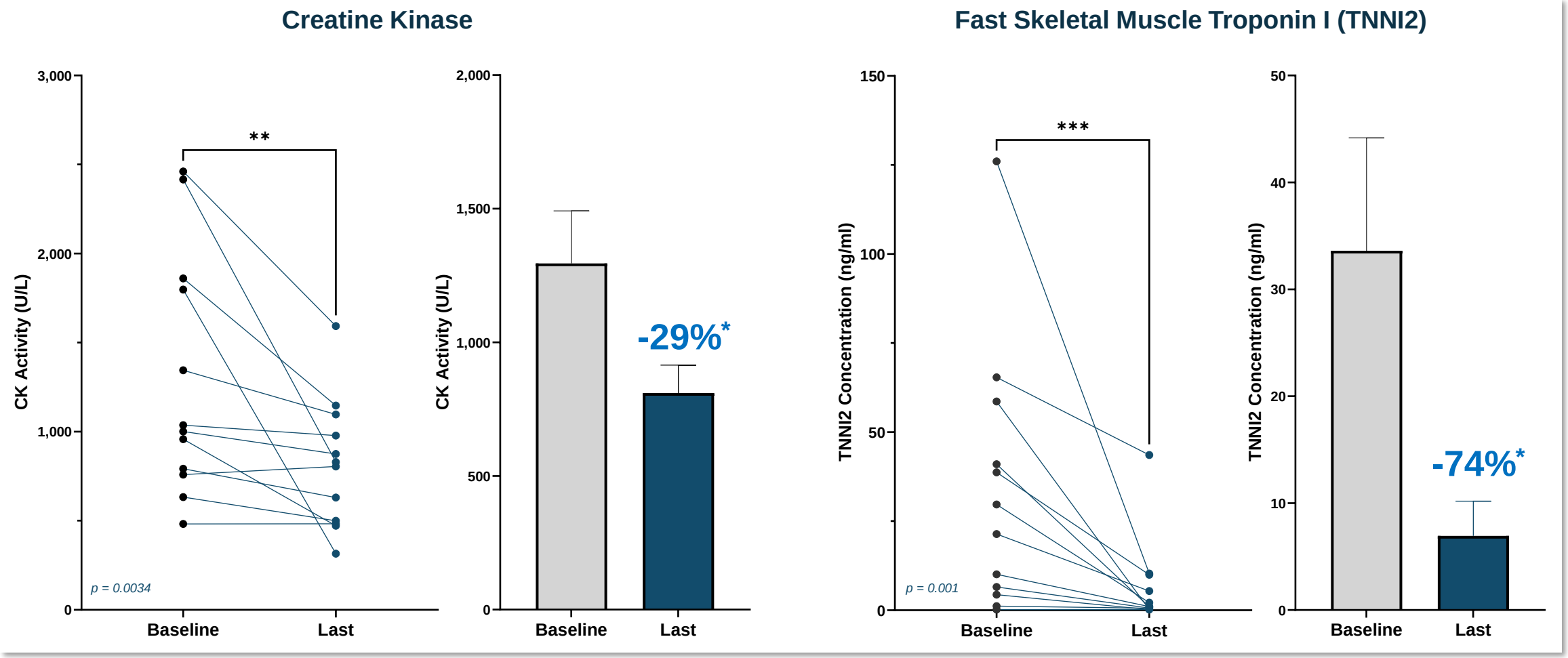




- Exposure with 15 mg dose reached the target exposures observed with the 20 mg dose in the Phase 1 BMD cohort
- At month four of dosing with EDG-5506, BMD patients continued to show an increased level of activity over activity levels at one month and activity levels observed in participants in the Phase 1b study (who were confined to the Phase 1 unit)

Means ± SEM; Source: Data on file

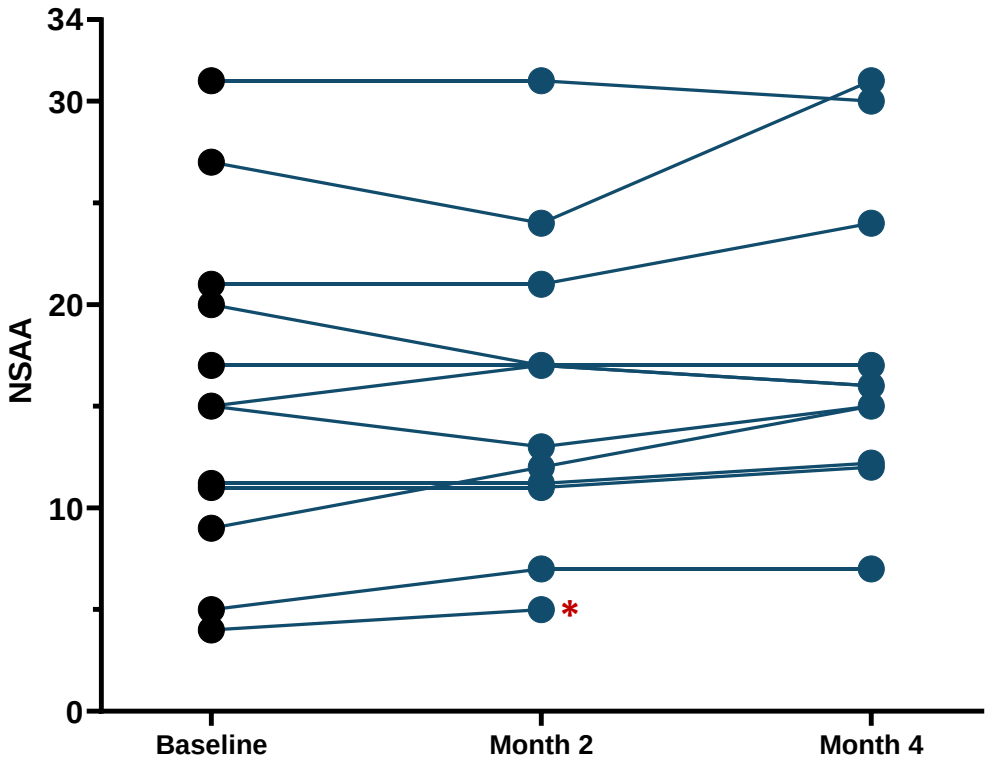
EDG-5506 Led to a Sustained Decrease in CK and Profound Suppression of TNNI2 Demonstrating Target Engagement

