Sevasemten: Topline Results from the CANYON Phase 2 Trial in Becker

December 16, 2024

Forward Looking Statement

This presentation contains forward-looking statements as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements in this presentation that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding Edgewise's cash runway, Edgewise's expectations relating to its clinical trials and clinical development of sevasemten (EDG-5506) and EDG-7500, including statements regarding the number of individuals to be recruited, timing of completion of recruitment and over-enrollment of the GRAND CANYON trial; statements regarding the potential of, and expectations regarding, Edgewise's product candidates and programs, including sevasemten and EDG-7500; statements regarding Edgewise's milestones; statements regarding whether data from the GRAND CANYON trial could support a marketing application; statements regarding the Company's plans to engage the FDA and European Medicines Agency; statements about sevasemten being the potential first treatment for Becker; and statements by Edgewise's chief executive officer and chief medical officer and Craig M. McDonald, M.D. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. The forward-looking statements contained herein are based upon Edgewise's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those projected in any forward-looking statements due to numerous risks and uncertainties, including but not limited to: risks associated with the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and operating as an early clinical stage company, including the potential for Edgewise's product candidates to cause serious adverse events; Edgewise's ability to develop, initiate or complete clinical trials for, obtain approvals for and commercialize any of its product candidates; Edgewise's ability to take advantage of potential benefits associated with designations granted by FDA and/or to maintain qualifications for applicable designations over time; the timing, progress and results of clinical trials for sevasemten and EDG-7500; Edgewise's ability to enroll and maintain patients in clinical trials; Edgewise's ability to raise any additional funding it will need to continue to pursue its business and product development plans; the timing, scope and likelihood of regulatory filings and approvals; the potential for any clinical trial results to differ from preclinical, interim, preliminary, topline or expected results, including that the primary endpoint of the GRAND CANYON trial (change from baseline in NSAA) will be met even though it was not met as a secondary endpoint in the CANYON trial; the potential that the outcome of preclinical testing and early clinical trials, including the results from the CANYON trial, may not be predictive of the success of later clinical trials, including that the trends from the CANYON trial will also be seen, and will be statistically significant, in the GRAND CANYON trial; Edgewise may gain further insights from its analysis of the CANYON trial results over time, including Edgewise's ongoing evaluation of additional secondary and exploratory endpoints; Edgewise's ability to develop a proprietary drug discovery platform to build a pipeline of product candidates; Edgewise's manufacturing, commercialization and marketing capabilities and strategy; the size of the market opportunity for Edgewise's product candidates; the loss of key scientific or management personnel; competition in the industry in which Edgewise operates; Edgewise's reliance on third parties; Edgewise's ability to obtain and maintain intellectual property protection for its product candidates; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in documents that Edgewise files from time to time with the U.S. Securities and Exchange Commission. These forward-looking statements are made as of the date of this presentation, and Edgewise assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

Agenda

Dr. Kevin Koch
Chief Executive Officer

Dr. Joanne Donovan
Chief Medical Officer

Dr. Craig M. McDonald
Distinguished Professor and Chair at the UC Davis Health Department of Physical Medicine and Rehabilitation

1. Introduction
2. Becker muscular dystrophy and sevasemten
3. Topline results: Phase 2 CANYON trial in Becker
4. Sevasemten future development plans
5. Clinical perspectives on the results
6. Closing remarks
7. Q & A

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

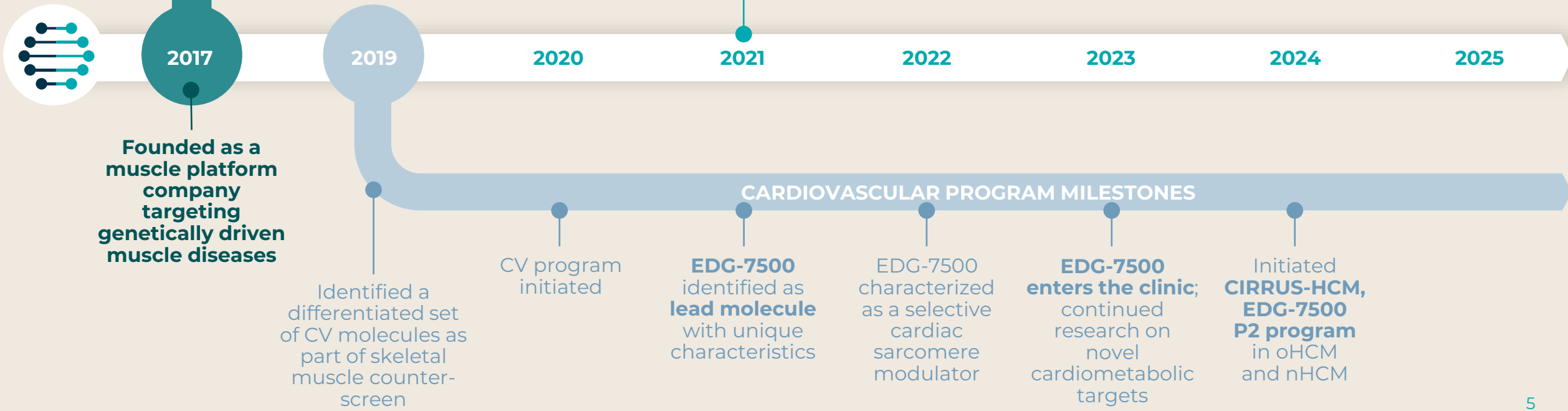
- Sevasemten pivotal program in muscular dystrophies including potential first treatment for Becker
- Advancing EDG-7500 in oHCM, nHCM, and other potential indications
- Novel cardiometabolic targets in discovery

Unwavering patient commitment

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

Abbreviations: oHCM, obstructive hypertrophic cardiomyopathy, nHCM, non-obstructive hypertrophic cardiomyopathy

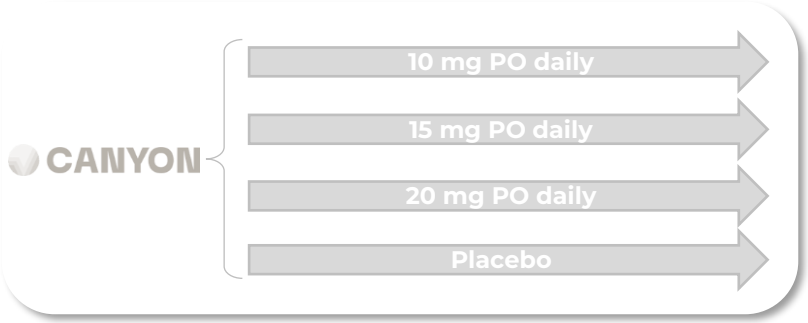
The Evolution of Edgewise



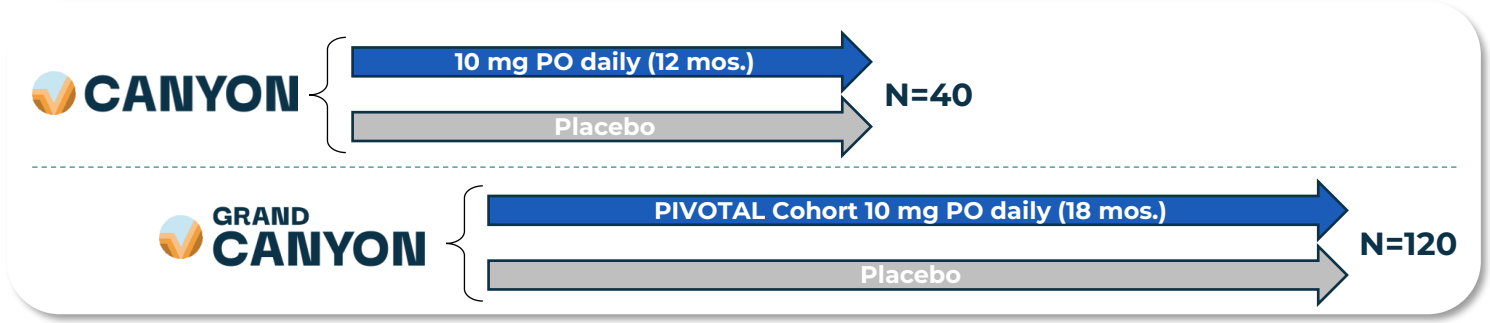
Abbreviations: HVs, healthy volunteers, CV, cardiovascular, oHCM, obstructive hypertrophic cardiomyopathy, nHCM, non-obstructive hypertrophic cardiomyopathy

