2-Year Topline Results from the ARCH Study of Sevasemten in Adults with Becker Muscular Dystrophy

April 16, 2024

NASDAQ: EWTX

Edgewise THERAPEUTICS

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Edgewise THERAPEUTICS

Dr. Kevin Koch

Chief Executive Officer

Dr. Joanne Donovan

Chief Medical Officer

Dr. Barry Byrne

UF Health Center & Powell Gene Therapy Center

AGENDA

1. Introduction to Edgewise Therapeutics
2. Contextualizing functional measurements in Becker
3. Results from the 2-year ARCH Becker trial
4. Opportunity in Becker
5. Closing remarks

Opening Remarks

Kevin Koch, CEO

Edgewise THERAPEUTICS

Leaders in muscle disease science

FOCUSED ON MUSCLE SCIENCE

- **Global leader** in muscle disease therapeutic development
- Deep knowledge of **integrated muscle physiology**
- Novel & holistic therapeutic approach to **protect muscle**

RAPIDLY ADVANCING PORTFOLIO

- **Advancing sevasemten to become the foundational therapy for muscular dystrophies**
- **Developing EDG-7500** to target select cardiovascular diseases
- Novel **cardiometabolic targets** in discovery

UNWAVERING PATIENT COMMITMENT

- **Mission-driven focus** on unmet needs in severe muscle conditions
- **Patients & families are critical voices** in all development programs

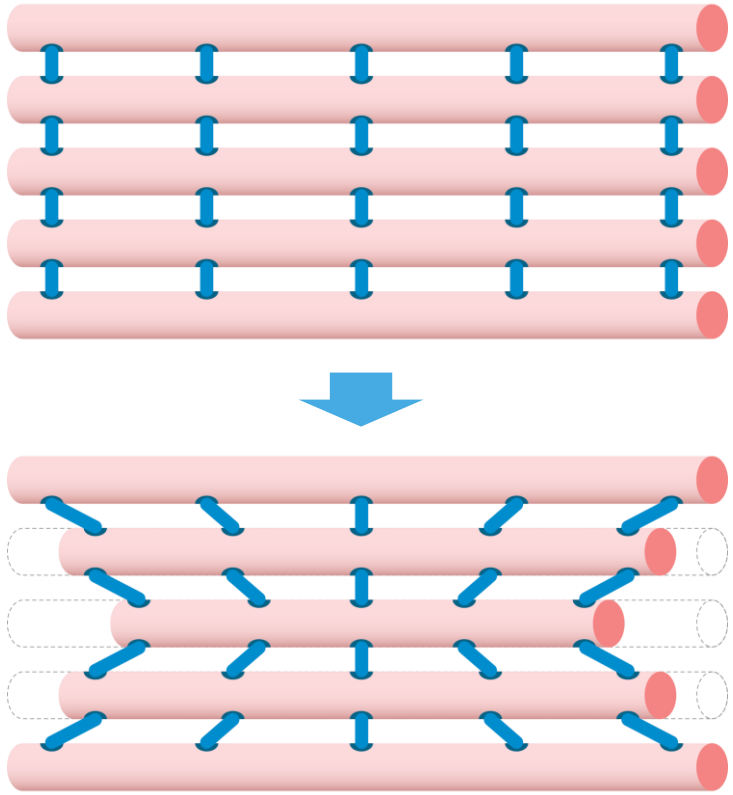
Our goal is to positively impact the course of Becker muscular dystrophy

- Becker is a severe, underappreciated condition with major unmet medical need and no standard of care
- No therapy has ever been approved specifically for Becker
- Can lead to relentlessly progressive loss of motor function
- Individuals with Becker lose mobility, function and independence in the prime of their lives

Source: NIH Genetics Home Reference - Duchenne and Becker muscular dystrophy; Romitti PA et. al., Pediatrics, 2015; Bushby KM, et. al., Lancet, 1991; Salari N, et. al., J Orthop Surg Res, 2022; : J Med Genet 2016;53:145–151; Lancet, 337 (8748), 1022–1024; J Orthop Surg Res 17, 96 (2022)

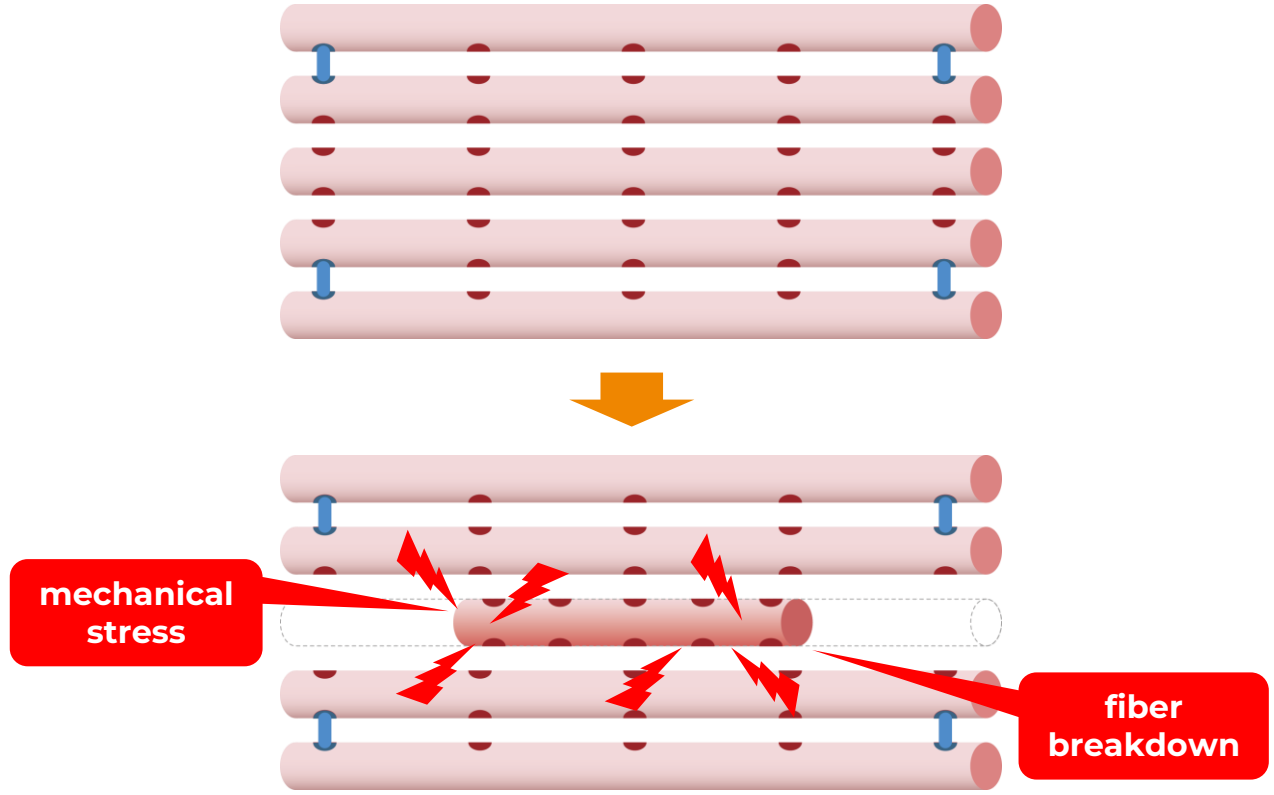
In Becker, fast muscle fibers are disproportionately injured by normal, everyday contractions

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's protective effects against contraction-induced injury in dystrophic muscles demonstrated 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

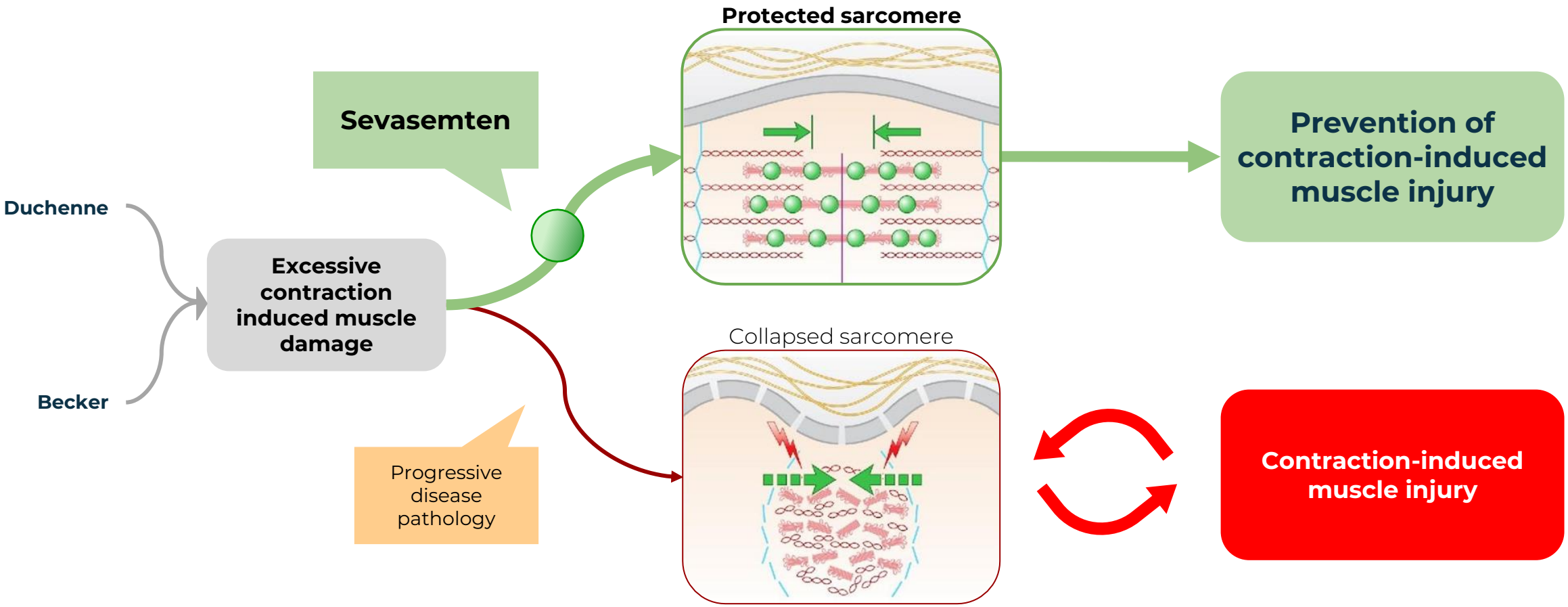
By minimally decreasing contraction while preserving function, contraction-induced injury is prevented