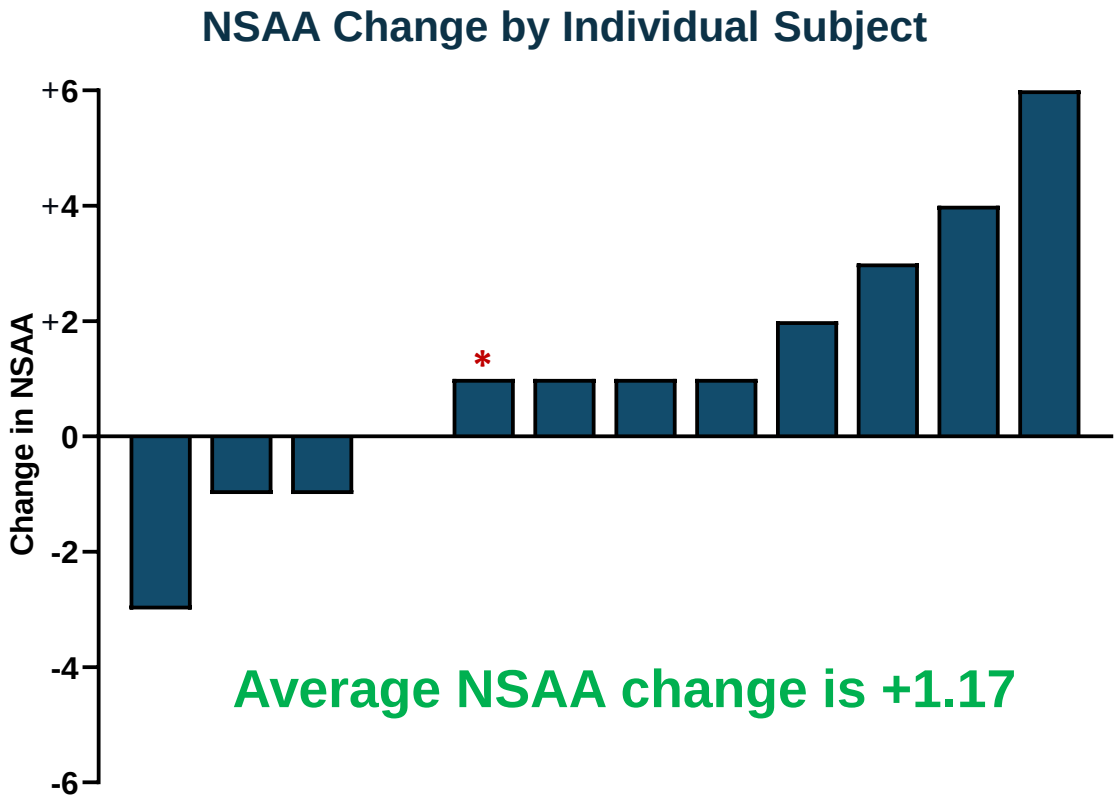


Individuals with the Highest Baseline Values Show Greatest Biomarker Effect, Suggesting Protection Against Activity-Induced Damage

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

NSAA Improvements Observed After 4 Months of EDG-5506 – NSAA Represents an Integrated Measure of Function



