Leaders in Muscle Disease Science

Edgewise Corporate Overview

July 2025

Edgewise® THERAPEUTICS

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. 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.

Focused on muscle science

- Global leader in muscle disease therapeutic development
- Deep knowledge of integrated muscle physiology
- Combined expertise in muscle biology and small molecule drug discovery to build our novel and differentiated muscle-focused platform

Rapidly advancing portfolio

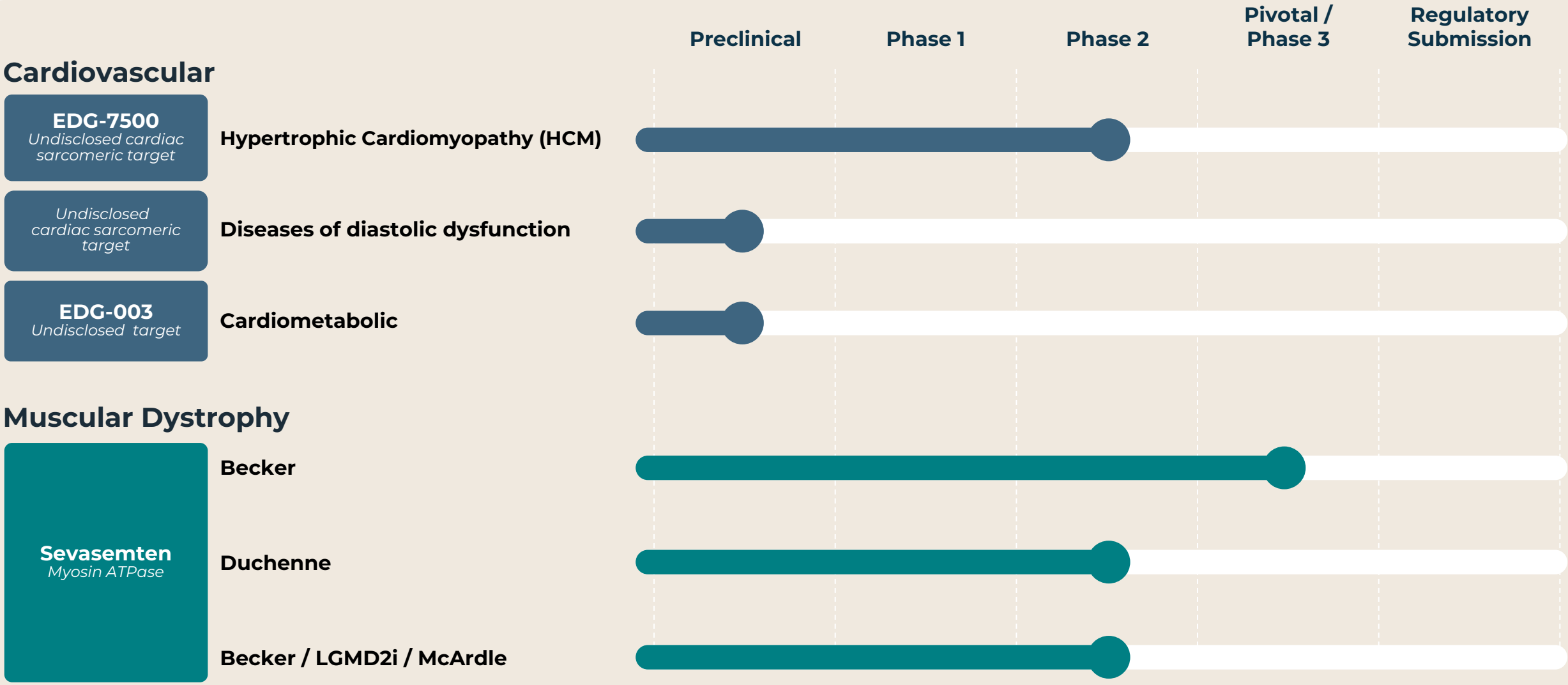
- Advancing EDG-7500 in oHCM and nHCM
- Advancing sevasemten in muscular dystrophies, including Becker for which there are no approved treatments
- Novel cardiometabolic targets advancing toward the clinic

Unwavering patient commitment

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

Abbreviations: nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy; Becker, Becker muscular dystrophy

Our Pipeline



Abbreviations: HCM, Hypertrophic cardiomyopathy; Becker, Becker muscular dystrophy; Duchenne, Duchenne muscular dystrophy; Limb-Girdle LGMD2i