Both videos have been sped up 3x

Reference: Russell AJ, et al. J Clin Invest. 2023;133(10):e153837. doi:10.1172/JCI153837

Sevasemten: A first-in-class fast myofiber (type II) myosin inhibitor designed to protect against contraction-induced muscle injury

Sevasemten Therapeutic Hypothesis

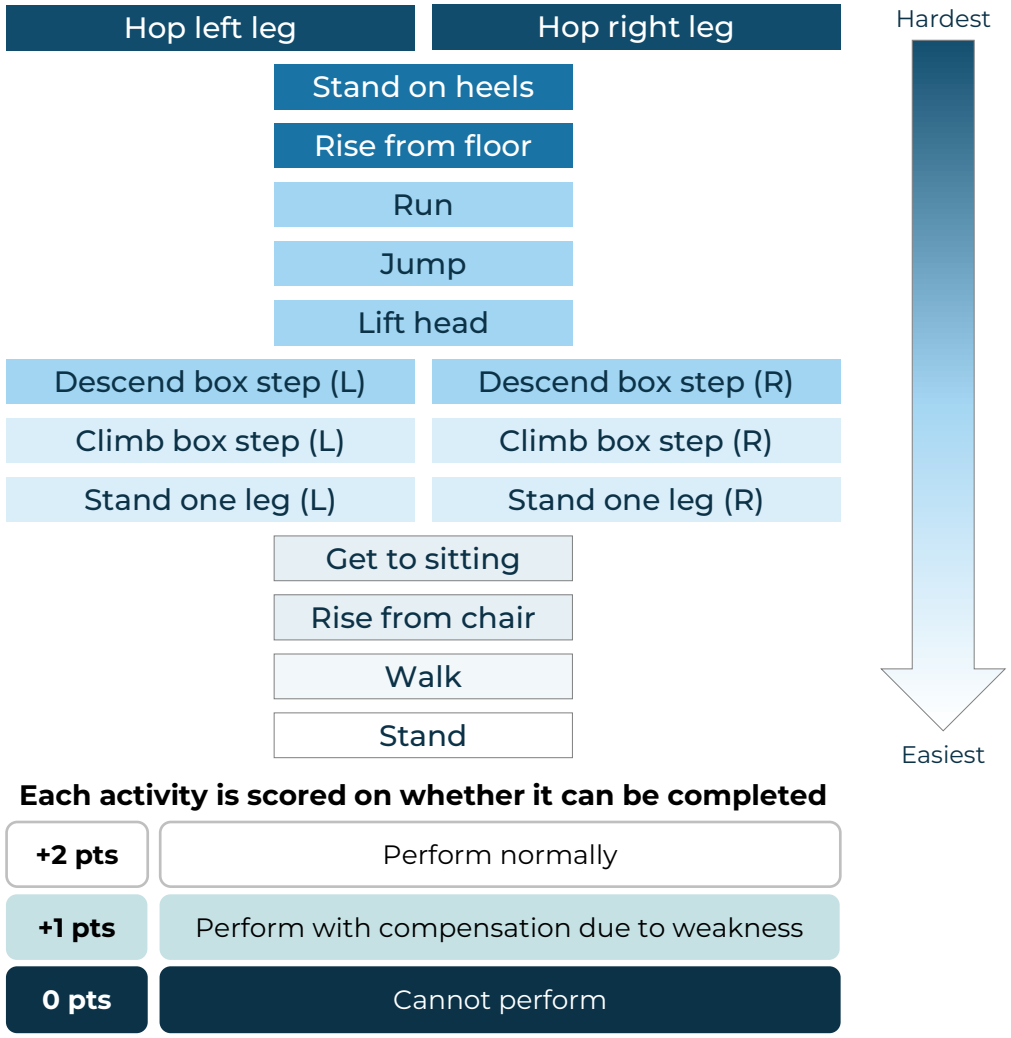


Contextualizing North Star Ambulatory Assessment (NSAA) in Becker Muscular Dystrophy

Barry Byrne, MD, PhD

NSAA: A well-established and validated measure of global function that is clinically meaningful in a real-world context

Composite evaluation of motor function across 17 tests with increasing difficulty



Each activity is scored on whether it can be completed

+2 pts	Perform normally
+1 pts	Perform with compensation due to weakness
0 pts	Cannot perform

Real-world implications for Becker individuals

Measure	Activity
Jump, hop, run	Playing sports
Stand on heels	Walking on uneven ground, cycling, difficulty getting out of a chair, striding, cycling
Rise from floor	Getting up after falling, playing on the floor with children
Climb box steps	Independent outdoor mobility particularly easy tasks like stairs and sidewalk curbs
Stand on one leg	Dressing oneself, putting on shoes/socks while standing, reaching high shelves
Gets to sitting	Sitting up in bed, adjust to falls
Rise from chair	Using a toilet independently, getting out of bed, using public transportation to get around
Walk	Walking to mailbox to pick up mail, hiking, everyday mobility
Stand	Grooming, preparing meals, adapting to mobility device, transferring to chair

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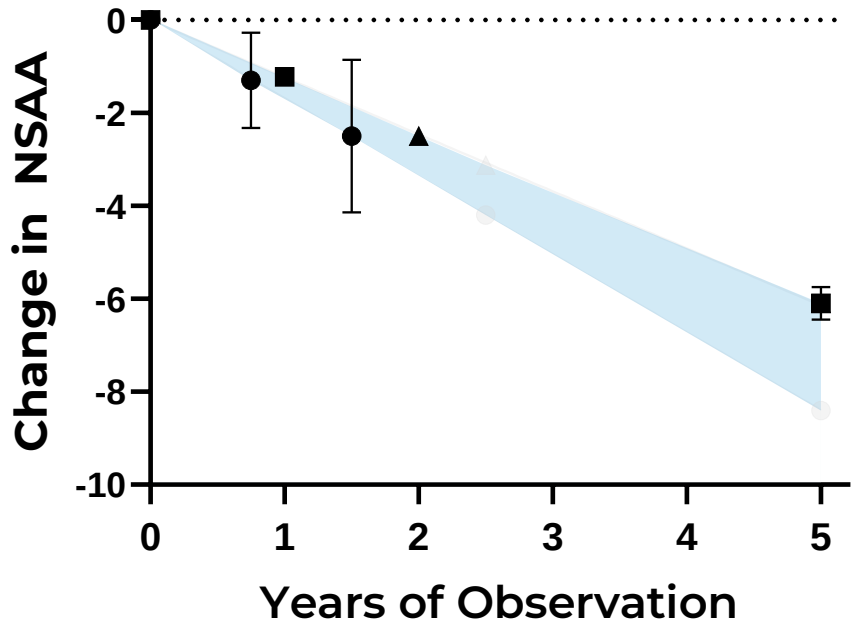
Analysis of NSAA data from the natural history of Becker publications

- The North Star Ambulatory Assessment (NSAA) is a multi-item scale utilized in muscular dystrophy natural history studies to longitudinally assess functional measures.
- Currently available natural history studies observe significant NSAA changes ranging from -1.2 to -2.4 average score declines over various periods of time up to 2 years in ambulatory Becker patients.[1,2,3]
- These natural history studies in Becker patients support that NSAA decline is consistent in Becker patients who are already progressing.

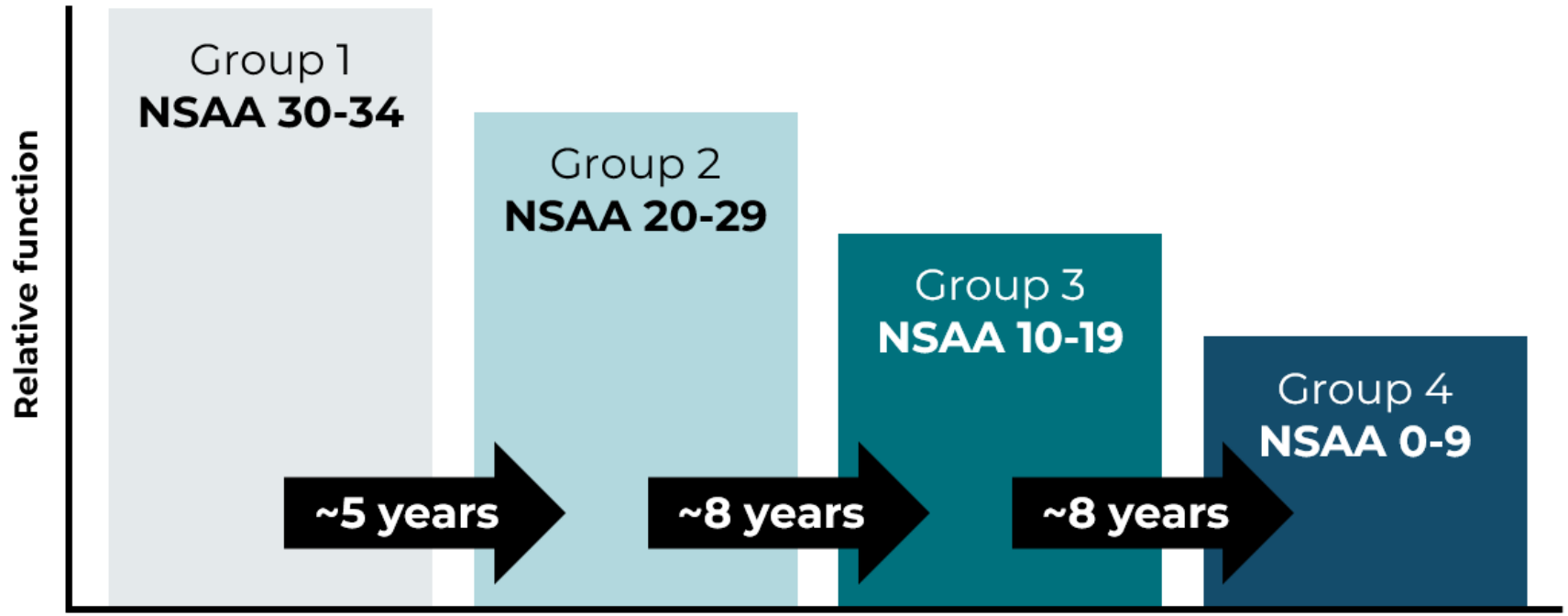
Natural history of Becker muscular dystrophy