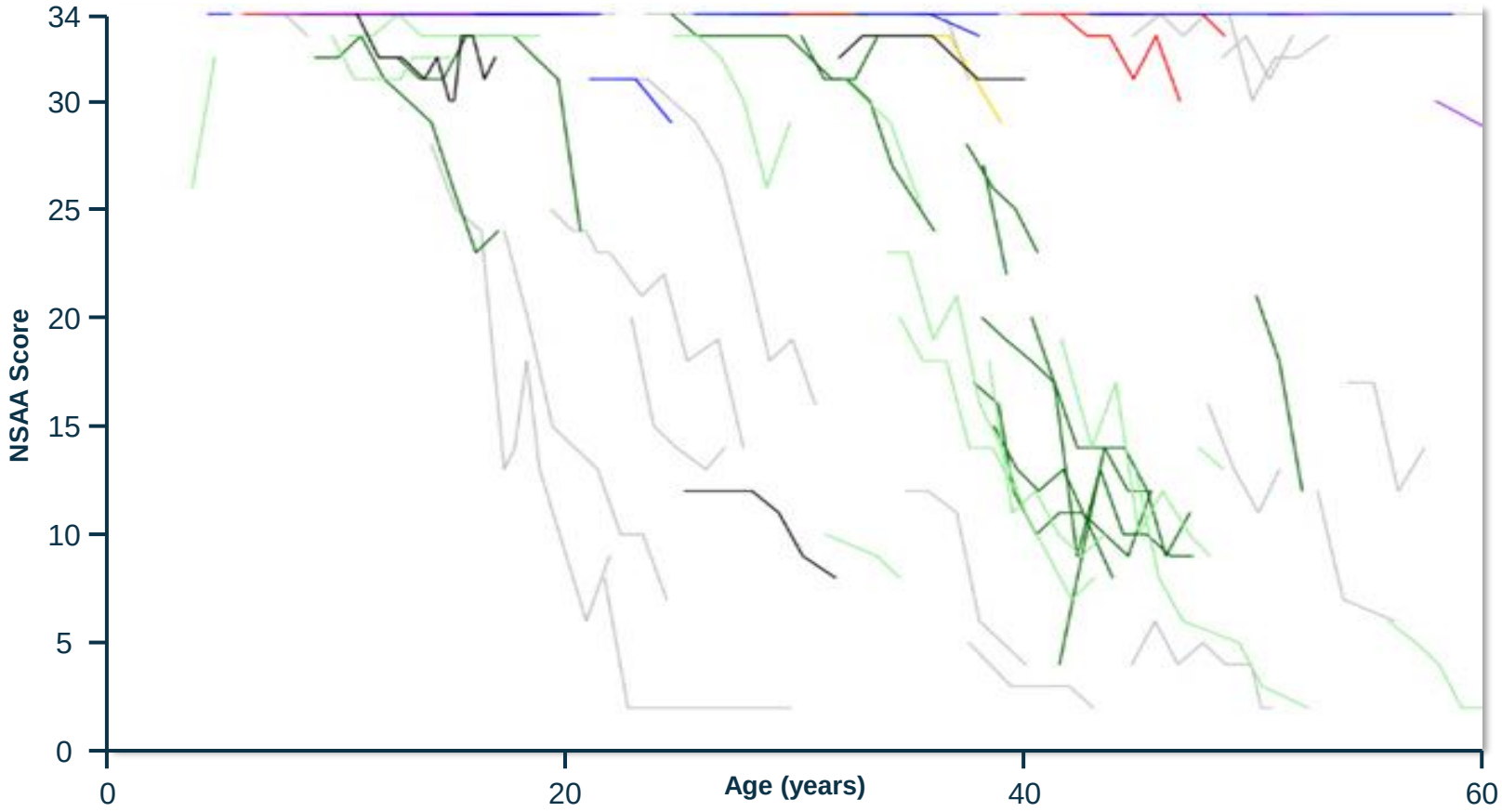


Average NSAA change is +1.17

9 of the 12 (75%) BMD Patients in the ARCH Study Showed an Improved or Stable NSAA Change Relative to their Baseline NSAA Scores

* Subject unable to perform activity at month 4 due to scooter accident
Source: Data on file

The Natural History of BMD Provides Helpful Context for Interpreting Changes in NSAA in Response to EDG-5506