Sevasemten for Becker

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

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

CANYON

ADULT PRIMARY EFFICACY ENDPOINT

Prespecified change from baseline in CK averaged across months 6, 9 and 12

Study not powered for NSAA

KEY INCLUSION CRITERIA

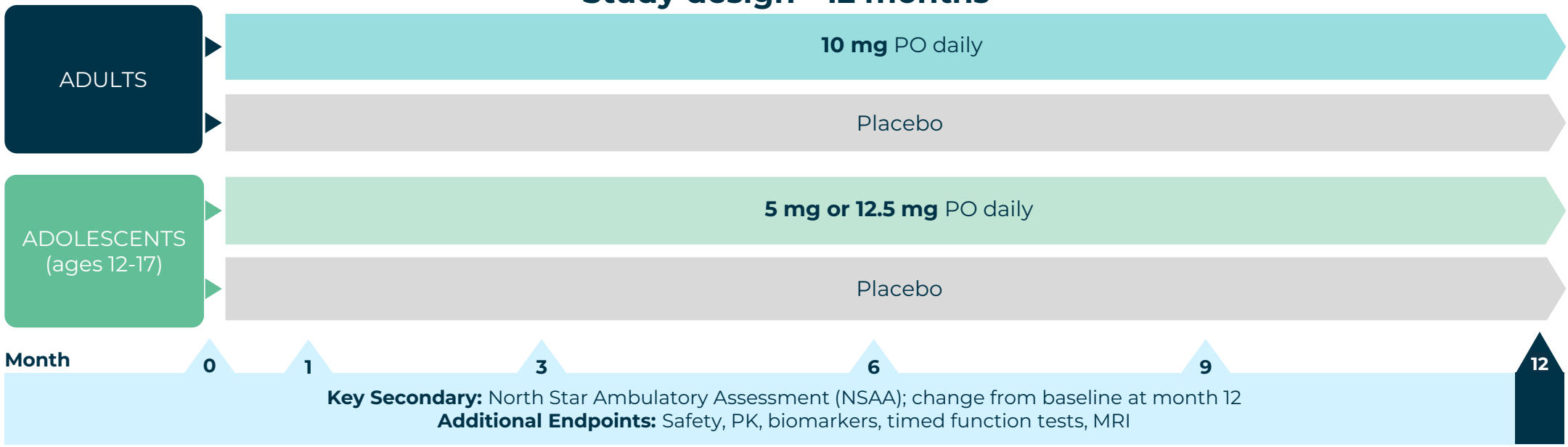
Ambulatory males aged 12 to 50 years with a dystrophin mutation and a Becker phenotype, not on corticosteroids, with a **NSAA between 5-32***

participants ENROLLED

Adults: **40**

Adolescents: **29**

Study design - 12 months



* Adolescents were selected based on NSAA above 5
Reference: NCT05160415
Abbreviations: CK, creatine kinase

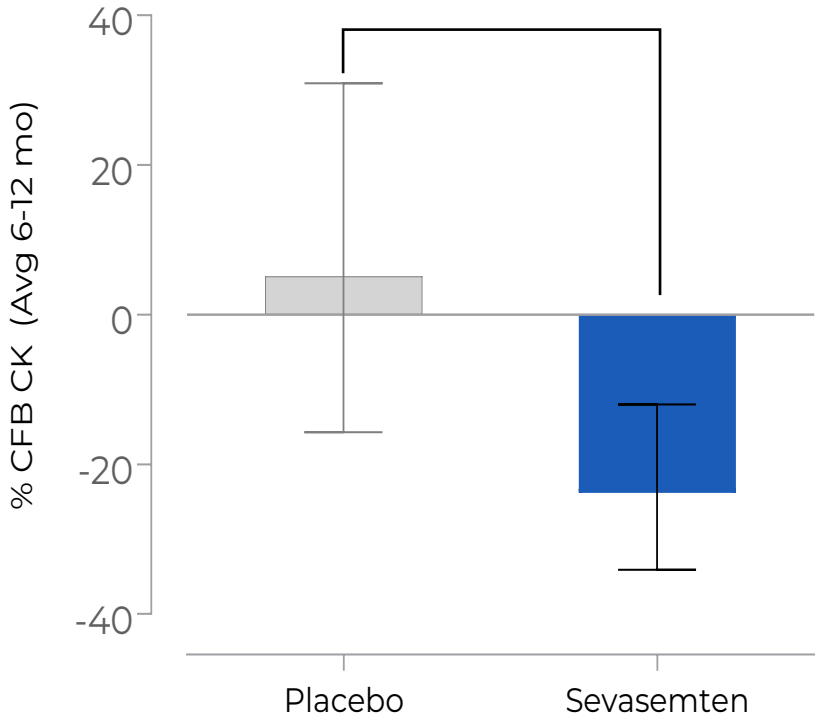
Edgewise THERAPEUTICS

CANYON Sevasemten was Well Tolerated

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%)