Reference: 1. Bello L, et al. Presented at MDA. 2022. 2. De Wel B, et al. Eur J Neurol. 2024. 3. Van de Velde NM, et al. Neurology. 2021.; 95% CI shown

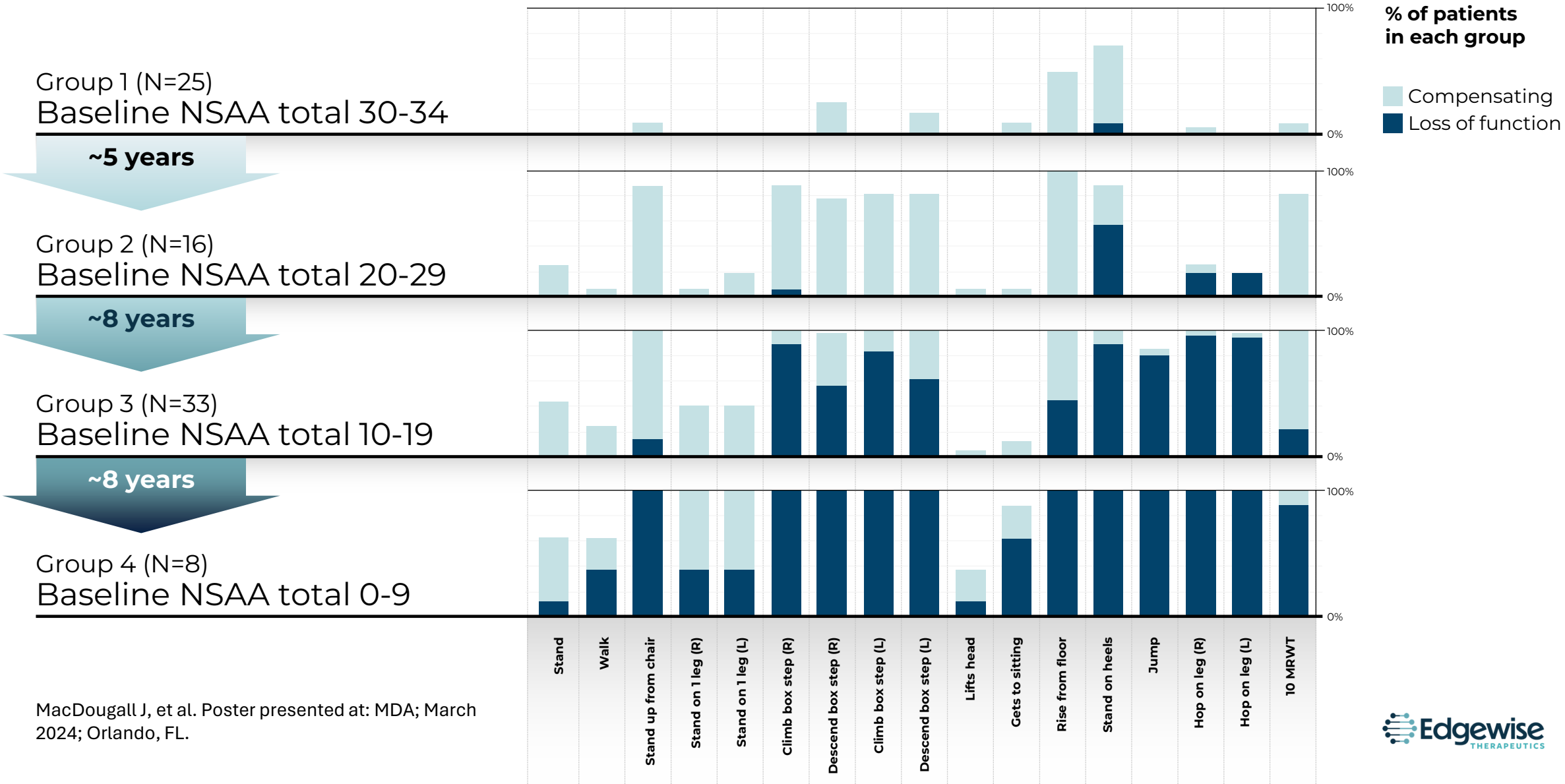
A cross sectional look at NSAA in Becker: Once declining, natural history shows average decrease of ~1.2 NSAA points/year

- Analysis of NSAA scores in Becker adults enrolled in Edgewise studies
  - Grouped by baseline scores: ≥30, 20-29, 10-19, <10
- What does a nominal NSAA mean to an individual with Becker?
  - At different NSAA scores, what functions are completely lost?
  - What functions require some degree of compensation because of weakness?



MacDougall J, et al. Poster presented at: MDA; March 2024; Orlando, FL.

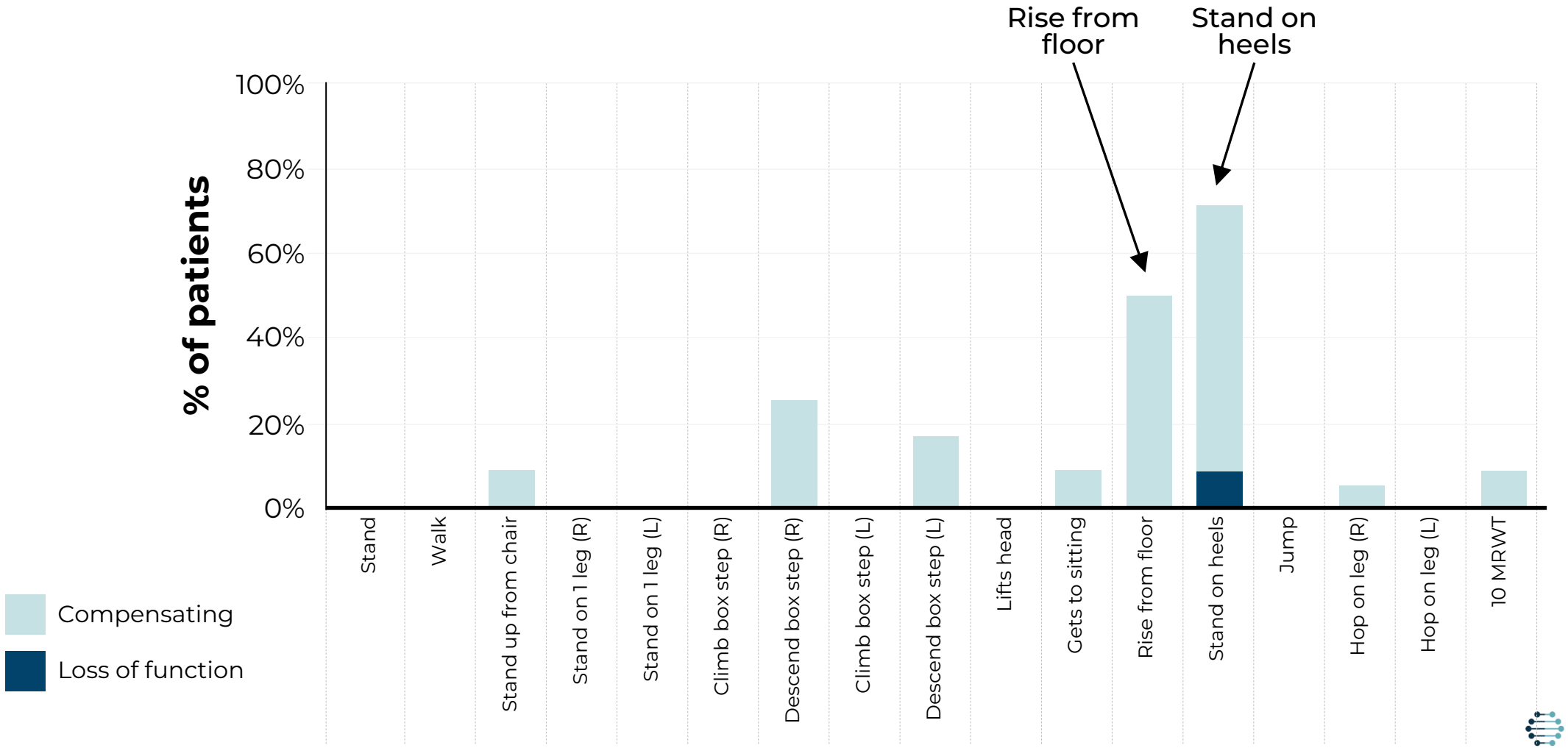
Individuals with Becker experience muscle decline compensation and rapid loss of function as NSAA scores decline



MacDougall J, et al. Poster presented at: MDA; March 2024; Orlando, FL.