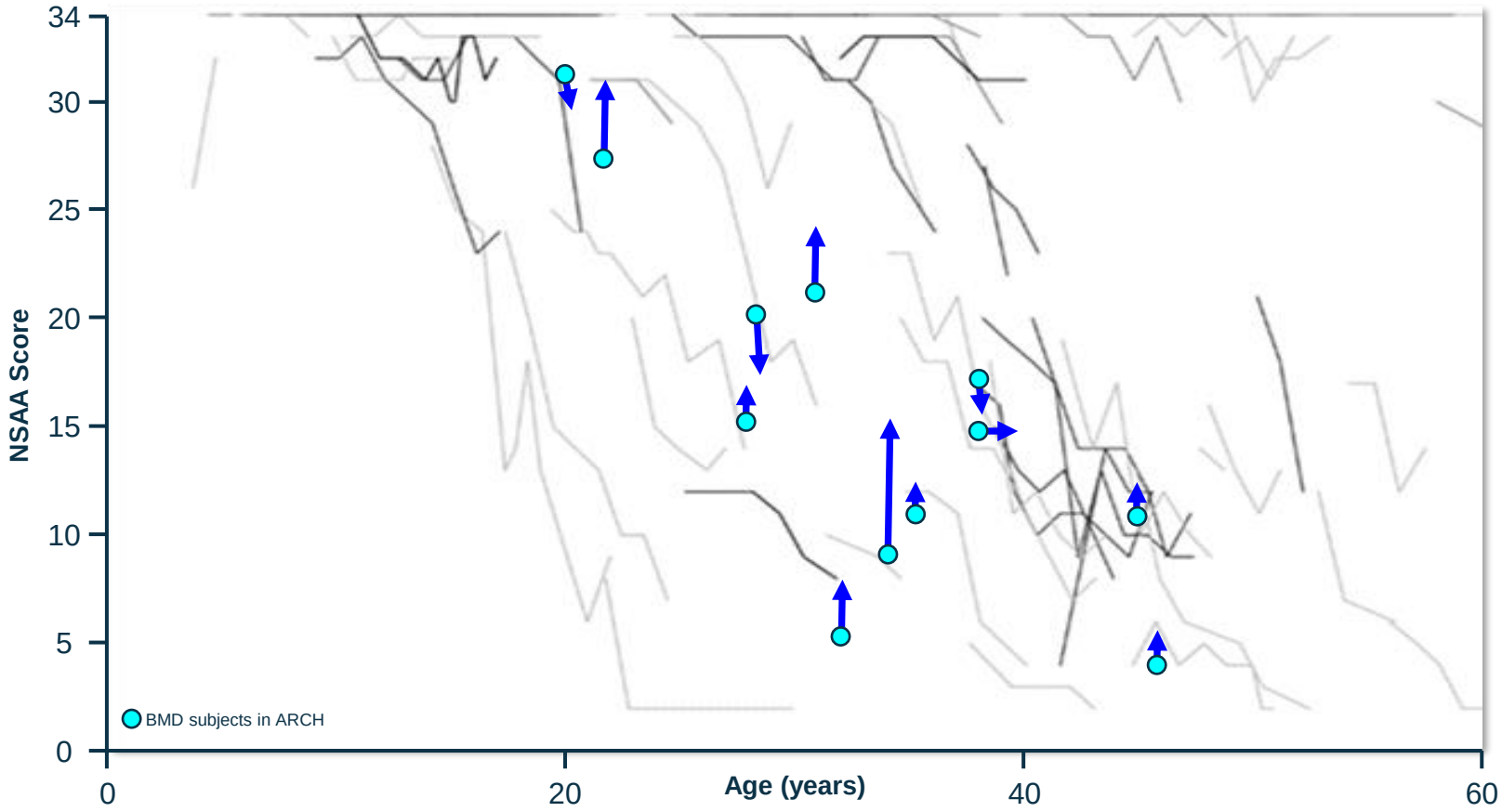


- Luca Bello's BMD Natural History Study, the most comprehensive study of its kind to date, demonstrates that **NSAA decline is consistent in BMD patients who are already progressing**
- BMD individuals with a baseline NSAA score of 10-32 exhibit an estimated yearly NSAA decline of **-1.22 points**
- Functional decline in BMD patients is further supported by Erik Niks' data demonstrating a **2.5 points NSAA decrease over 2 years** in unselected ambulatory BMD patients

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

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

The NSAA Improvements After 4 Months of EDG-5506 Dosing are Remarkable Relative to Trajectories from the Bello Natural History



Longitudinal NSAA Evaluations Across Participants in the Bello NHx Cohort

	Group	Est. Yearly δ
NSAA	10-32 (n=33)	**-1.22**

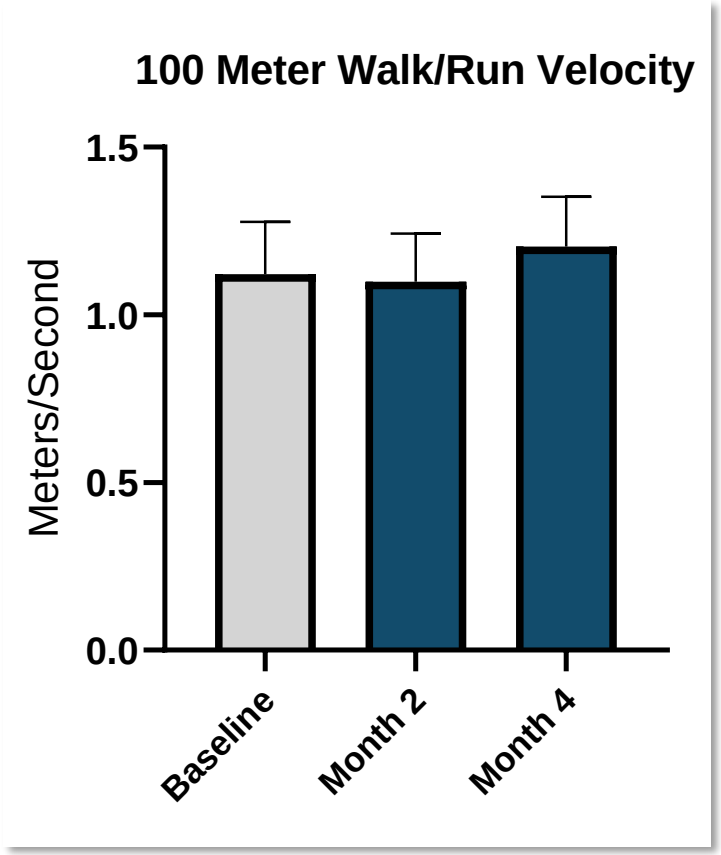
Edgewise NSAA Changes After 4 Months of EDG-5506 Dosing

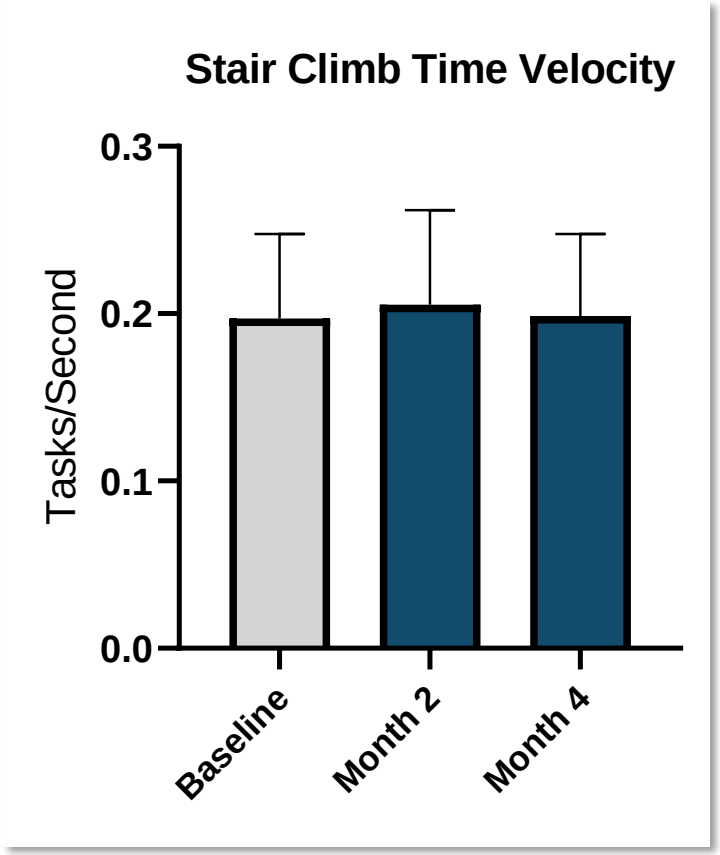
	Group	δ After 4 Months
NSAA	All (n=12)	**+1.17**