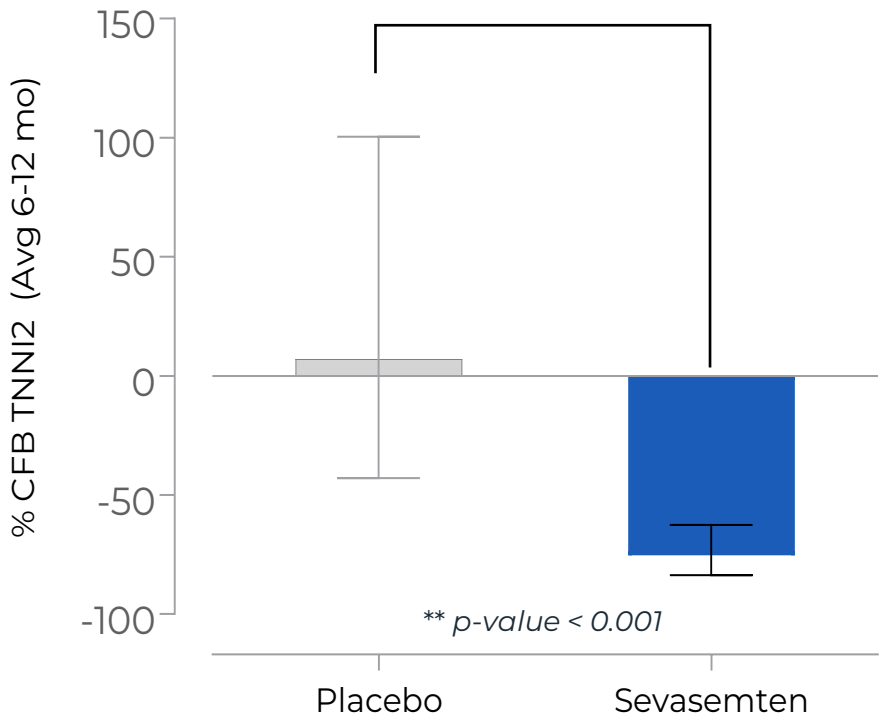
Sustained Decrease in Key Biomarkers of Muscle Damage after 12 Months of Treatment