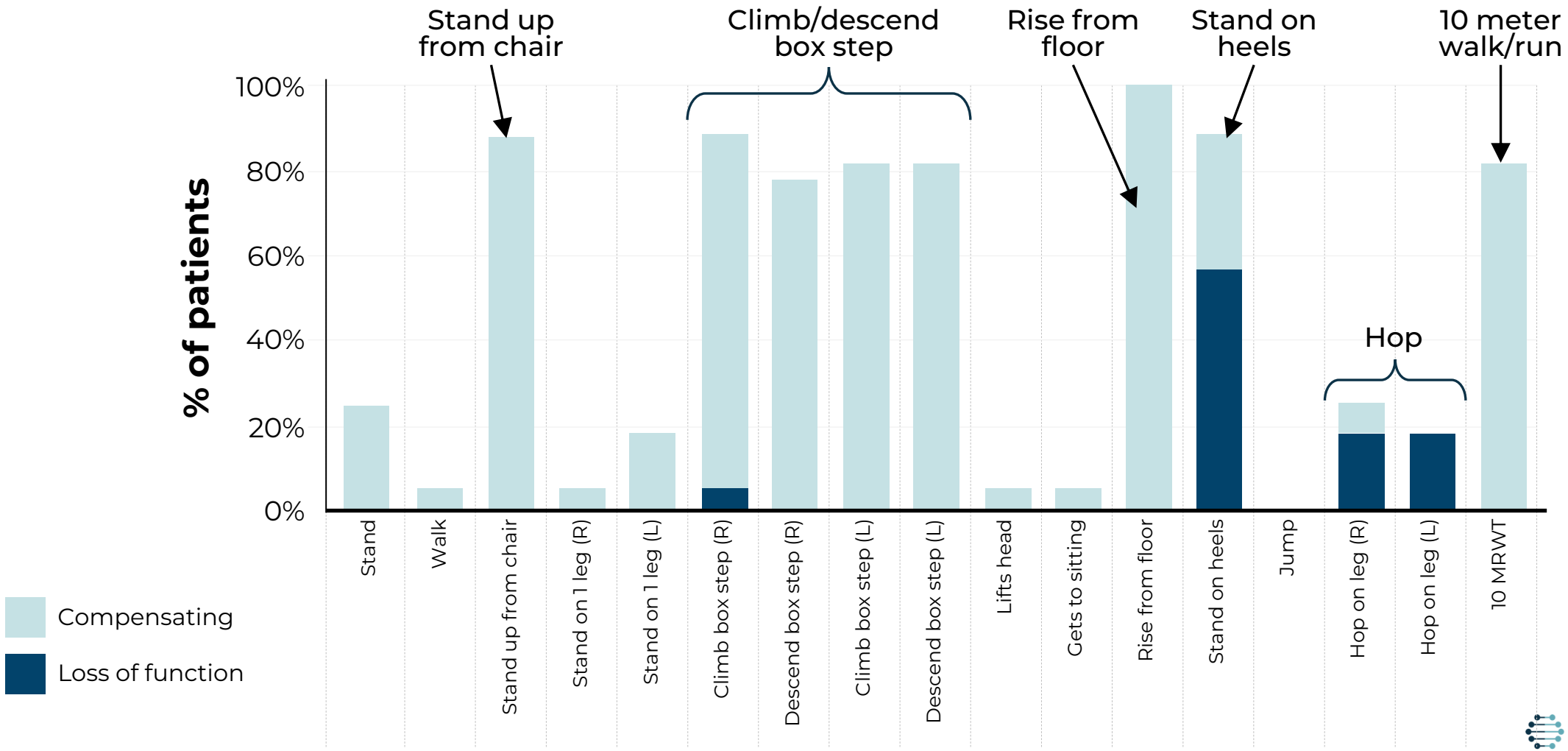
NSAA: Baseline loss of function by item in Becker patients

Becker Group 1: Baseline NSAA total 30-34 (N=25)



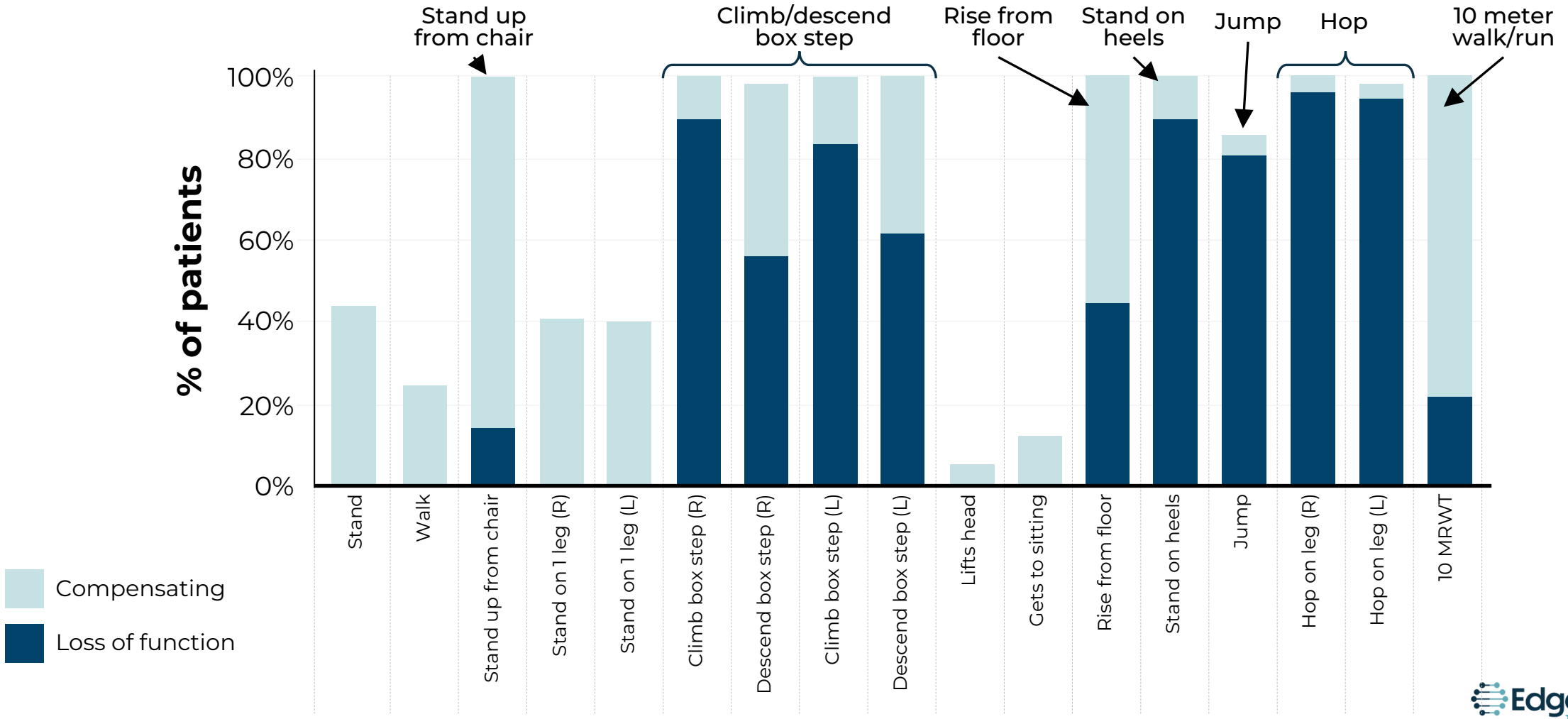
NSAA: Baseline loss of function by item in Becker patients

Becker Group 2: Baseline NSAA total 20-29 (N=16)



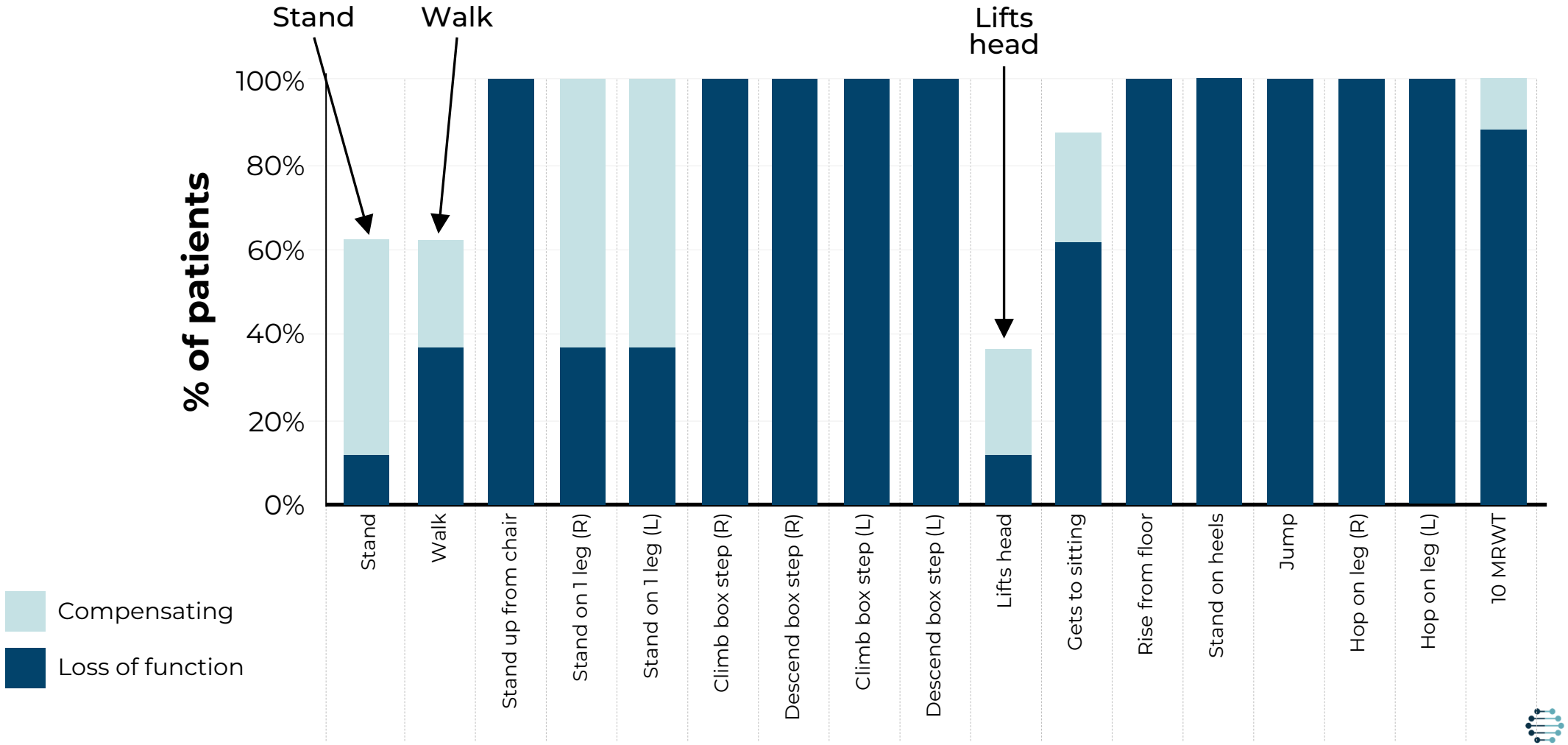
NSAA: Baseline loss of function by item in Becker patients

Becker Group 3: Baseline NSAA total 10-19 (N=33)



NSAA: Baseline loss of function by item in Becker patients

Becker Group 4: Baseline NSAA total 0-9 (N=8)



Caring for individuals with Becker
The impact of a nominal change in NSAA on daily living

Progressive Disease, Rapid Decline

Becker muscular dystrophy is a serious dystrophinopathy. Once function begins to decline, individuals continue to irreversibly lose muscle and their disease progresses.