ARCH, CANYON and the Evolution to GRAND CANYON Expedited the Development Timeline for Sevasemten in Becker

Original CANYON Design



Expanded CANYON/GRAND CANYON Design

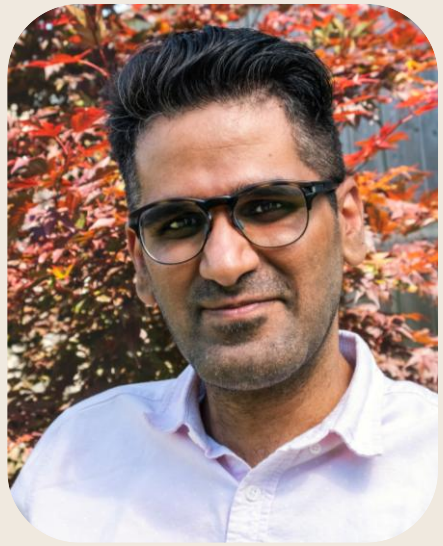


- The Phase 2 CANYON study was originally designed as a dose-finding study to evaluate the effect of sevasemten on safety, pharmacokinetics, biomarkers, and function in individuals with Becker
- 12-month data from the ARCH study supported the hypothesis that a reduction in contraction-induced muscle damage has the potential to preserve and improve muscle function while preventing disease progression
- ARCH identified key factors, including the dose of sevasemten, to allow expansion of CANYON to include the GRAND CANYON cohort as a potentially registrational cohort with NSAA as the primary endpoint
- GRAND CANYON is the first pivotal cohort of an investigational therapy for Becker. Data from GRAND CANYON, if positive, could support a marketing application

This strategic pivot significantly reduced development timelines to support a potential approval of sevasemten for individuals living with Becker

Becker Muscular Dystrophy and Sevasemten

Dr. Joanne Donovan



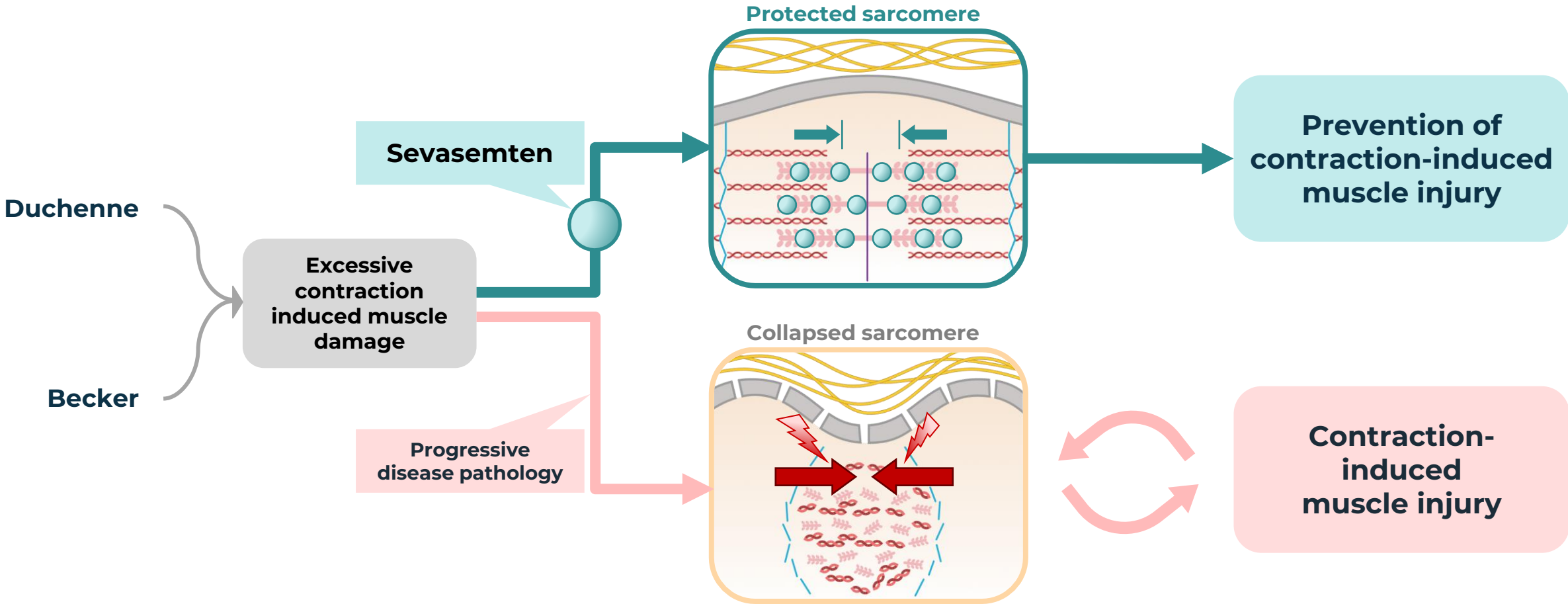
Our goal is to positively impact the course of Becker muscular dystrophy

- Becker is a rare, genetic, life-shortening, debilitating and degenerative neuromuscular disorder
- The disease predominately affects males and imposes significant physical, emotional, financial and social impacts on the individuals and their caregivers
- Individuals with Becker lose mobility, function and independence in the prime of their lives
- There is currently no treatment for Becker

> ***"I was told, 'You're lucky you don't have Duchenne.' It's frustrating that you live longer, but you are constantly going downhill"***
>
> – Individual living with Becker

Sevasemten: A First-in-Class Fast Myofiber (Type II) Myosin Inhibitor Designed to Protect Against Contraction-Induced Muscle Injury

Sevasemten Therapeutic Hypothesis



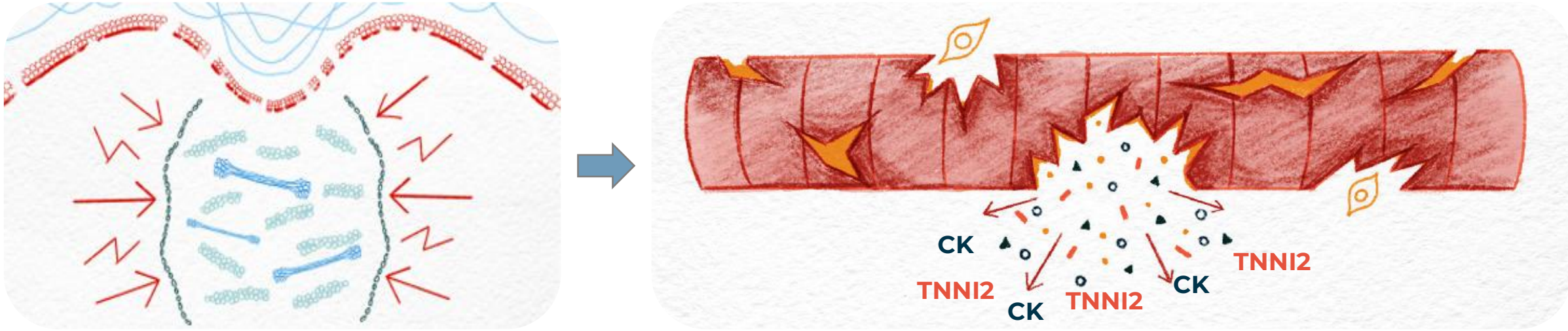
Sevasemten is an investigational therapy that has not been approved for use in muscular dystrophies by any regulatory agency, as its safety and effectiveness have not been established for the treatment of these diseases.
Abbreviations: CK, creatine kinase