Primary Endpoint:
CK % Change from Baseline



TNNI2 % Change from Baseline

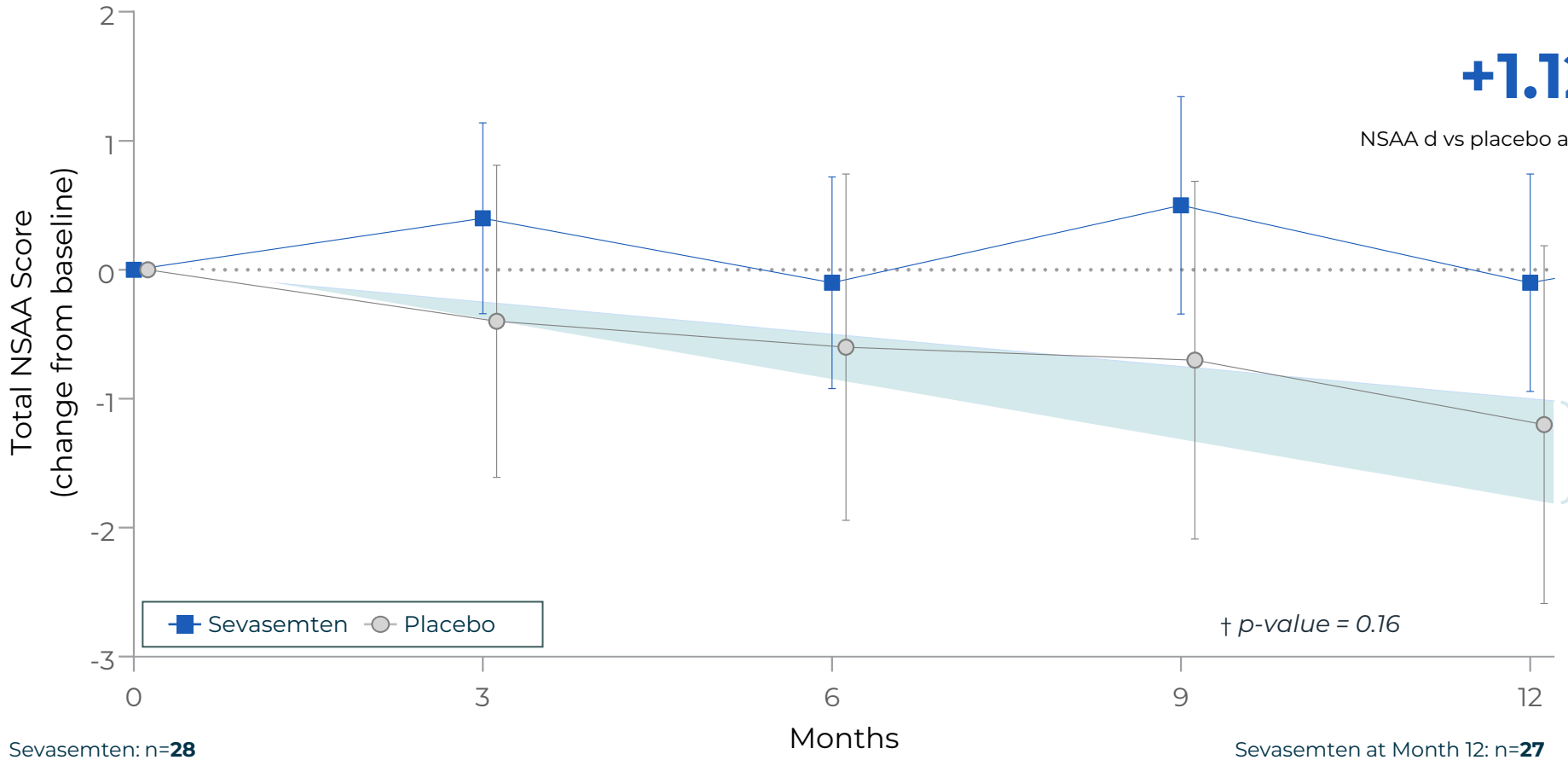
-77% **



LS Means, LS Mean differences and 95% CI shown for Safety Population
CK and TNNI2 values were log-transformed. LS (least squares) means, LS mean differences and CIs were back-transformed to percent scale; CFB, change from baseline; CK, creatine kinase; TNNI2, fast skeletal troponin I; NSAA, The North Star Ambulatory Assessment

NSAA Remained Stable Over Time in Sevasemten Group; NSAA Between-Group Difference: **1.12**

NSAA Score Change from Baseline



+1.12†

NSAA d vs placebo at month 12

Natural history studies show mean annual decreases of 1 to 1.7 NSAA points; **placebo group declined consistent with natural history**

Sevasemten: n=**28**

Initial Placebo: n=**12**

Sevasemten at Month 12: n=**27**

Placebo at Month 12: n=**12**

Through Month 12, LS Means and 95% CI shown for Safety Population
Post-Month 12 timepoints, observed means and 95% CI are presented

Sevasemten Efficacy in Becker Continues to be Assessed in the MESA Open Label Study with 99% of Eligible Participants Currently Enrolled

ARCH — **Phase 1**: 24-month Open Label Study (N=12)
COMPLETE

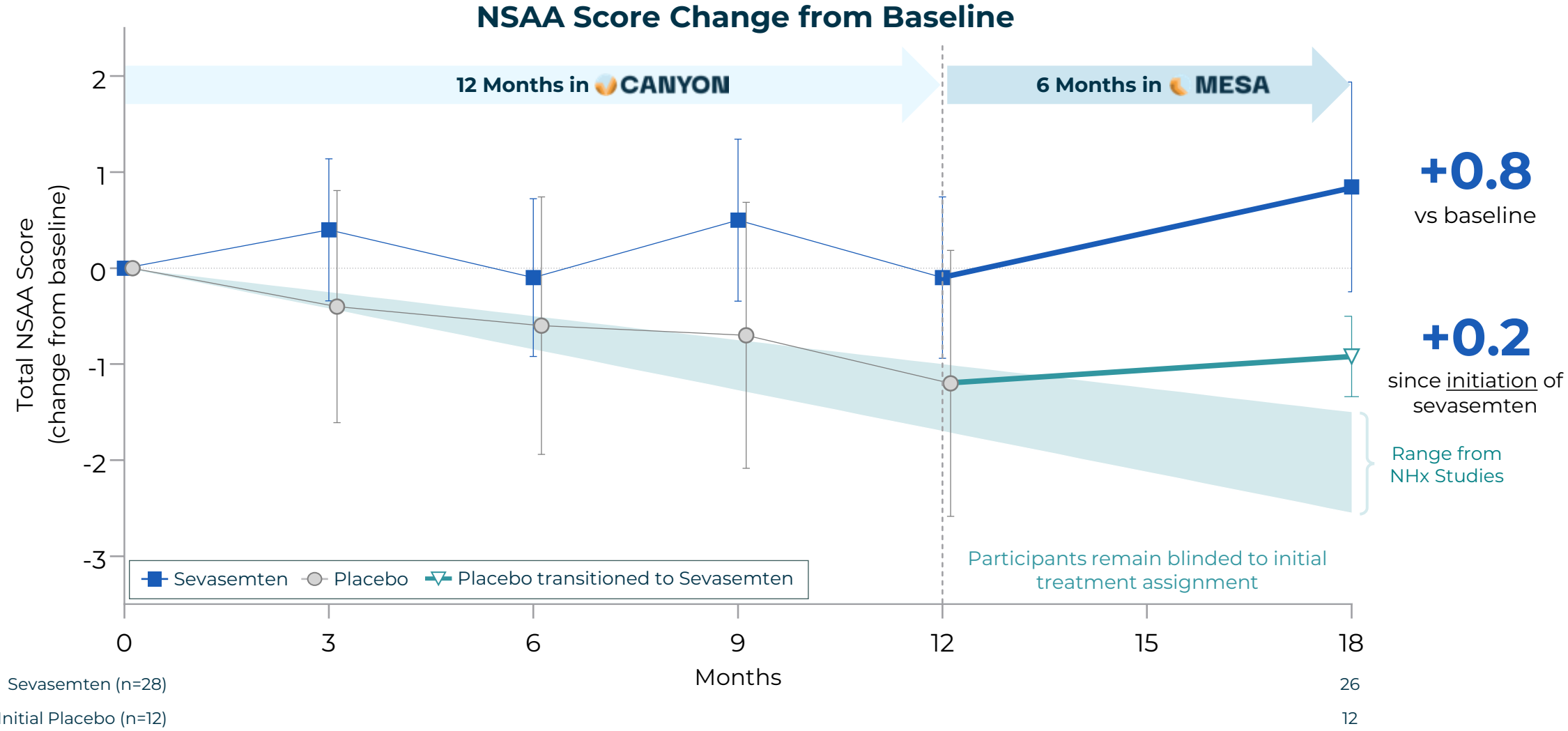
DUNE — **Phase 2**: 16-weeks Placebo Controlled Exercise Challenge Study (N=9)
COMPLETE