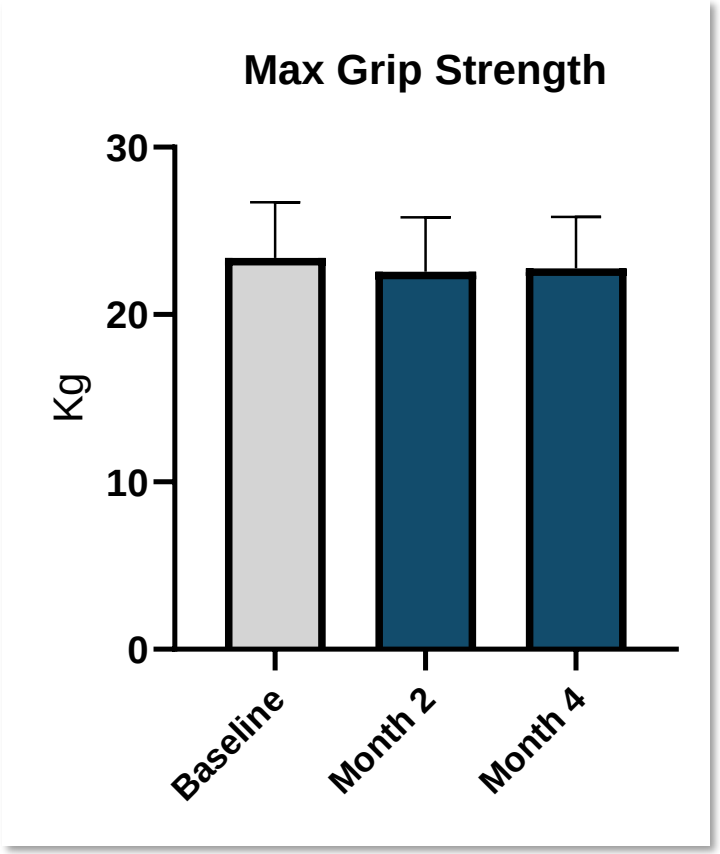
Encouraging Divergence Between Bello BMD Natural History External Control (N=33) and ARCH Study Population (N=12) After 4 Months of EDG-5506 Treatment

Source: Data on file; Data presented by Luca Bello at MDA (2022)

100 Meter Walk/Run, Four Stair Climb and Grip Strength Were Unchanged After 4 Months of EDG-5506 Dosing



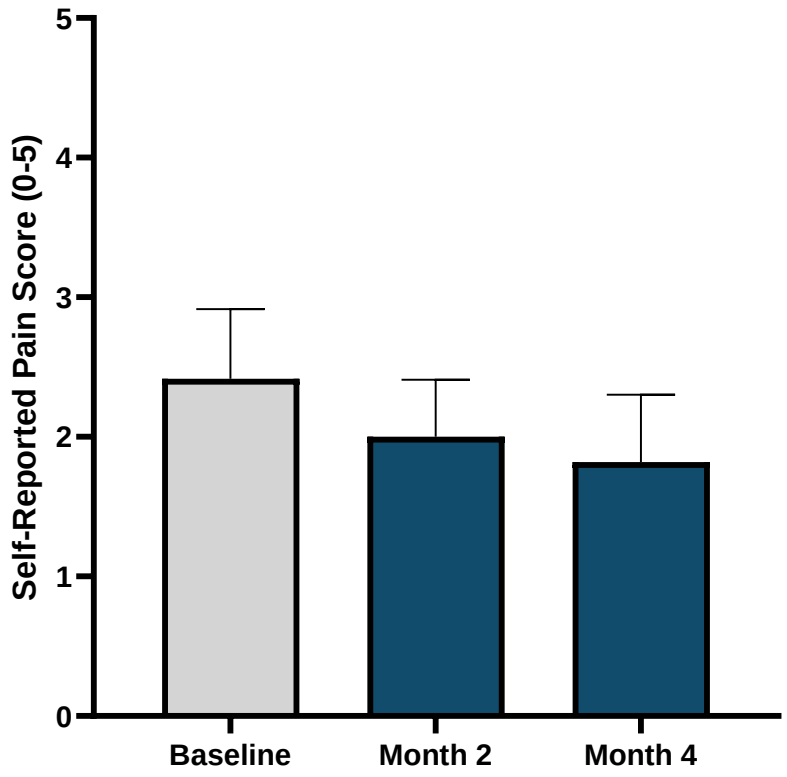




Stabilization Across Other Functional Measures in Addition to Max Grip Strength at 4 Months Trends Favorably for EDG-5506