Maintaining Function

Change in one point on NSAA is viewed as impactful on quality of life.

Stabilizing function or even reducing the slope of decline is an important goal in Becker muscular dystrophy.

Effects of Sevasemten (EDG-5506) on Function and Biomarkers of Muscle Damage in Adults with Becker

Joanne Donovan, MD, PhD
Chief Medical Officer

ARCH

An open-label, single-center study to assess sevasemten safety and pharmacokinetics in Becker

PRIMARY OBJECTIVE

Safety & tolerability

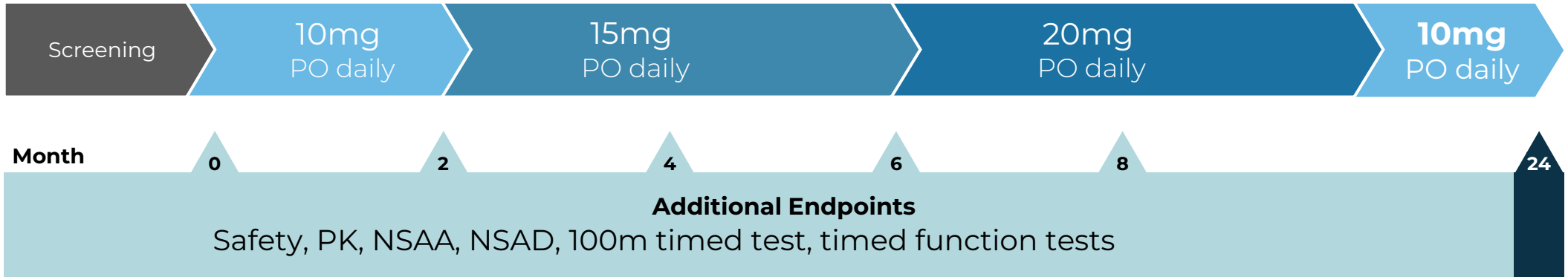
KEY INCLUSION CRITERIA

Ambulatory males aged 18 to 55 years with a dystrophin mutation and a Becker phenotype, not taking corticosteroids, who could complete 100m timed test

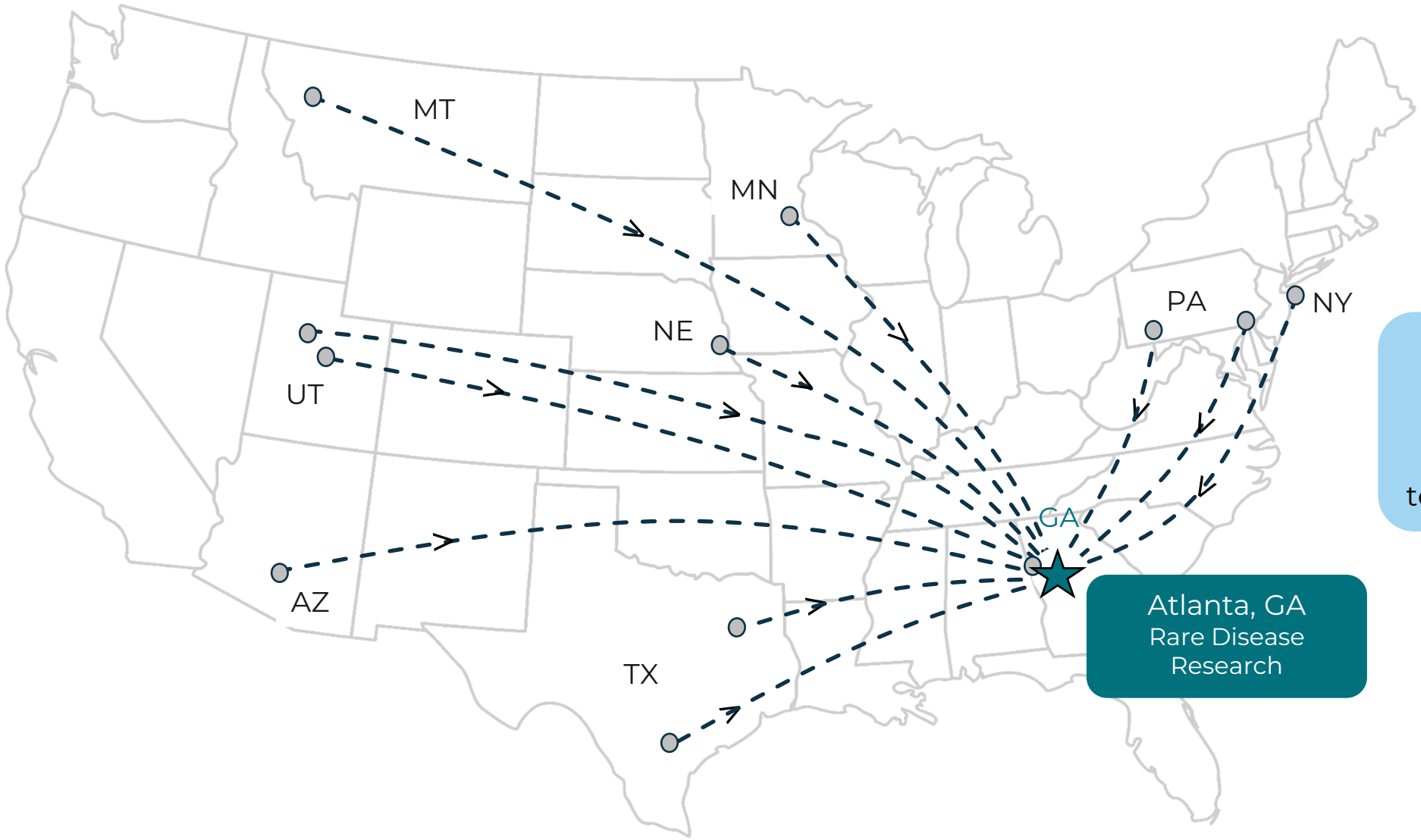
PATIENTS ENROLLED

12

Study design - 24 months



Desire for therapeutics in Becker exemplified by distance travelled by ARCH Patients



Over the course of two years, ARCH participants traveled **190,000 miles** to participate in the study

Significant functional impairment & decreased muscle mass at baseline

CHARACTERISTIC	BECKER PARTICIPANTS (n=12)	AGE NORMATIVE VALUES
Age (SD)	33 (8) 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 (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.

Sevasemten remains well-tolerated at all doses

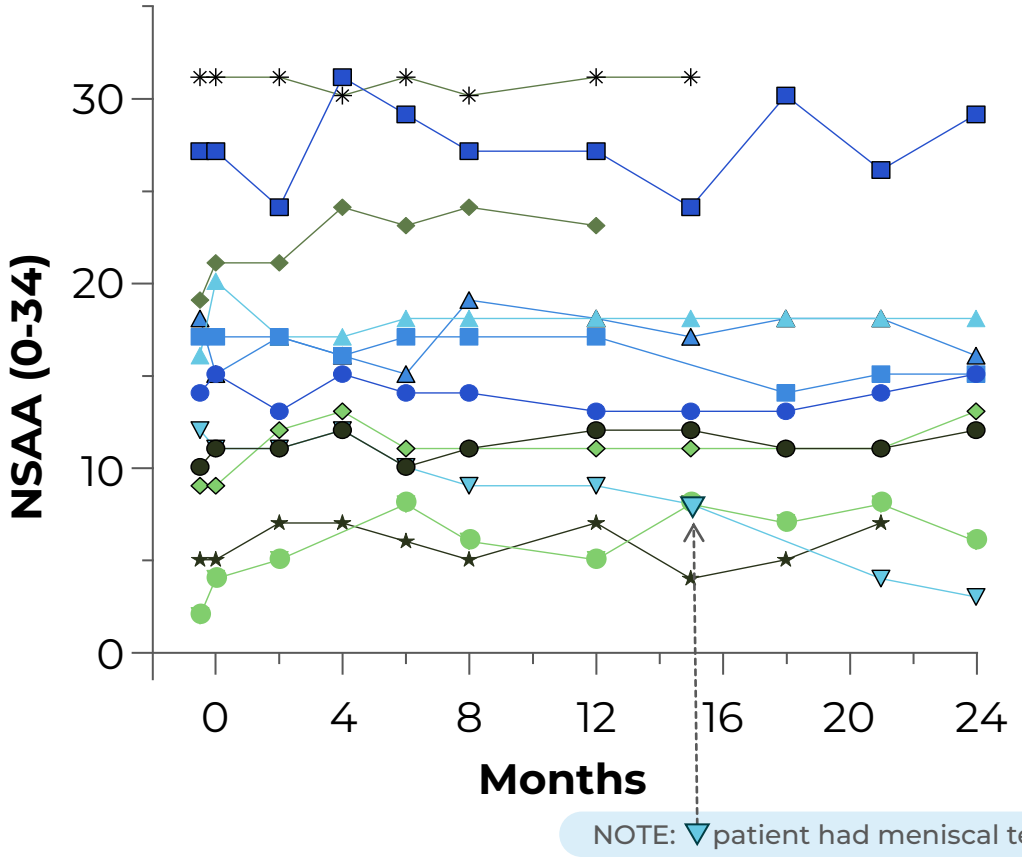
Treatment Emergent AE (seen in >1 subject)	After One Year	After Two Years
COVID-19	4	5
Fall*	3	4
Dizziness	4	4
Arthralgia	4	4
Nasopharyngitis	3	3
URI	3	3
Procedural pain	2	3
Headache	3	3
Somnolence	3	3
GERD	2	3
Influenza	2	3
Sinusitis	2	2