CANYON — **Phase 2**: 12-month Placebo Controlled Study (N=40 Adults)
COMPLETE

GRAND CANYON — **Pivotal Cohort**: 18-month Placebo Controlled Study (N=175 Adults)
ACTIVE, Not Recruiting

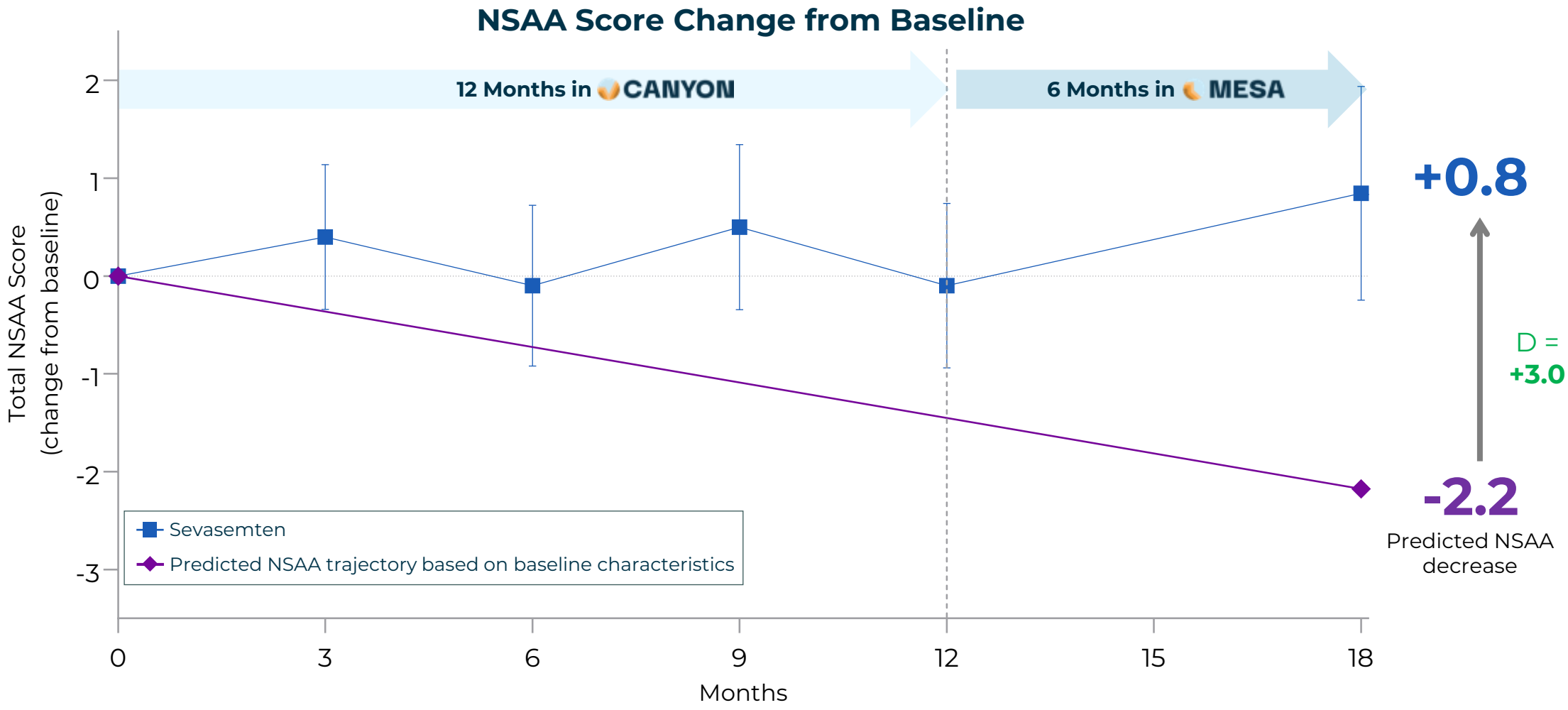
MESA — Open-label extension study in adults and adolescents with Becker
As of March 2025, **85 participants** enrolled in MESA (99% of eligible)

After Transitioning to MESA, CANYON Participants Showed an Increase in NSAA over 18 Months