Means ± SEM; Source: Data on file

Self-Reported Pain Scores Also Trended Better Following 4 Months of EDG-5506 Dosing



- While the ARCH study is not placebo controlled, a positive trend in self-reported pain scores was observed after 4 months of EDG-5506 dosing
- Additionally, other patient-reported outcomes, such as mental health, fatigue and sleep, also trended better
- A more comprehensive analysis of the PROs and PROMIS-57 is ongoing

Means ± SEM; Source: Data on file

Key Takeaways Following 4 Months of EDG-5506 Dosing in BMD Patients Enrolled in ARCH

- EDG-5506 **continues to be well-tolerated** following an increase to 15 mg daily dosing
- PK at 15 mg led to **target exposures** in line with the Phase 1 two-week study
- BMD patients treated with EDG-5506 **continued to exhibit increased activity** relative to baseline
- CK and Fast Skeletal Muscle Troponin I showed a **sustained decrease** through 4 months despite participants continuing to exhibit full daily activity levels
- **Trends toward functional benefit in NSAA that are remarkable** based on natural history data; **pain scores also trended positively**

Ongoing and Upcoming Clinical Studies with EDG-5506

Phase 1 OL Study (BMD) *(NCT05160415)* **ARCH**	*Steady-state PK, biomarker response and longer-term safety*	***Fully Enrolled***
Natural History Study in BMD *(NCT05257473)*	*Observational natural history study in BMD adults and adolescents*	***Enrolling***
Phase 2 BMD *(NCT05291091)* **CANYON**	*Dose Ranging* → *OLE*	***Enrolling***
Phase 2 DMD Dose Ranging Study **LYNX**	*Dose Ranging* → *OLE*	*2H22 Start*
Phase 2 LGMD 2I, BMD and McArdle Exercise Study **DUNE**	→ *OLE*	*2H22 Start*

Abbreviations: LGMD, limb-girdle muscular dystrophy

Phase 2 Study in Adults and Adolescents with BMD

CANYON

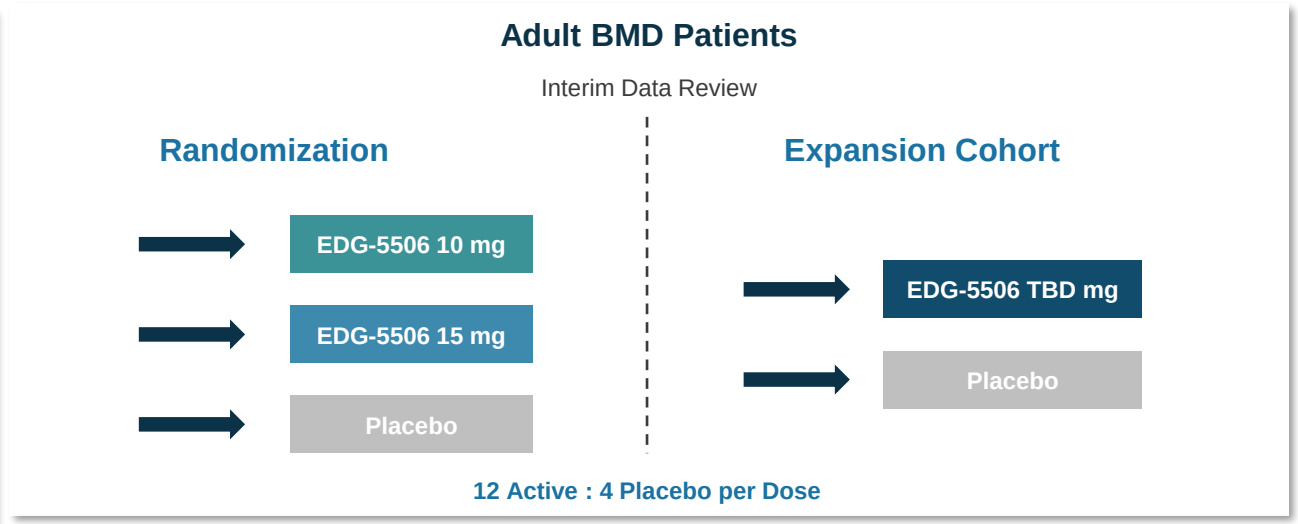
A Phase 2 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Effect of EDG-5506 on Safety, Biomarkers, PK, and Functional Measures in Adults and Adolescents With BMD