- 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)

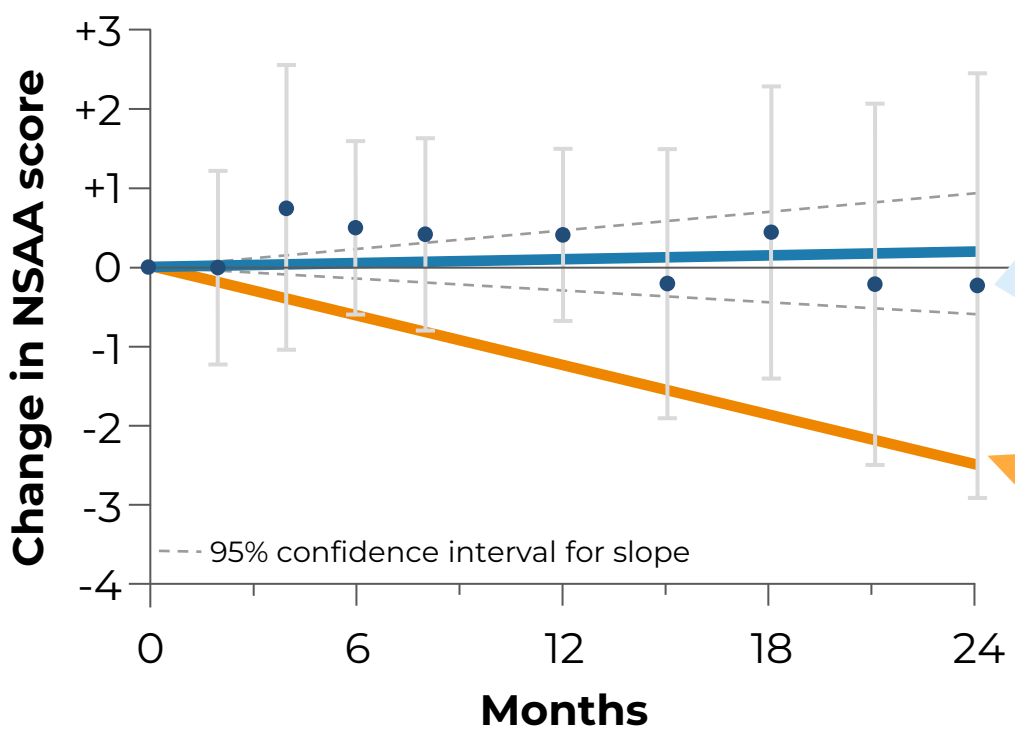
*Falls are typical for Becker patients and are not related to dizziness
AEs, adverse events; SAE, serious adverse events
Reference: Data on File

NSAA stabilized and continues to diverge from natural history at 24 months: Full data set

NSAA responses



NSAA change*



-0.2 mean change in NSAA with sevasemten at 24 months

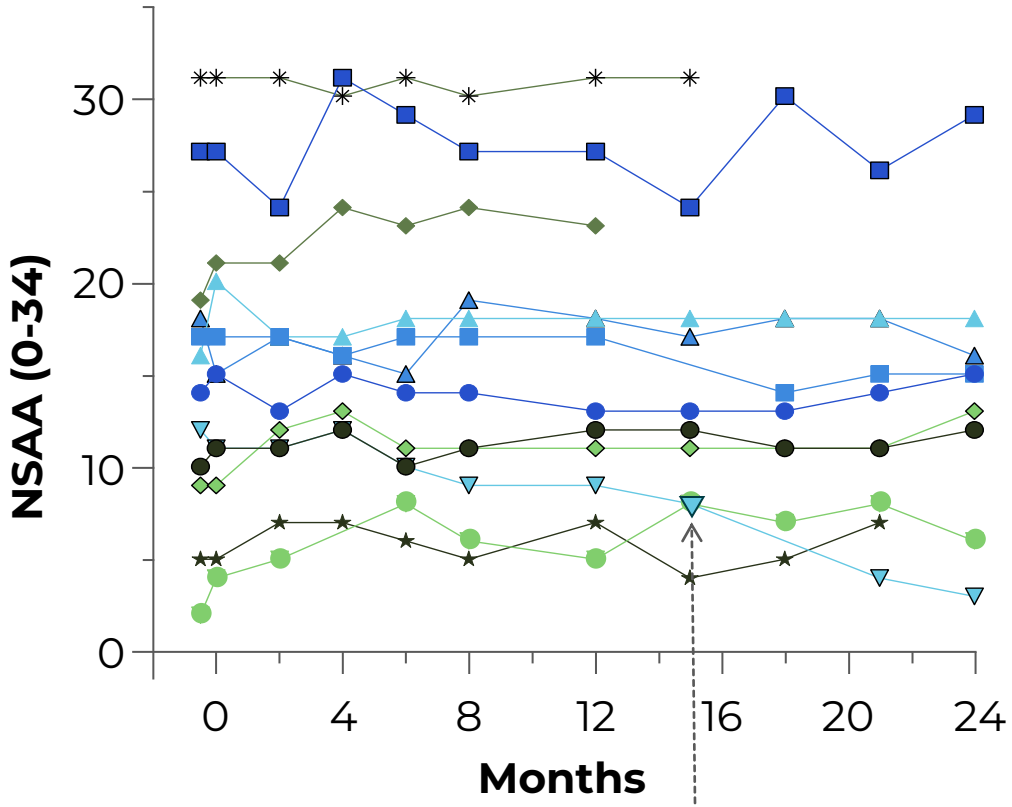
-2.4 Becker natural history average change

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

*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

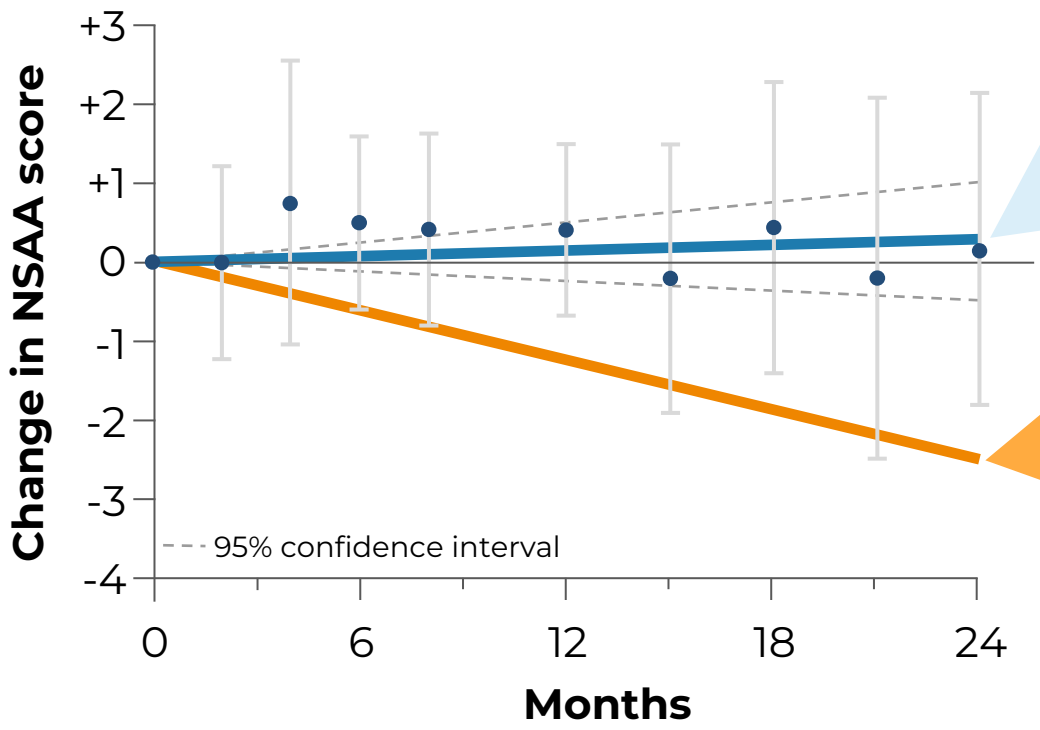
NSAA stabilized and continues to diverge from natural history at 24 months: Last observation carried forward

NSAA responses



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

NSAA change*



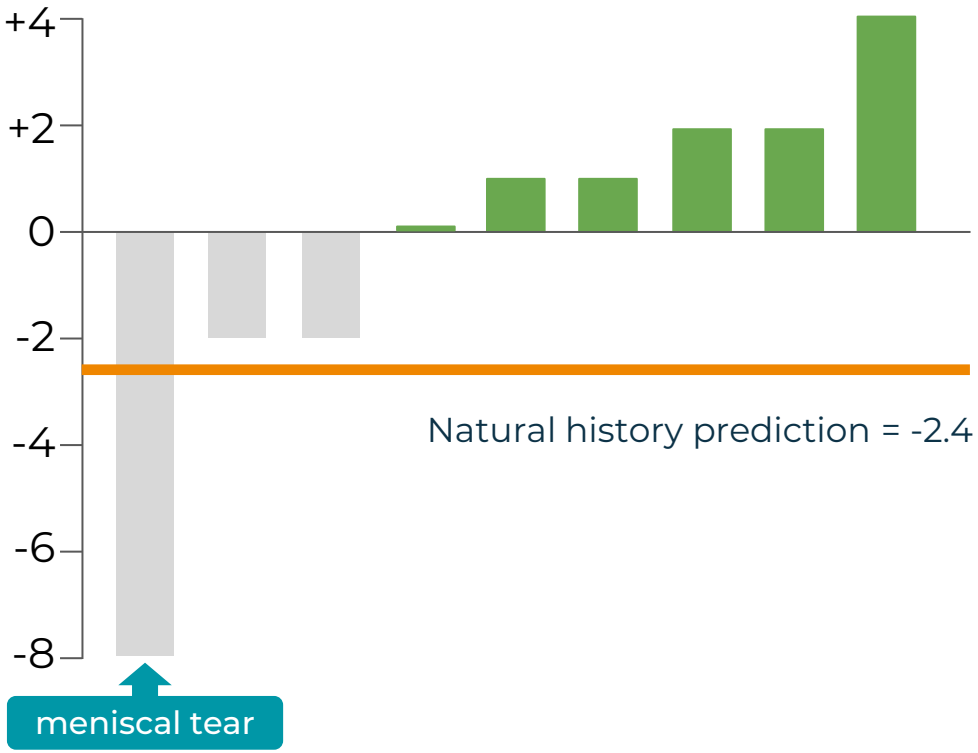
+0.2 mean change in NSAA with sevasemten at 24 months