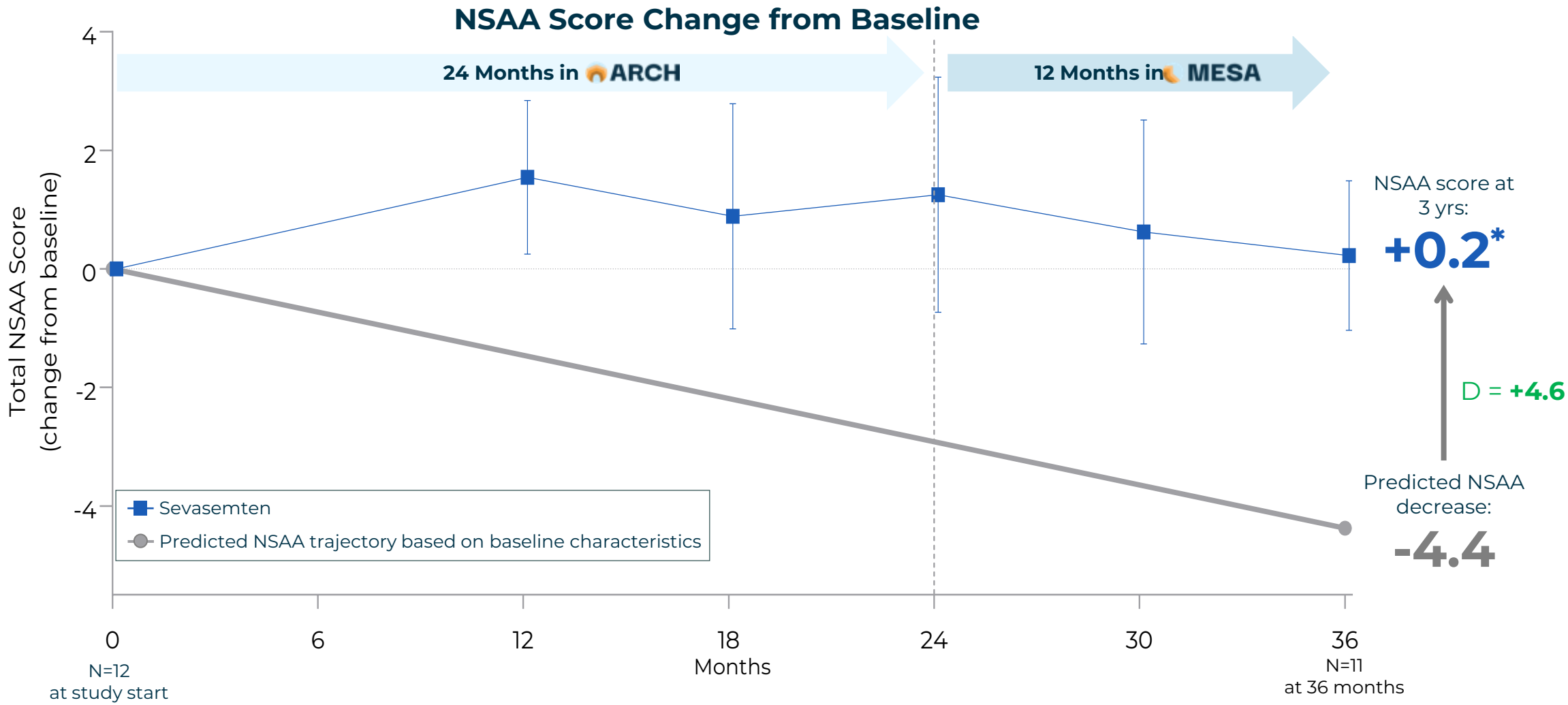
Through Month 12, LS Means and 95% CI shown for Safety Population
Post-Month 12 timepoints, observed means and 95% CI are presented

CANYON Participants' NSAA Scores Diverge from Predicted NH; 92% Improved vs their Predicted Scores



Through Month 12, LS Means and 95% CI shown for Safety Population
Post-Month 12 timepoints, observed means and 95% CI are presented;
NH, Natural History