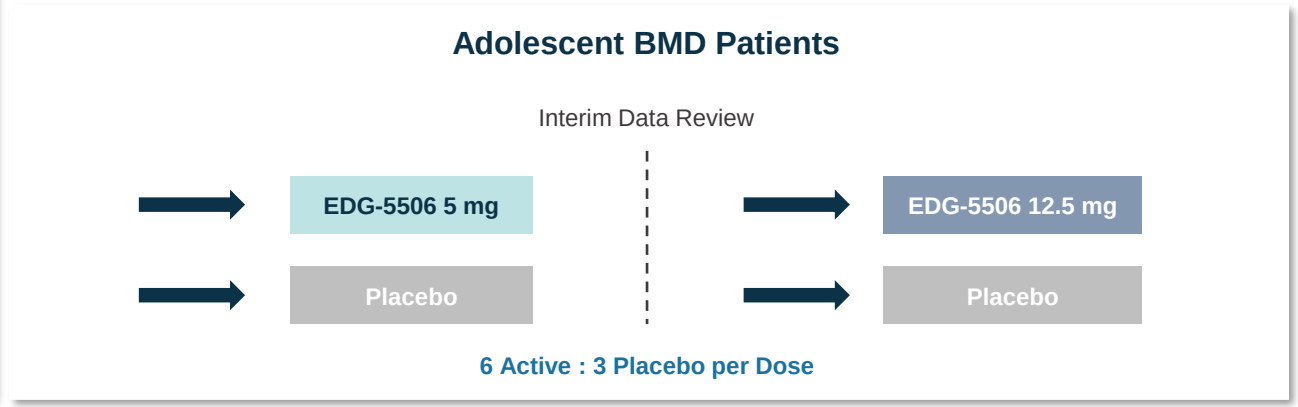
Trial Design

- Population: 66 ambulatory adults and adolescents with a genetic diagnosis of BMD
  - NSAA between 10 and 32
- ~12 sites in US and Europe
- Duration: 1 year

Summary of Endpoints

- Primary Endpoint: Changes in biomarkers of muscle damage and number and severity of adverse events
- Secondary Endpoints – Change from baseline in:
  - Fat fraction of upper leg muscles assessed by MRI
  - NSAA and NSAD
  - 10-meter walk/run test
  - 100-meter timed test
  - 4-stair climb
  - Time to rise from floor





Phase 2 Study in Boys with DMD

LYNX

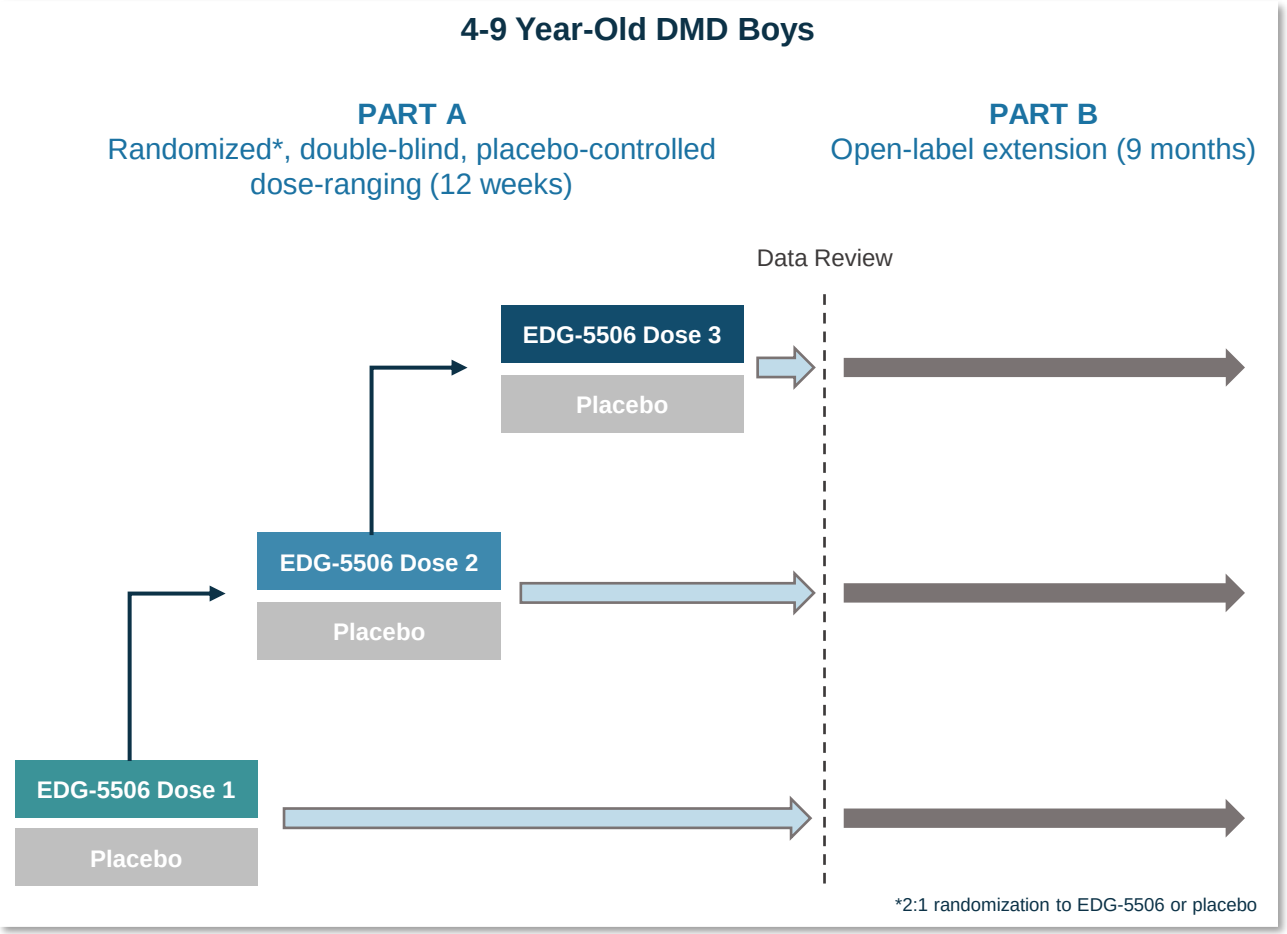
A 2-Part Phase 2 Study of Safety, Pharmacokinetics and Biomarkers in Children with Duchenne Muscular Dystrophy Including a Randomized, Double-Blind, Placebo-Controlled Part A, Followed by an Open-Label Part B