-2.4 Becker natural history average change

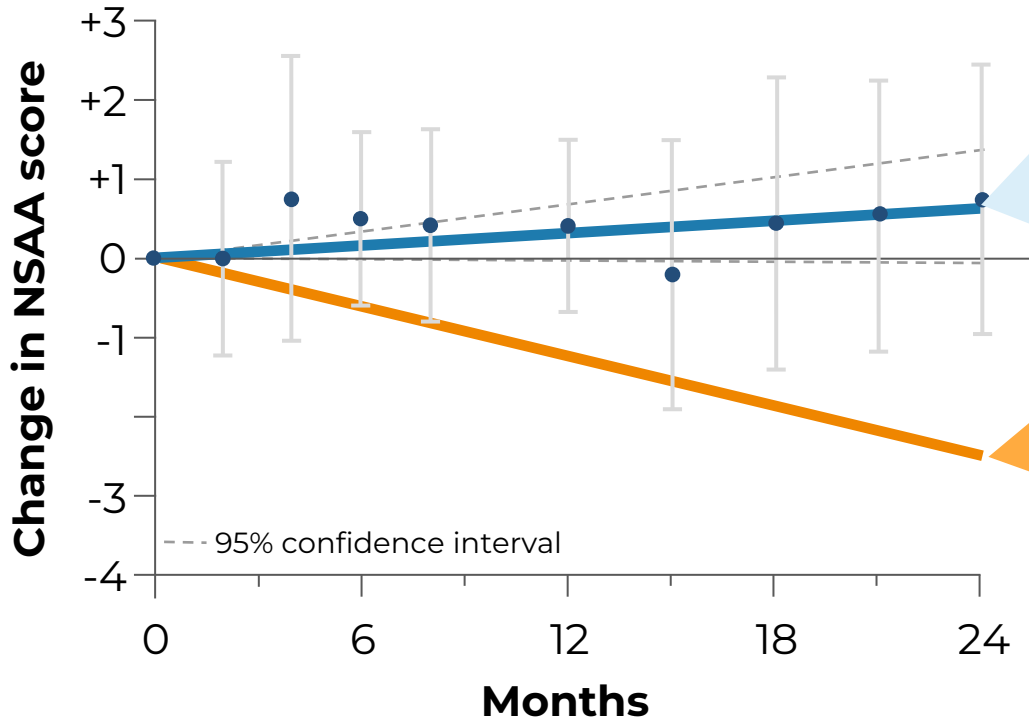
*All data through 24 months, including participant who is recovering from meniscus surgery, LOCF to 24 months only
Natural history based on data presented by Bello at MDA (2022) and van de Velde NM et. al., Neurology, 2021
Mean ± 95% CI; Abbreviations: NSAA, North Star Ambulatory Assessment
Reference: Data on file

NSAA predominantly stable or improved at 24 months

Individual ARCH participant NSAA responses at 24 months**



NSAA change*



+0.75 mean change in NSAA with sevasemten at 24 months

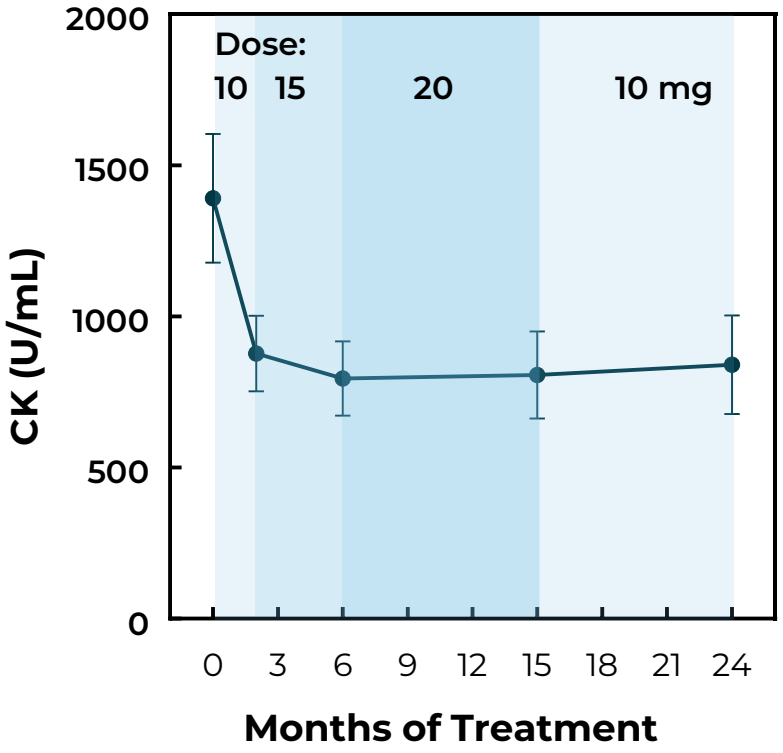
-2.4 Becker natural history average change

N=9 with data at 24 months (3 withdrawal, 1 knee surgery)

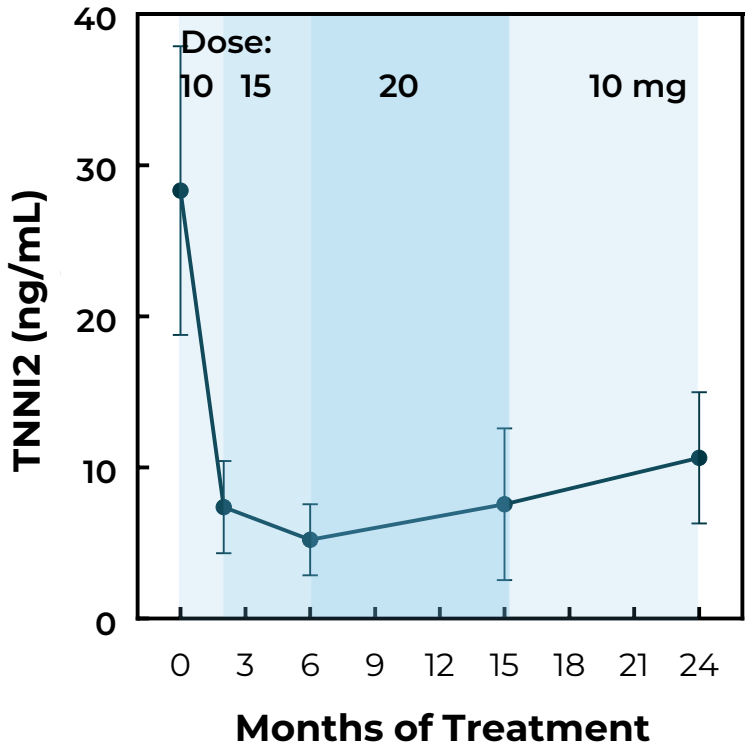
Natural history based on data presented by Bello at MDA (2022) and van de Velde NM et. al., Neurology, 2021
Mean ± 95% CI; Abbreviations: NSAA, North Star Ambulatory Assessment
Reference: Data on file

Biomarkers of muscle damage show rapid and sustained decreases with sevasemten

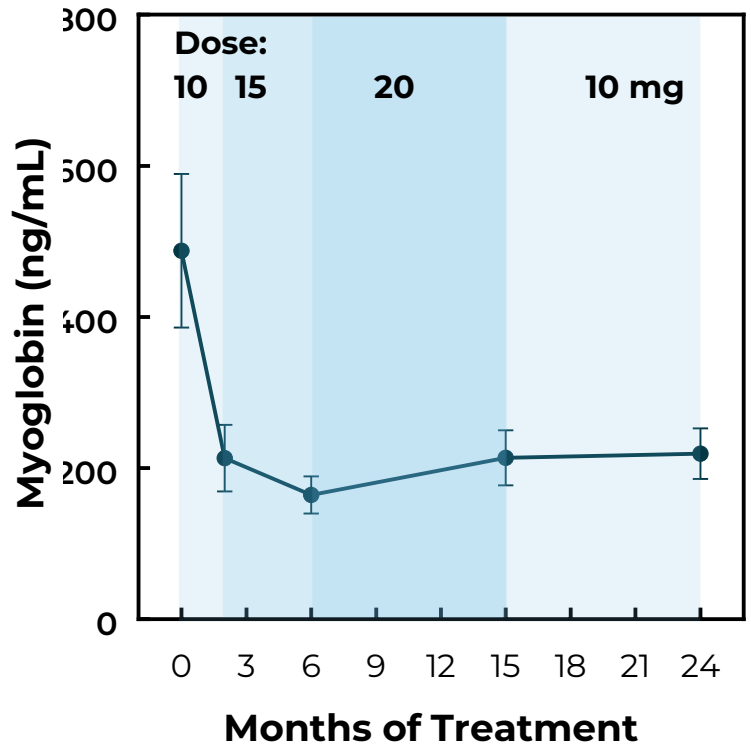
Creatine Kinase (CK)



Fast skeletal muscle troponin I (TNNI2)