Elevated Circulating Levels of Muscle Injury Biomarkers, including CK and TNNI2, Indicate Ongoing Muscle Damage in Muscular Dystrophies

Contraction-Induced Muscle Injury in Muscular Dystrophies

Contraction induced muscle damage causes excessive degeneration

Fast fibers are subsequently injured leading to release of muscle injury biomarkers into the circulation



Circulating Levels of Muscle Injury Biomarkers Can be Measured to Determine Ongoing Muscle Damage in Muscular Dystrophies

Abbreviations: CK, Creatine Kinase; TNNI2, Fast Skeletal Muscle Troponin I

Our Commitment to Becker: Completed and Ongoing Clinical Trials

ARCH	**Phase 1 Becker**	*Open-label, safety, PK, function* → *OLE*	***Complete***
DUNE	**Phase 2 Becker, LGMD2i, & McArdle**	*Exercise challenge study* → *OLE*	***Complete***
CANYON	**Phase 2 Becker**	*PK, biomarkers and longer-term safety* → *OLE*	***Complete***
GRAND CANYON	**Pivotal Cohort Becker** *(NCT05291091)*	*Function (NSAA), PK, biomarkers and longer-term safety* → *OLE*	***Recruiting***
MESA	**Becker Open Label Extension Study** *(NCT06066580)*	*Open-label long-term safety, biomarkers and functional measures*	***Enrolling by invitation***
GRASP-01-002	**Becker Natural History Study** *(NCT05257473)*	*24-Month, observational study*	***Recruiting***

Abbreviations: LGMD, limb-girdle muscular dystrophy; NSAA, North Star ambulatory assessment; PK, pharmacokinetics

CANYON Topline Results

A Phase 2 Multi-Center Study to Assess Sevasemten Safety and Effect on Biomarkers in Adults with Becker

CANYON

ADULT PRIMARY EFFICACY ENDPOINT

Change from baseline in CK averaged across Months 6, 9 and 12

KEY INCLUSION CRITERIA

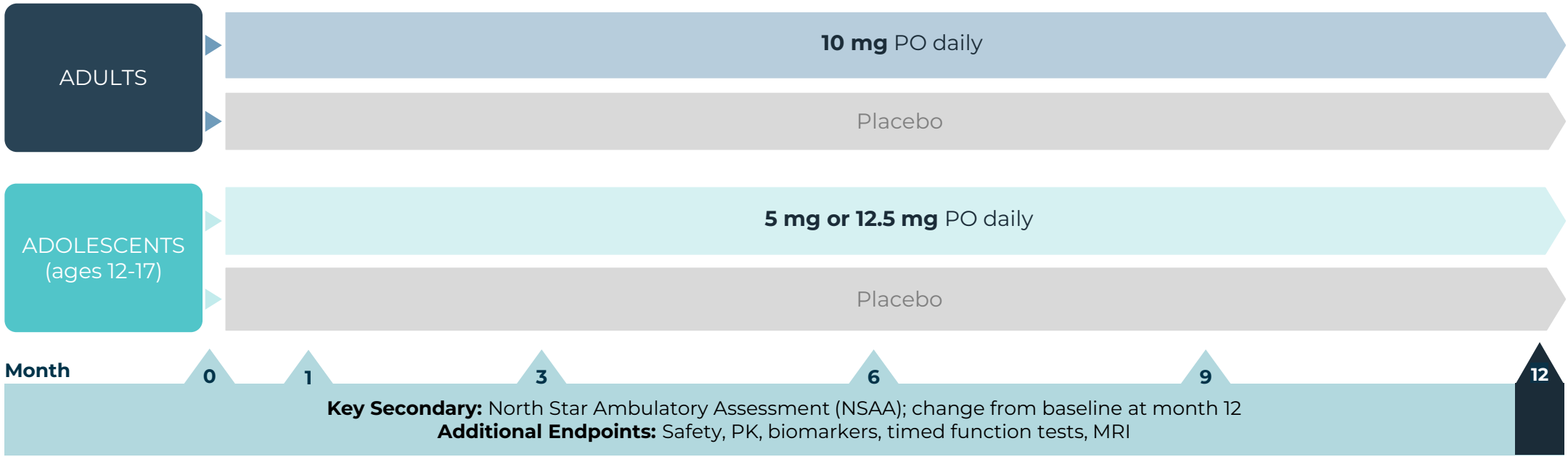
Ambulatory males aged 12 to 50 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, with a **NSAA between 5-32***

PATIENTS ENROLLED

Adults: **40**

Adolescents: **29**

Study design - 12 months



* Adolescents were not selected based on NSAA
Reference: NCT05160415
Abbreviations: CK, creatine kinase

Edgewise THERAPEUTICS

CANYON Summary of Key Study Metrics

3* countries

16 sites

* Trial sites in the US, UK and the Netherlands

Enrollment: Largest Becker study to date

Total of 80 patients screened and 69 patients enrolled:

- Adults: 40
- Adolescents: 29

Low discontinuation rate

- 4% overall
- 2.5% in adult cohort (1 out of 40 enrolled)

99% of eligible participants enrolled in MESA open-label extension

- Approximately, 85 Becker patients currently enrolled in MESA

Becker Mutation Overview: Slow Progressor Genotypes were Largely Excluded with Functional Cut-Off Criteria

Mutation type	Adults (N=40)	Adolescents (N=29)
Becker mutations associated with progression	**39**	**26**
45-x	20	11
Other	19	15
None/very slow progression Becker mutations	**1**	**3**
X-51	1 (sevasemten)	2 (sevasemten)
Del 48	0	0
45-55 (associates with late myopathy)	0	1 (sevasemten)

Reference: Bello L., *et. al.*, *Sci Rep.*, 2016

CANYON Overview of Baseline Function in Safety Population

Functional test	Adults Sevasemten (n=28)	Adults Placebo (n=12)	ARCH (N=12)
Mean total NSAA score, points (SD)	18.4 (7.66)	24.2 (8.19)	15.1 (8.4)
Mean 4SC velocity, 1/seconds (SD)	0.22 (0.128)	0.34 (0.173)	0.19 (0.164)
Mean RFF velocity, 1/seconds (SD)*	0.14 (0.114)	0.21 (0.128)	0.16 (0.196)
Mean 10MWR velocity, meters/second (SD)	1.52 (0.731)	2.00 (0.884)	1.15 (0.521)
Mean 100MTT velocity, meters/second (SD)	1.50 (0.856)	1.78 (0.782)	1.08 (0.496)

*At baseline, 1 placebo and 9 sevasemten treated participants were unable to rise from floor

Abbreviations: NSAA, North Star Ambulatory Assessment

Functional Measures Not Well Matched at Baseline; Patients in Sevasemten Group had Lower Baseline NSAA

Functional test	Adults Sevasemten (n=28)	Adults Placebo (n=12)	Difference (from placebo)	P-value vs. Placebo
Mean total NSAA score, points (SD)	18.4 (7.66)	24.2 (8.19)	**-5.8**	**0.04**
Mean 4SC velocity, 1/seconds (SD)	0.22 (0.128)	0.34 (0.173)	**-0.12**	**0.02**
Mean RFF velocity, 1/seconds (SD)*	0.14 (0.114)	0.21 (0.128)	**-0.07**	**0.09**
Mean 10MWR velocity, meters/second (SD)	1.52 (0.731)	2.00 (0.884)	**-0.48**	**0.08**
Mean 100MTT velocity, meters/second (SD)	1.50 (0.856)	1.78 (0.782)	**-0.28**	**0.32**