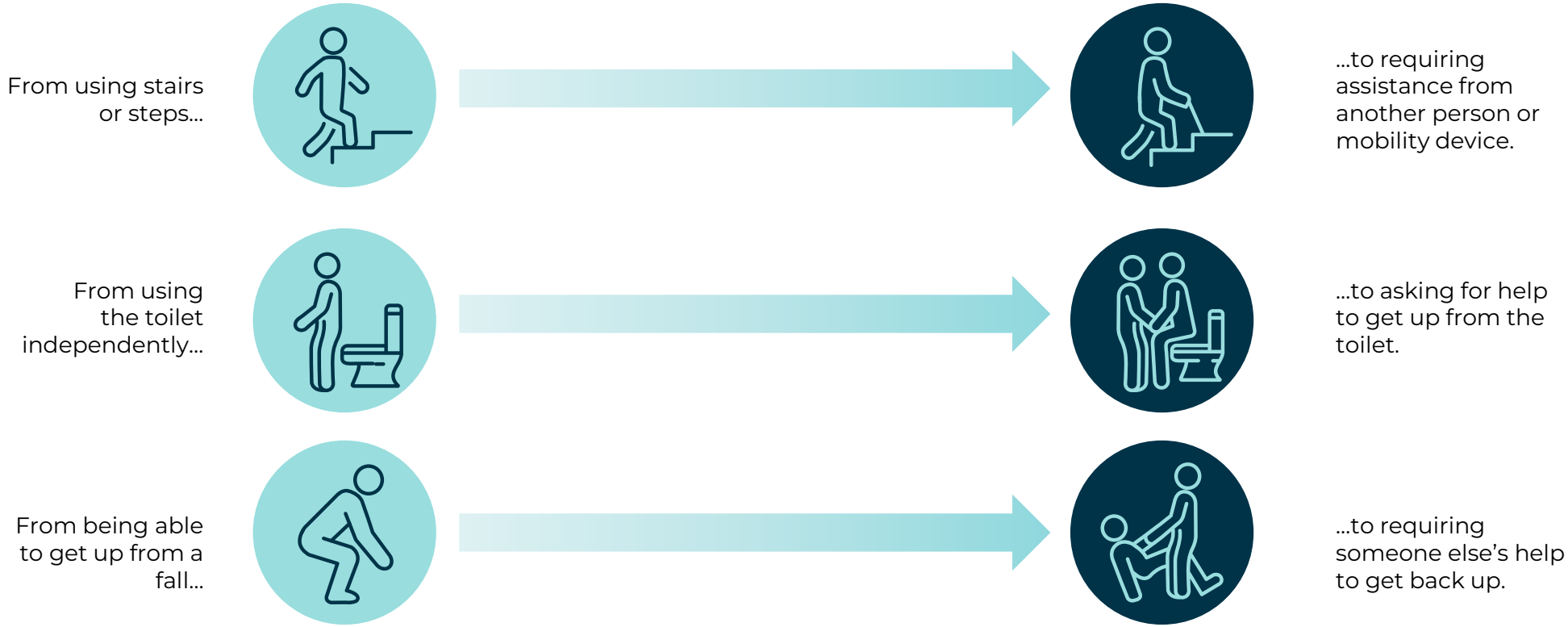
ARCH Participants Remained Stable After 3 Years vs a Predicted -4.4 Point NSAA Decline



* Subject with meniscal tear at month 15 excluded from subsequent NSAA measures
Means and 95% CI shown for Safety Population
NHx comparators not available for time points earlier than 12 months

For Individuals with Becker, Functional Decline Has a Daily Impact

Even a 1-Point NSAA decline could look like:



Abbreviations: NSAA, North Star Ambulatory Assessment

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

GRAND CANYON

REGISTRATIONAL COHORT

PRIMARY ENDPOINT

NSAA at 18 months

KEY INCLUSION CRITERIA

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

ENROLLMENT

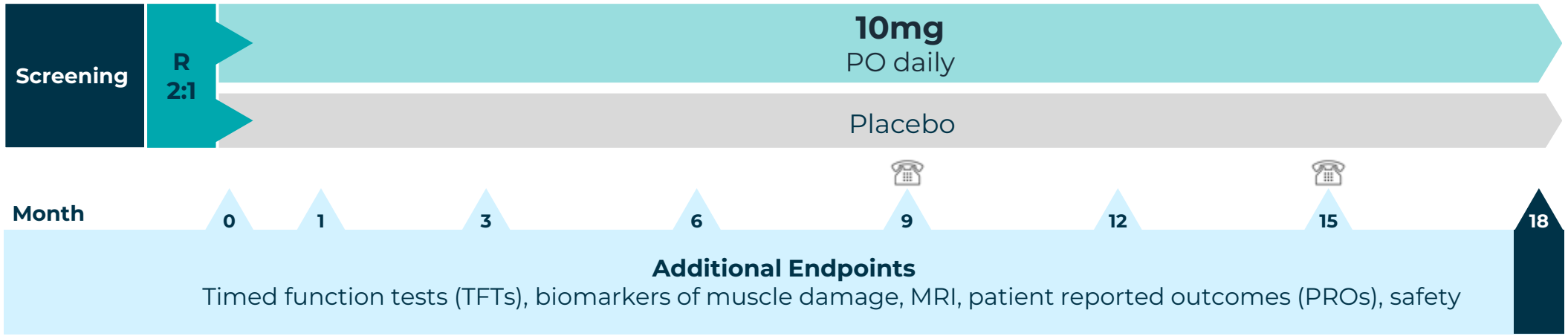
175

POWERED AT

>98%

for observing a significant difference assuming a mean NSAA difference of 1.7 points over placebo at 18 months