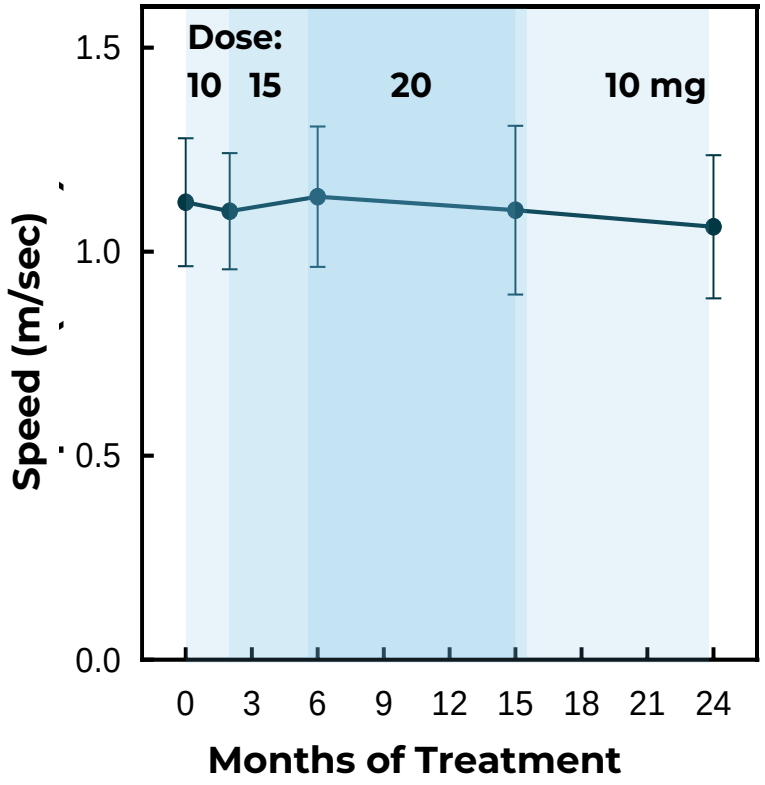
Myoglobin



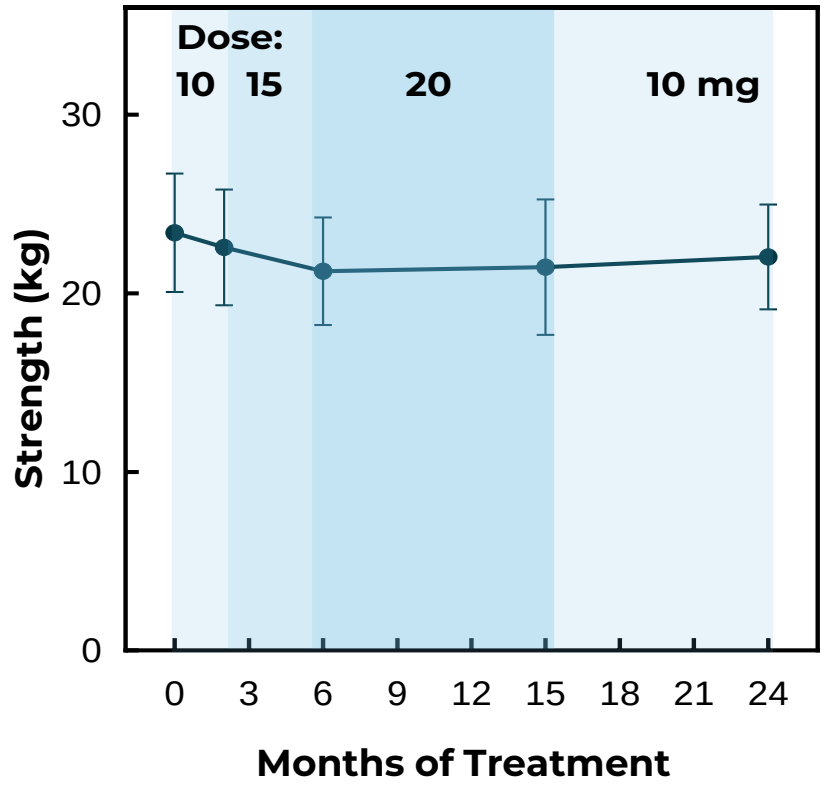
Mean ± SEM
Reference: Data on File

No significant change at 24 months in hand grip strength or measures of endurance

100-Meter Timed Test Velocity



Maximum Grip Strength



Mean ± SEM
Reference: Data on File

Outcomes of the ARCH study

Safety	Biomarkers	Function	Pivotal dose identified
Well-tolerated at all doses	Demonstration of **rapid, sustained and significant decreases** in multiple biomarkers of muscle damage	**Stabilization of functional assessments** with trends toward improvement	Maximal biomarker response at 10 mg dose PK/PD supportive of **10 mg dose for pivotal cohort**

ARCH informed the design of GRAND CANYON, which is potentially registrational

CANYON

The largest interventional Becker study to date

Topline data from CANYON is anticipated in Q4

PRIMARY ENDPOINT

CK at 12 months

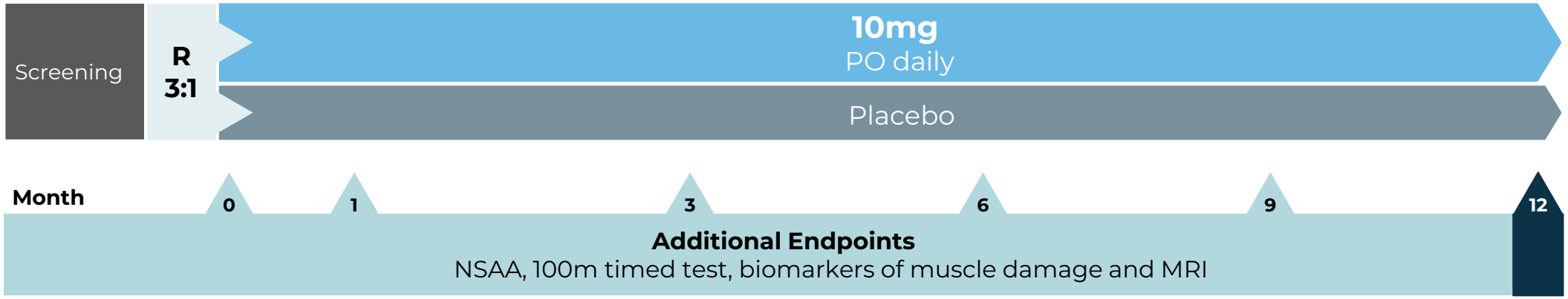
KEY INCLUSION CRITERIA

Adult individuals with Becker with NSAA 5-32, not on corticosteroids

ENROLLMENT

40

Study design - 12 months



CANYON could become a transformative trial for Edgewise

- CANYON data may allow refinement of the statistical analysis plan of the GRAND CANYON pivotal cohort to optimize trial success

- Positive data from CANYON may support pathway to explore early approval of sevasemten for Becker
    - Statistically significant changes in biomarkers of muscle damage and strong trends / statistically meaningful changes in secondary endpoints, including NSAA (with confirmatory GRAND CANYON ongoing)

Topline data from CANYON anticipated in: **4Q24**

Global, multi-center, placebo-controlled pivotal cohort assessing efficacy & safety of sevasemten in Becker

POTENTIAL REGISTRATIONAL TRIAL

PRIMARY ENDPOINT

NSAA at 18 months

KEY INCLUSION CRITERIA

Adult individuals with Becker with NSAA 5-32, not on corticosteroids

TARGET ENROLLMENT

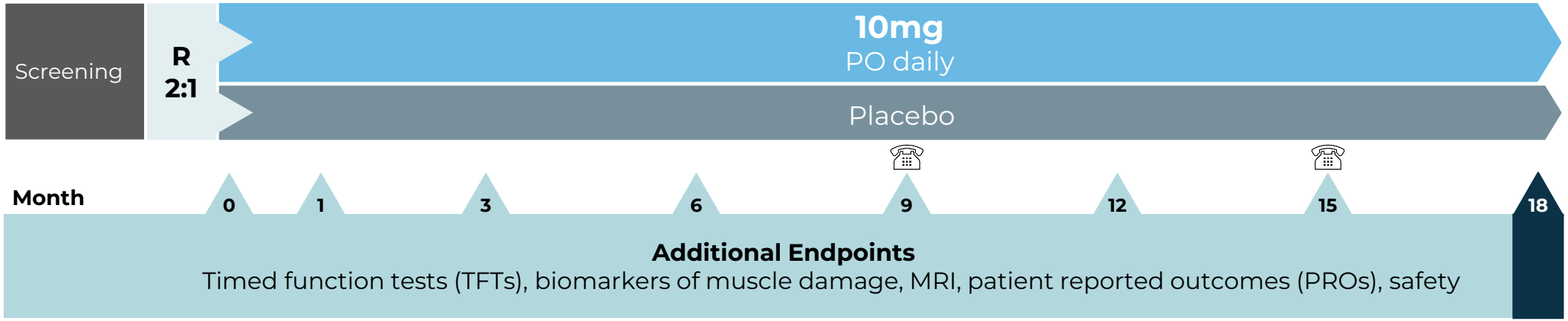
120

POWERED AT

>90%

for observing a difference corresponding to the natural history NSAA decline of 1.2 points/year

Study design - 18 months



We aim to change the lives of individuals with Becker

NUMBER OF APPROVED BECKER THERAPIES

0

AGE AT WHICH BECKER PATIENTS CAN BECOME WHEELCHAIR OR OTHER MOBILITY DEVICE DEPENDENT

>16 years of age

NUMBER OF BECKER PATIENTS IN US, EU-5, & JAPAN

~12,000

Additionally, Duchenne gene therapies are creating a "new" population of Becker-like patients with significant remaining unmet need

ESTABLISHED TREATMENT CENTERS WITH NEUROMUSCULAR SPECIALISTS

>80%

of physicians surveyed will reach out to their Becker patients previously lost to follow-up if sevasemten is approved

Source: Parent Project Muscular Dystrophy: Fifteen Year Registry Report; Edgewise Therapeutics independent quantitative and qualitative market research (Bluestar BioAdvisors); Edgewise research; Emery AE, Neuromuscul. Disord., 1991; MD STARnet Data and Statistics; Duchenne muscular dystrophy. National Center for Advancing Translational Sciences; Duan D et al., Nat. Rev. Dis. Primers, 2021

Well-capitalized to execute important milestones across both sevasemten and EDG-7500

CASH, CASH EQUIVALENTS & MARKETABLE SECURITIES

$550M

DEBT

$0

COMMON SHARES OUTSTANDING (NASDAQ: EWTX)

93M

CASH RUNWAY THROUGH 2027

As of January 31, 2024

Thank You