*At baseline, 1 placebo and 9 sevasemten treated participants were unable to rise from floor

The baseline imbalance observed is a direct consequence of a small study and should resolve in the larger GRAND CANYON cohort (n=120)

Abbreviations: NSAA, North Star Ambulatory Assessment

Sevasemten was Well Tolerated: Overview of Treatment Emergent Adverse Events (TEAE)

Functional test	Sevasemten (n=28) n (%)	Placebo (n=12) n (%)	Total (N=40) n (%)
Any TEAE*	26 (92.9)	10 (83.3)	36 (90)
Severe TEAE	0 (0)	0 (0)	0 (0)
Serious Adverse Events	1 (3.6)	0 (0)	1 (2.5)
Any drug related TEAE	16 (57.1)	5 (41.7)	21 (52.5)
Discontinuation due to TEAE	1 (3.6)	0 (0)	1 (2.5)
Deaths	0 (0)	0 (0)	0 (0)

* A treatment emergent adverse event (TEAE) is any adverse event (AE) that starts during or after the first dose of investigational product through the end of the safety follow-up period

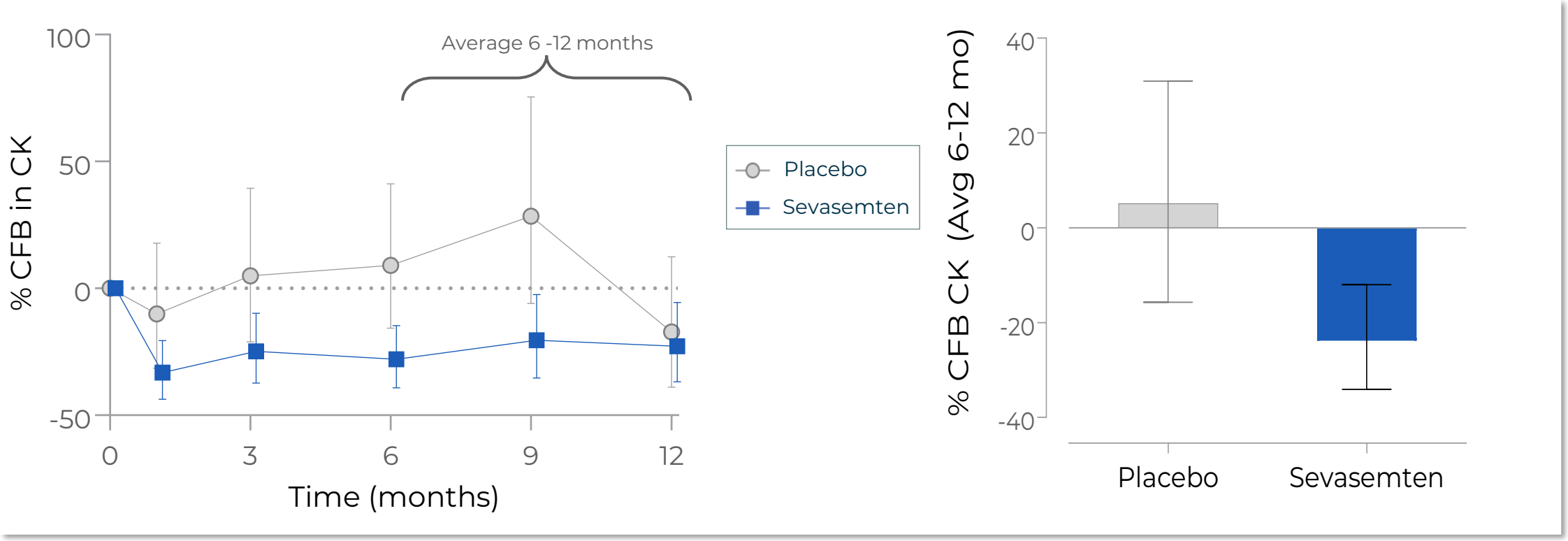
Sevasemten was Well Tolerated: TEAEs Occurring in ≥5% of Total

System Organ Class/Preferred Term	Sevasemten (n=28) n (%)	Placebo (n=12) n (%)	Total (N=40) n (%)
Any TEAE	**26 (92.9%)**	**10 (83.3%)**	**36 (90%)**
Eye disorders			
Vision blurred	1 (3.6%)	2 (17%)	3 (8%)
Gastrointestinal disorders			
Abdominal pain	1 (4%)	1 (8%)	2 (5.%)
Vomiting	2 (7%)	0 (0%)	2 (5.%)
General disorders and administration site conditions			
Fatigue	5 (18%)	3 (25%)	8 (20%)
Chest discomfort	2 (7%)	0 (0%)	2 (5%)
Influenza like illness	2 (7%)	0 (0%)	2 (5%)
Infections and infestations			
COVID-19	6 (21%)	2 (17%)	8 (20%)
Nasopharyngitis	6 (21%)	2 (17%)	8 (20.%)
Upper respiratory tract infection	5 (18%)	2 (17%)	7 (18%)
Influenza	4 (14%)	1 (8%)	5 (13%)
Injury, poisoning and procedural complications			
Fall	8 (29%)	2 (17%)	10 (25%)
Back injury	1 (4%)	1 (8%)	2 (5%)
Investigations			
Ejection fraction decreased	0 (0%)	2 (17%)	2 (5%)
Musculoskeletal and connective tissue disorders			
Arthralgia	2 (7%)	1 (8%)	3 (8%)
Back pain	3 (11%)	0 (0%)	3 (8%)
Osteopenia	2 (7%)	0 (0%)	2 (5%)
Tendonitis	2 (7%)	0 (0%)	2 (5%)
Nervous system disorders			
Headache	9 (32%)	2 (17%)	11 (28%)
Dizziness	9 (32%)	0 (0%)	9 (23%)
Somnolence	5 (18%)	1 (8%)	6 (15%)
Migraine	3 (11%)	1 (8%)	4 (10%)
Dizziness postural	2 (7%)	1 (8%)	3 (8%)
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	4 (14%)	0 (0%)	4 (10%)
Cough	3 (11%)	0 (0%)	3 (8%)
Nasal congestion	2 (7%)	0 (0%)	2 (5%)

Statistically Significant Decrease in the Primary Endpoint of CK: **28%** Reduction vs Placebo