Trial Design

- Population: ~27 participants aged 4 to 9 years inclusive will be randomized to EDG-5506 or placebo in a 2:1 ratio; three dose cohorts will be enrolled sequentially
- Up to 12 sites across the US
- Placebo-controlled, randomized for 3 months with open-label extension to 1 year

Summary of Endpoints

- Primary Endpoint: safety and tolerability of EDG-5506 in children with DMD
- Additional Endpoints:
  - PK of EDG-5506 in children with DMD
  - Effect on biomarkers of muscle damage
  - Functional measures
  - Self-reported/caregiver-reported outcomes



Implications of the 4-Month ARCH Study Data on Our Ongoing and Upcoming Clinical Programs in DMD and BMD

- **The CANYON trial was designed to obtain dose-ranging data on safety and biomarkers, and was powered on biomarker change**

- **The ARCH 4-month data support potential expansion of CANYON to power for functional efficacy, and potentially accelerate the program**

- **The LYNX trial will focus on 3-month biomarker changes to select dose for a pivotal study with an extension to evaluate functional relationship**

Closing Remarks

Kevin Koch, CEO

Edgewise THERAPEUTICS

Summary of Today's EDG-5506 Presentation

Remarkable improvement in NSAA after only 4-months of EDG-5506 dosing

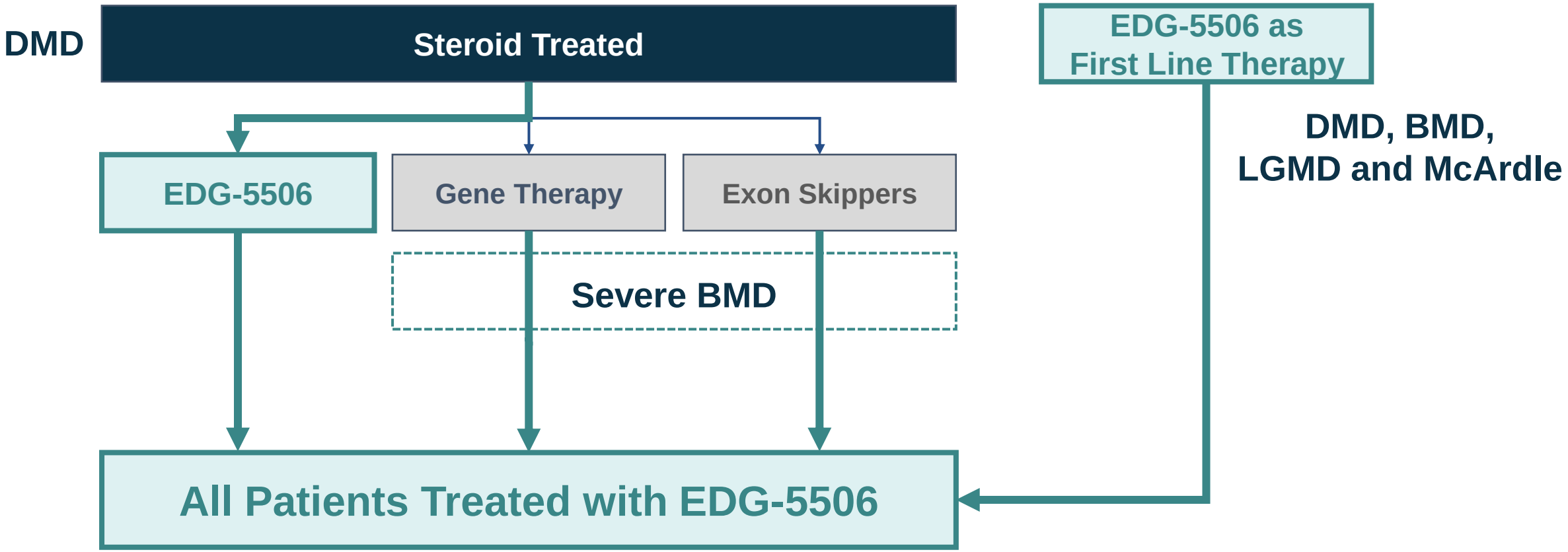
Sustained and highly statistically meaningful decreases in biomarkers of muscle damage

Continues to be generally well tolerated

6-month data expected to be presented at the upcoming World Muscle Society Conference in October

DMD Phase 2 clinical trial expected to commence in 2H22

EDG-5506's Mutation Agnostic MOA Allows Potential Combination with All Therapeutics in Development for Muscular Dystrophy



Additional upside exists in other myopathies

Strong Execution in 1H22 has Positioned Edgewise to be able to Achieve Multiple Milestones

DMD Phase 2 Dose-Ranging Study Start	2H22
BMD Open Label Study Data 6 Month Readout	2H22
Phase 2 Exercise Challenge Start in LGMD2i and McArdle	2H22
Selection of a Novel Cardiac Candidate	2H22

Well-Capitalized to Execute Important Value-Driving Milestones Across Both EDG-5506 and Pipeline Programs

$248M[(1)]

Cash, Cash Equivalents and Marketable Securities

No Debt

49.8M[(1)]

Common Shares Outstanding

NASDAQ: EWTX

(1) As of June 30, 2022


Edgewise
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Thank You and Questions