CK between-group difference LSMean: **-28%**

(95% CI -44% to -6%); **p-value = 0.02**



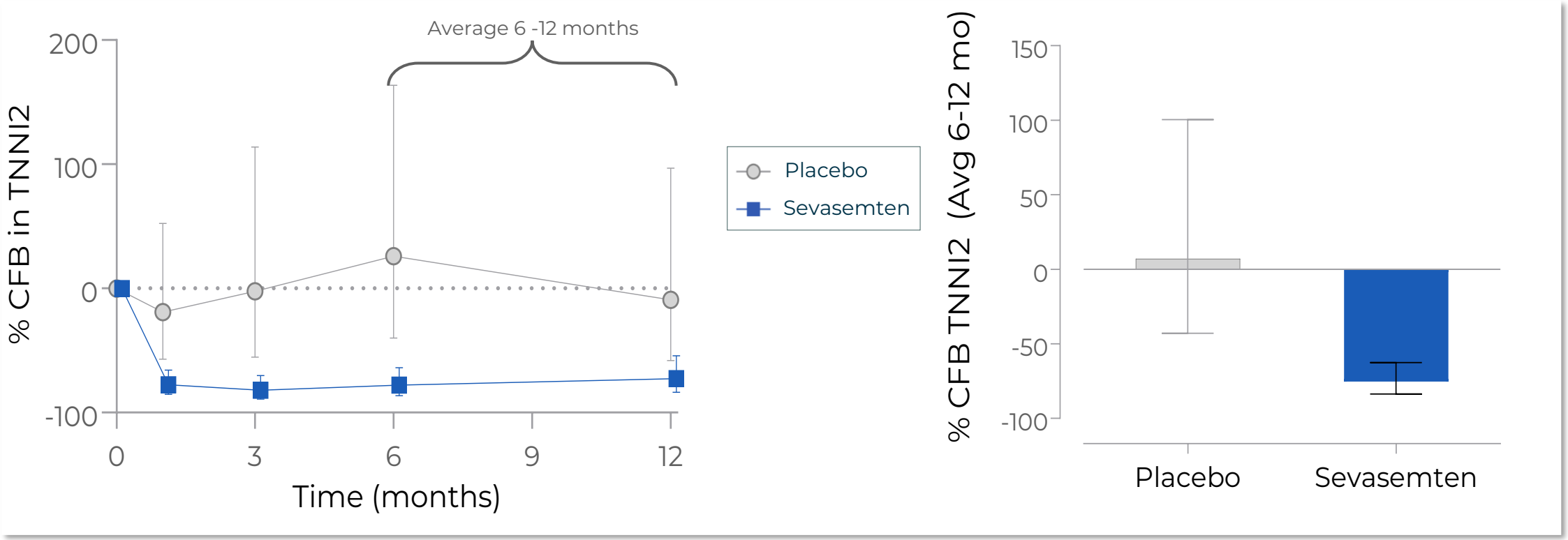
CK showed rapid and sustained decreases with sevasemten treatment

Note: CK values are log-transformed. LS (least squares) means, LS mean differences and CIs were back-transformed to percent scale
Abbreviations: CFB, change from baseline, CI, confidence interval, CK, creatine kinase

TNNI2 Decreased **77%** from Baseline in the Sevasemten Treatment Group vs Placebo

TNNI2 between-group difference LSMean: **-77%**

(95% CI -89% to 51%); **p-value < 0.001**



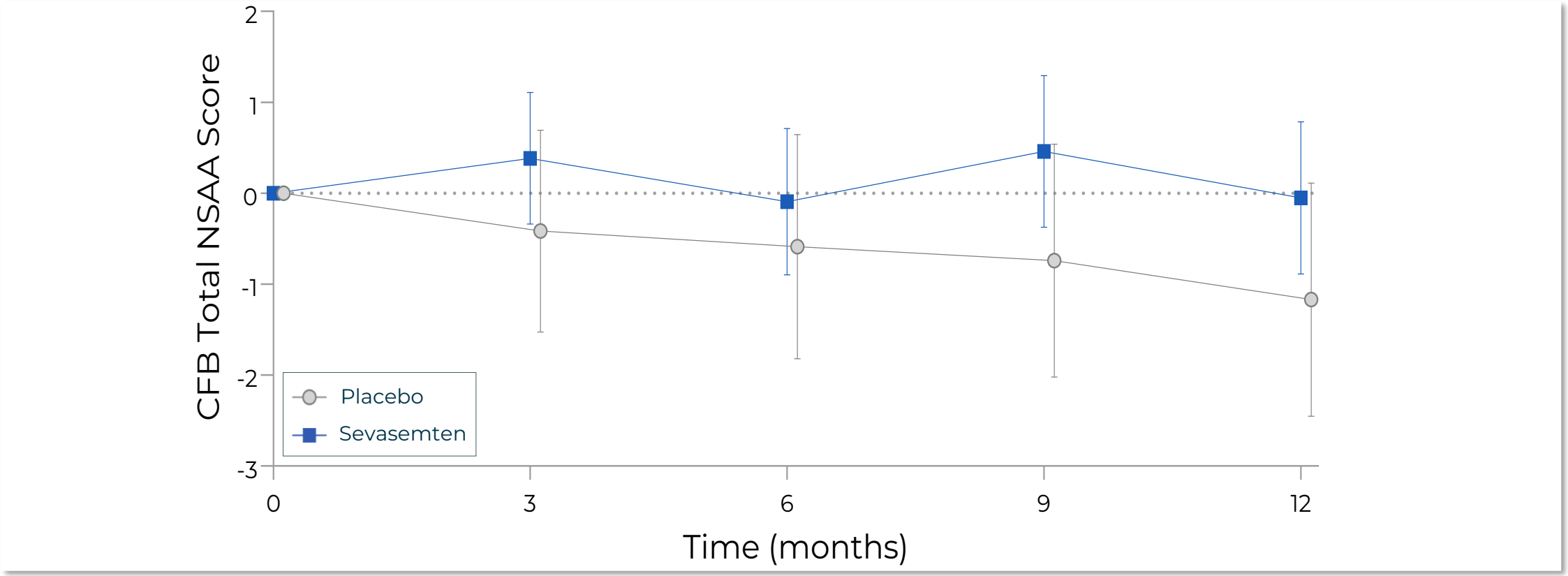
TNNI2, an on-target biomarker of fast muscle fiber damage, also demonstrated rapid and sustained decreases with sevasemten treatment

Note: TNNI2 values are log-transformed. LS means, LS mean differences and CIs were back-transformed to percent scale
Abbreviations: CFB, change from baseline, CI, confidence interval, TNNI2, troponin I2

Key Secondary Endpoint: NSAA **Remained Stable** Over Time in Sevasemten Group

NSAA between-group difference LSMean: **1.12**

(95% CI -0.4 to 2.7); **p-value = 0.16**



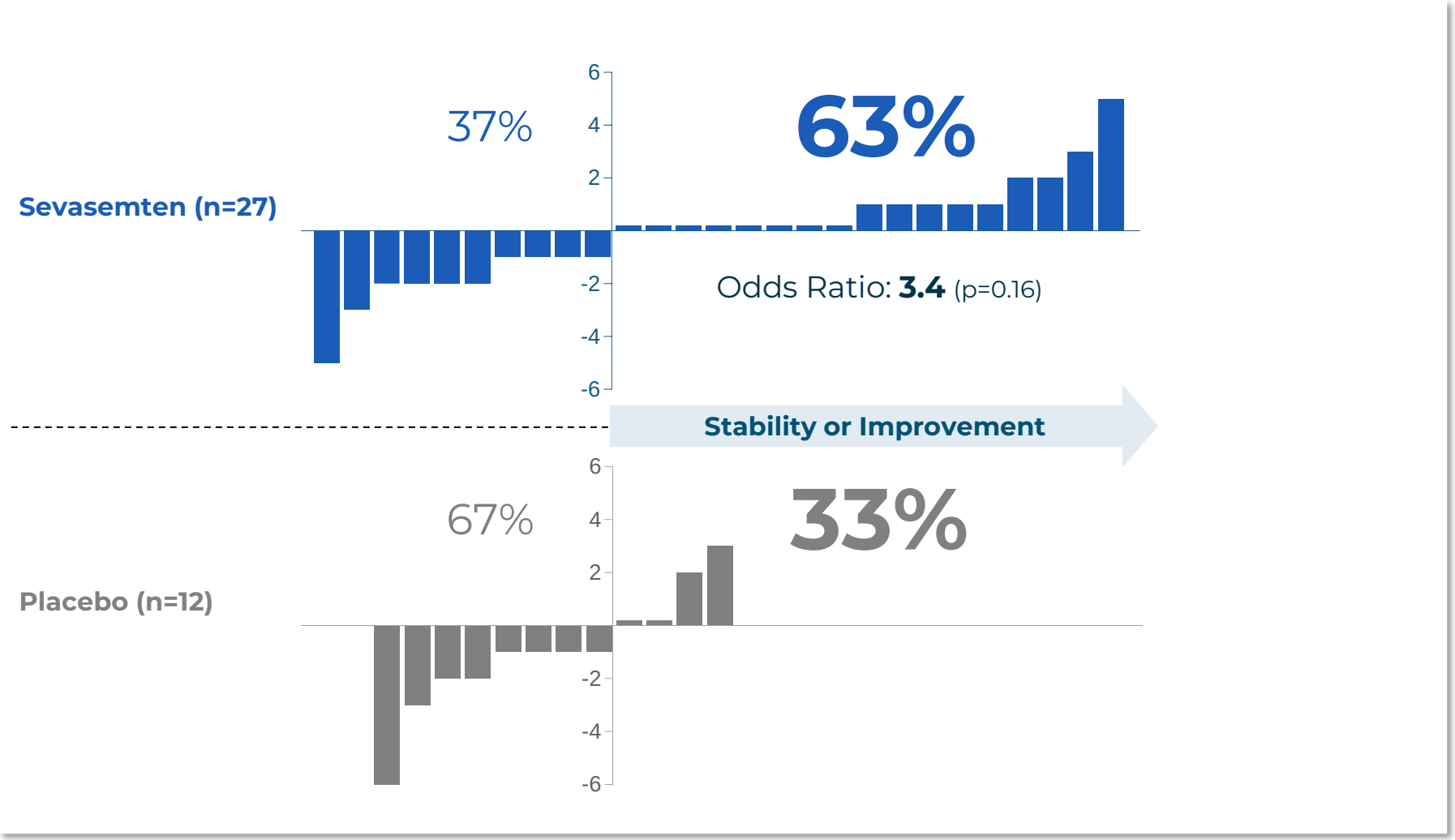
Positive trends in NSAA favoring sevasemten with placebo declining in line with natural history

Abbreviations: NSAA, North Star Ambulatory Assessment

CANYON

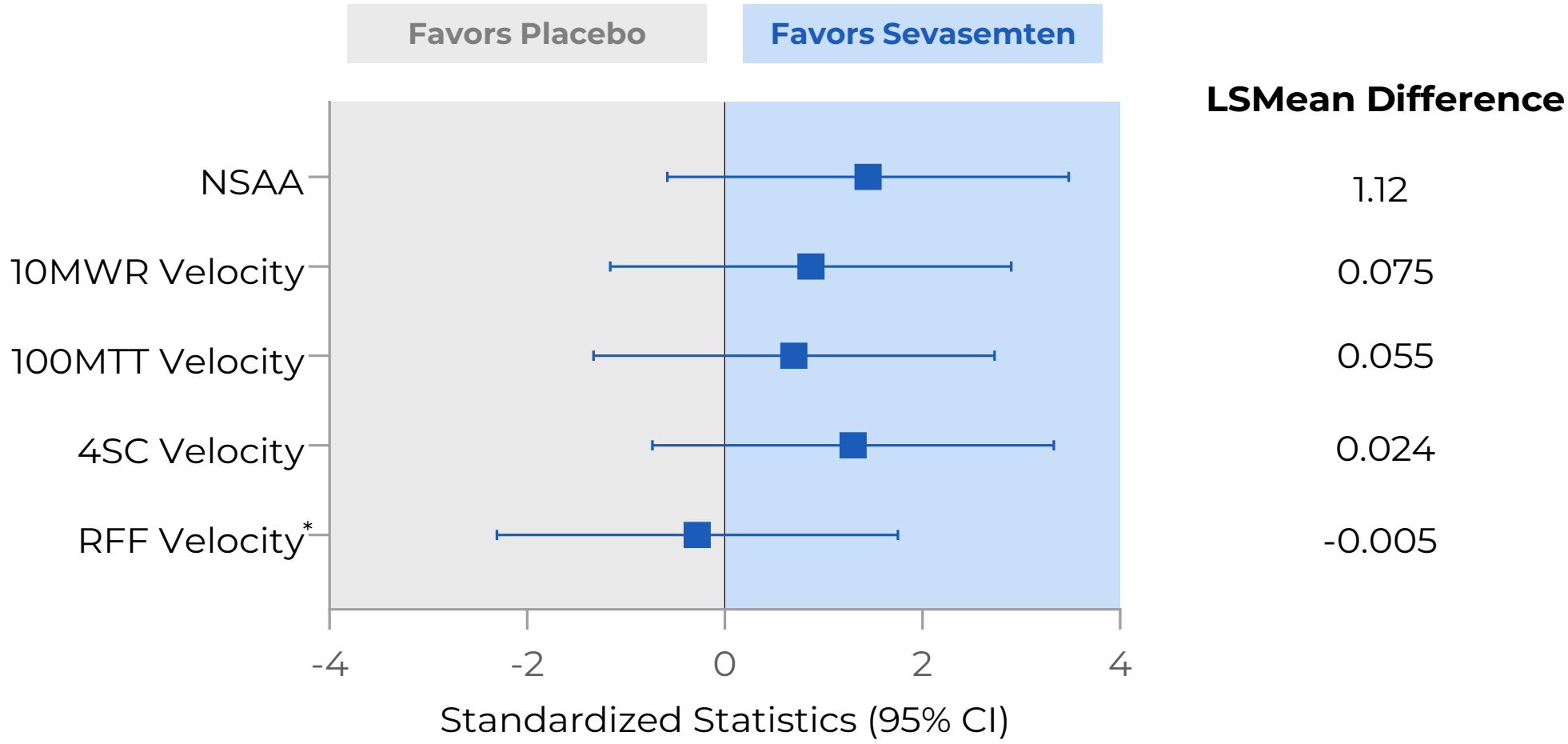
63% of Patients Treated with Sevasemten Showed **Stable or Improved Function** After 12 Months

Sevasemten NSAA Responder Analysis



Abbreviations: NSAA, North Star Ambulatory Assessment

Trends in Other Functional Measures Favor Sevasemten Treatment Arm



* At baseline, 9 sevasemten and 1 placebo treated participants were unable to rise from floor. At Month 12, 9 sevasemten and 2 placebo treated participants were unable to rise from floor
Note: For the figures, LSM differences and CIs were standardized by dividing by the SE. LSM differences presented on the right of the figure are on original scale (without SE adjustment)

Abbreviations: NSAA, North Star Ambulatory Assessment, CI, confidence interval

CANYON Summary of Trial Results

Safety

- Well-tolerated, at all doses, in adults and adolescents
- No safety concerns identified

Biomarkers

- Primary endpoint achieved: 28% average decrease in CK versus placebo (p=0.02)
- Plasma TNNI2 decreased 77% from baseline versus placebo (p<0.001)

Function

- Sevasemten treated patients showed stabilization of NSAA with trends toward improvement
- Placebo group (n=12) declined in line with natural history

Secondary & Exploratory

- The imbalance between groups confounded interpretation of a few endpoints (e.g., MRI); evaluation of the full data set ongoing

Abbreviations: CK, creatine kinase, NSAA, North Star Ambulatory Assessment

Sevasemten
Future Development Plans

Global, Multi-Center, Placebo-Controlled Pivotal Cohort Assessing Efficacy & Safety of Sevasemten in Becker

POTENTIAL REGISTRATIONAL COHORT

PRIMARY ENDPOINT

NSAA at 18 months

KEY INCLUSION CRITERIA

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

ENROLLMENT

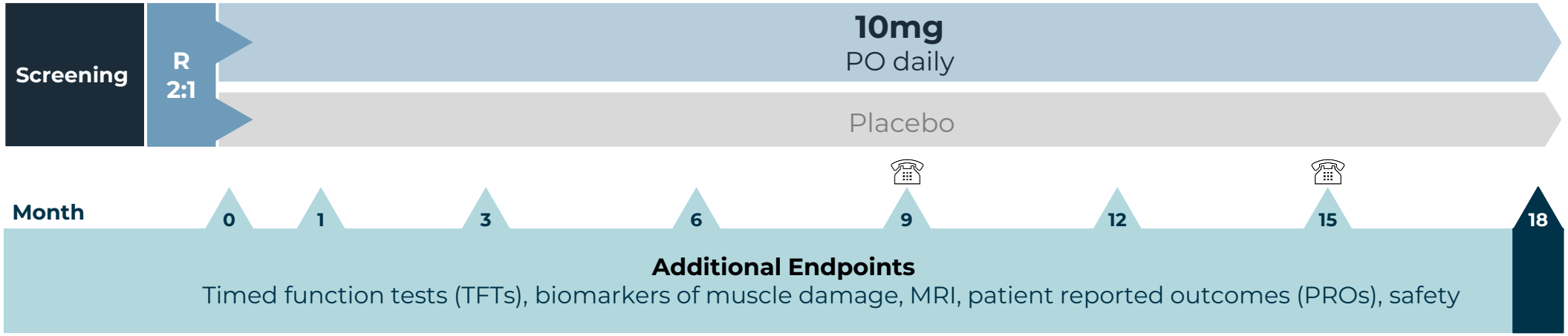
>120

POWERED AT

>90%

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

Study design - 18 months

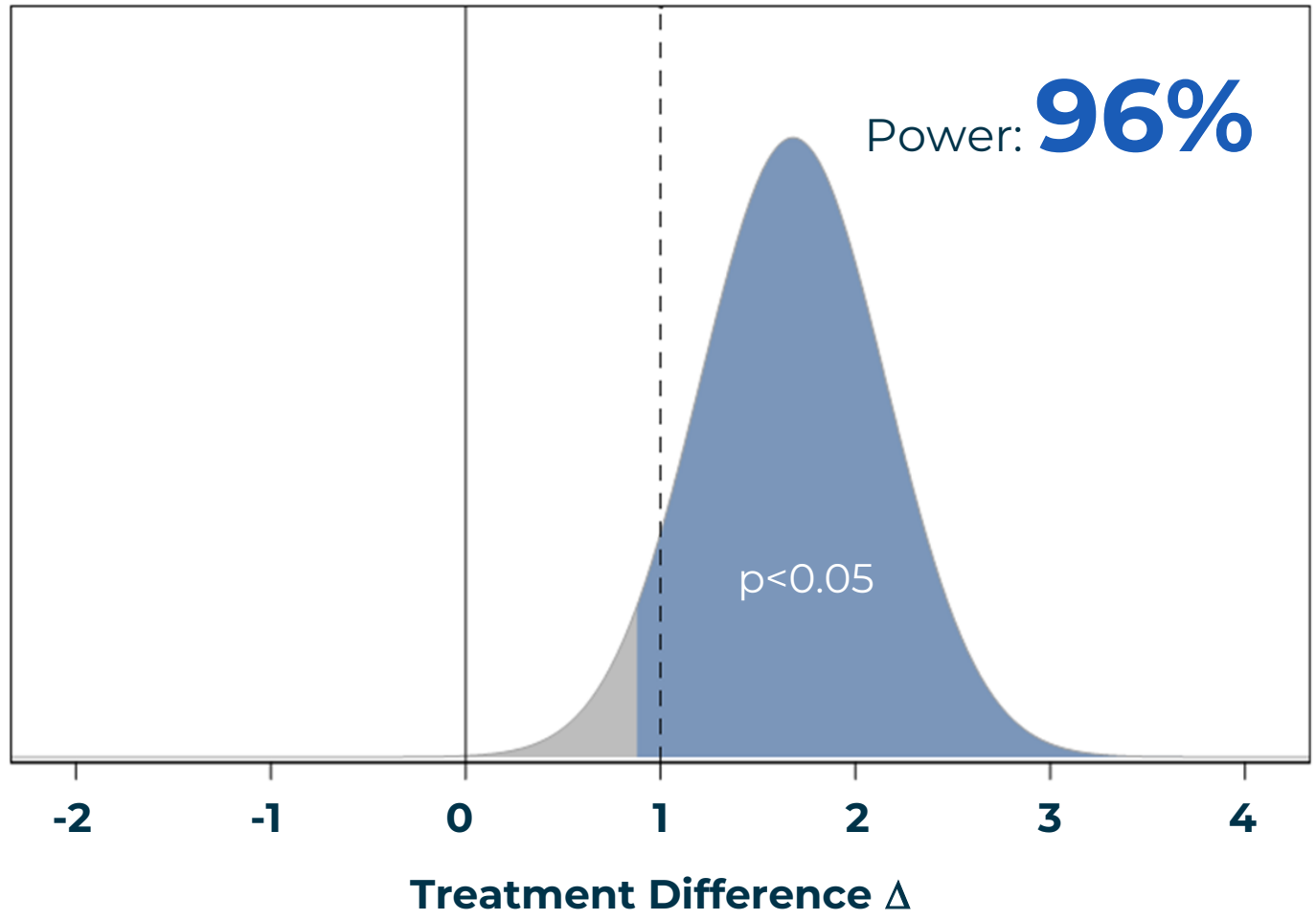


Abbreviations: PO, by mouth; NSAA, North Star Ambulatory Assessment

GRAND CANYON Powered at 96% to Show a 1.68 Point NSAA Difference at 18 Months

Power Calculation Assumptions:

- N=120 patients with 2:1 randomization
- Month 12 CANYON treatment difference $\Delta = 1.12$
- Assumed 50% increase in NSAA treatment effect at month 18 vs month 12 ($\Delta = 1.68$)
- 10% drop-out rate
- Standard deviation (σ) = 2.16
- Tipping point = 0.87 (represents point where the p-value is ~0.05 given the study size and assumed standard deviation based on t-test)



Abbreviations: NSAA, North Star Ambulatory Assessment

Sevasemten for Becker Next Steps

1

CANYON results support engagement with FDA & EMA
about marketing authorization filing strategies for sevasemten in Becker

2

GRAND CANYON is near full enrollment
in 51 sites across the United States, Europe*, New Zealand, Australia and Israel;
on track to over-enroll by Q1 2025

3

To date, 99% of eligible Becker participants
who have completed ARCH, CANYON, GRAND CANYON and DUNE
have enrolled in MESA

4

Increased confidence in GRAND CANYON future success
based on sevasemten clinical experience to date, Becker natural history data, and internal modeling

*European sites include the UK, Netherlands, Belgium, Denmark, Spain, France, Germany and Italy

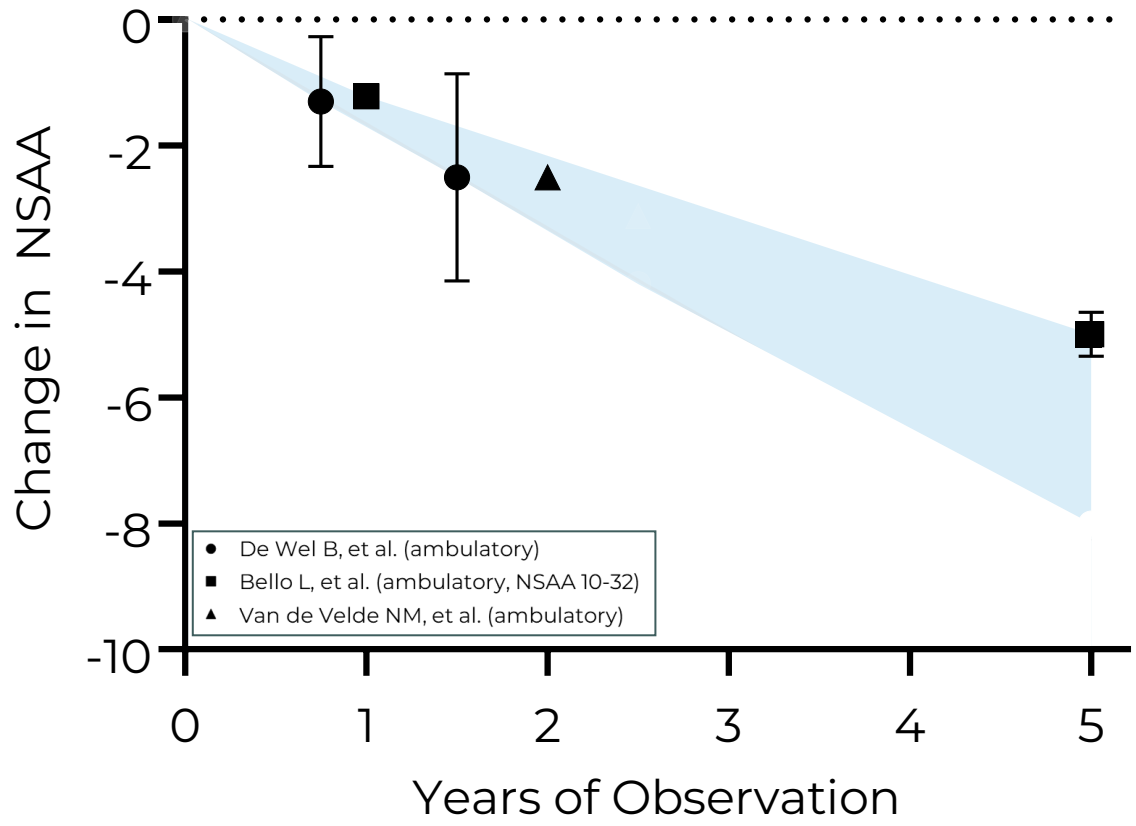
CANYON Clinical Implications and Sevasemten's Potential Role in Becker

Dr. Craig M. McDonald

Natural History Data in Becker Support that Functional Decline, Measured by NSAA, is Consistent and Predictable

Natural history of Becker muscular dystrophy

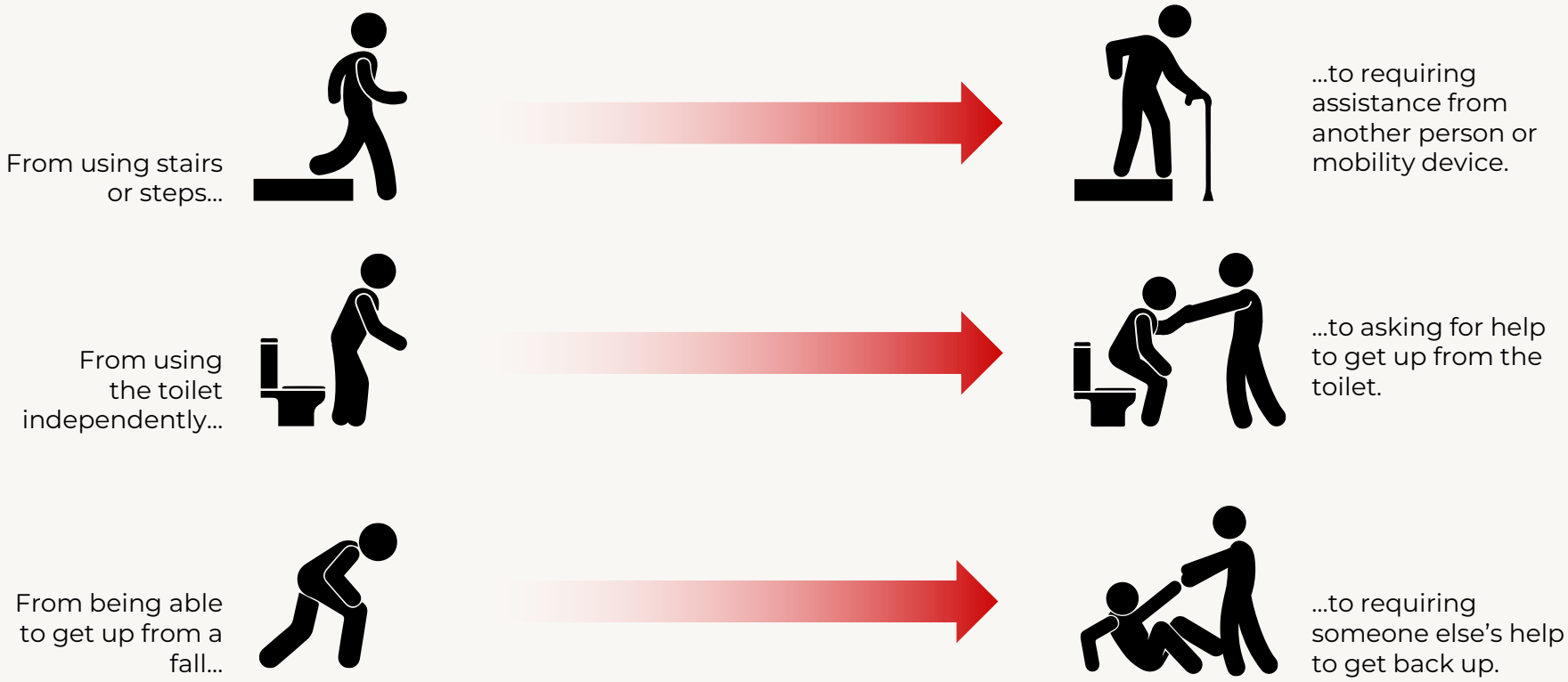
- NSAA is utilized in muscular dystrophy natural history studies to longitudinally assess function
- Multiple natural history studies in individuals with Becker demonstrate a **NSAA average score decline of 1.0 to 1.8 points annually** .[1,2,3]
- Becker Natural history studies support that NSAA decline is consistent in Becker patients who are already progressing



Reference: 1. Bello L, et al. 2016. 2. De Wel B, et al. Eur J Neurol. 2024. 3. Van de Velde NM, et al. Neurology. 2021.;4. Bello L et al 2024 WMS; 95% CI shown

A Clinician's Perspective on How to Interpret a 1-point NSAA Change in Becker

For individuals living with Becker, **this decline could look like:**



Abbreviations: NSAA, North Star Ambulatory Assessment

Closing Remarks

Kevin Koch, CEO

We Aim to Change the Lives of Individuals with Becker

~12,000 PEOPLE WITH BECKER IN US, EU-5 & JAPAN

~16 AGE PEOPLE WITH BECKER CAN BECOME MOBILITY DEVICE DEPENDENT

0 APPROVED THERAPIES

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

Edgewise Upcoming Value-Generating Milestones

		H2 2024	H1 2025	H2 2025
Skeletal **Sevasemten**	**Becker**	Phase 2 CANYON 1-year placebo-controlled data ✓	GRAND CANYON Recruitment complete (Q1)	
	Duchenne		Phase 2 LYNX & FOX Controlled dose-ranging data	Phase 3 trial Initiation
Cardiac **EDG-7500**	**Hypertrophic Cardiomyopathy**	Phase 1/Phase 2 EDG-7500 data in HVs & oHCM ✓	Phase 2 28-day study Initial Data readout	Phase 2 12-week oHCM & nHCM
		Phase 2 28-day study Initiate in oHCM & nHCM ✓	EDG-CV candidate IND in HF	Cardiometabolic Drug *In vivo* POC

Abbreviations: HV, healthy volunteers; oHCM, obstructive hypertrophic cardiomyopathy; nHCM, non-obstructive hypertrophic cardiomyopathy; CV, cardiovascular; IND, Investigational New Drug application; POC, proof of concept

Well-Capitalized to Execute Important Milestones Across Both EDG-7500 & Sevasemten

CASH, CASH EQUIVALENTS & MARKETABLE SECURITIES

~$493M

DEBT

$0

COMMON SHARES OUTSTANDING (NASDAQ: EWTX)

~94M

CASH RUNWAY THROUGH 2027

As of September 30, 2024

Q & A