Study design - 18 months



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

Edgewise is Poised to Deliver the First Therapy for Individuals with Becker

Clinical Outcomes

- ✓ **ARCH**: Long-term safety, reduced biomarkers of muscle damage and trends in improvement in function (NSAA) over 24 months
- ✓ **CANYON**: Well-tolerated, met primary endpoint (CK), showed stabilization of NSAA with trends toward improvement vs placebo over 12 months
- ✓ **ARCH/MESA and CANYON/MESA**: Continued positive trends in NSAA demonstrating sustained disease stabilization and a continued slowing of progression
- ✓ **GRAND CANYON** ongoing: Highly powered to show a statistically significant difference in NSAA versus placebo over 18 months

Regulatory Path

- ✓ Rare disease population (~12K in 7MM) with no approved therapies
- ✓ Completed successful Type C meeting with FDA with clear path to approval

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

1 NOVEL MOA IN DEVELOPMENT: SEVASEMTEN

Bryan
Living with Becker

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

Sevasemten for Duchenne

Our Goal is to Develop a New Therapeutic Approach that Could Become the Standard of Care in Duchenne

- Despite recent advances, the Duchenne community remains in need of new therapeutic options
- Sevasemten's mutation-agnostic MOA enables the potential for a foundational therapy—used alone or in combination with other treatments
- Edgewise is the only company focused specifically on contraction-induced muscle injury in Duchenne

> ***"I don't want to be like this for my whole life. I want to experience what other people normally get a chance to do."***
>
> – Individual living with Duchenne

LYNX

A 2-Part, Multi-Center, Randomized, Placebo-Controlled, Phase 2 Study of Sevasemten in Boys with Duchenne

PRIMARY ENDPOINT

Safety after 24 months

KEY INCLUSION CRITERIA

Aged 4-9, ambulatory, on stable dose steroids, <10 sec 4SC, <10 sec stand from supine

ENROLLMENT

66

PART A:

12-week placebo-controlled dose-escalation (sequentially enrolled)

Cohort 1	R 2:1	**Sevasemten, 2.5 mg**	Placebo
Cohort 2	R 2:1	**Sevasemten, 5 mg**	Placebo
Cohort 3	R 2:1	**Sevasemten, 7.5/10 mg**	Placebo
Cohort 4	R 2:1	**Sevasemten, 15 mg**	Placebo
Cohort 5	R 2:1	**Sevasemten, 30 mg**	Placebo
Cohort 2NS	R 2:1	**Sevasemten, 5 mg (steroid-naive)***	Placebo

Week 0 → 12

Exploratory Endpoints

NSAA, 100-meter timed test, SV95C, timed function tests, PRO, and muscle strength testing

PART B:

92-week OLE

Open-Label Extension with Dose Escalation

0 → 92

*Age 4-7

Doses listed were the starting doses for each cohort; changes were made to dosing as the trial continued.

CK, creatine kinase; R, randomization; AE, adverse event; SAE, serious adverse event; NSAA, North Star Ambulatory Assessment

1. ClinicalTrials.gov. NCT05540860. https://clinicaltrials.gov/ct2/show/NCT05540860. 2. Data on File.

Sevasemten was Well-Tolerated in the Placebo-Controlled Period; Safety Profile Similar in Open-Label Period

System Organ Class/Preferred Term TEAEs Occurring in ≥5% of Total Active	Placebo (N=23)	Cohort 1 2.5 mg (N=7)	Cohort 2 5.0 mg (N=6)	Cohort 3 7.5/10.0 mg (N=8)	Cohort 4 15.0 mg (N=10)	Cohort 5 30.0 mg (N=8)	Cohort 2NS 5.0 mg (N=4)	Pooled Active (N=43)
Any TEAE	16 (70%)	5 (71%)	4 (67%)	7 (88%)	10 (100%)	8 (100%)	4 (100%)	38 (88%)
Gastrointestinal disorders								
Vomiting	3 (13%)	0	2 (33%)	3 (38%)	2 (20%)	2 (25%)	1 (25%)	10 (23%)
General disorders and administration site conditions								
Fatigue	6 (26%)	1 (14%)	0	1 (13%)	3 (30%)	3 (38%)	1 (25%)	9 (21%)
Infections and infestations								
Nasopharyngitis	0	2 (29%)	0	0	2 (20%)	0	2 (50%)	6 (14%)
Viral upper respiratory tract infection	2 (9%)	0	0	0	3 (30.0%)	0	0	3 (7%)
Injury, poisoning and procedural complications								
Fall	2 (9%)	2 (29%)	0	0	1 (10%)	1 (13%)	1 (25%)	5 (12%)
Musculoskeletal and connective tissue disorders								
Muscle spasms	0	1 (14%)	0	0	2 (20%)	0	0	3 (7%)
Nervous system disorders								
Dizziness	3 (13%)	0	0	1 (13%)	3 (30%)	4 (50.%)	0	8 (19%)
Headache	6 (26%)	1 (14%)	0	0	2 (20%)	0	0	3 (7%)
Somnolence	0	1 (14%)	0	0	1 (10%)	3 (38%)	0	5 (12%)
Respiratory, thoracic and mediastinal disorders								
Cough	6 (26%)	0	0	0	1 (10%)	2 (25%)	0	3 (7%)

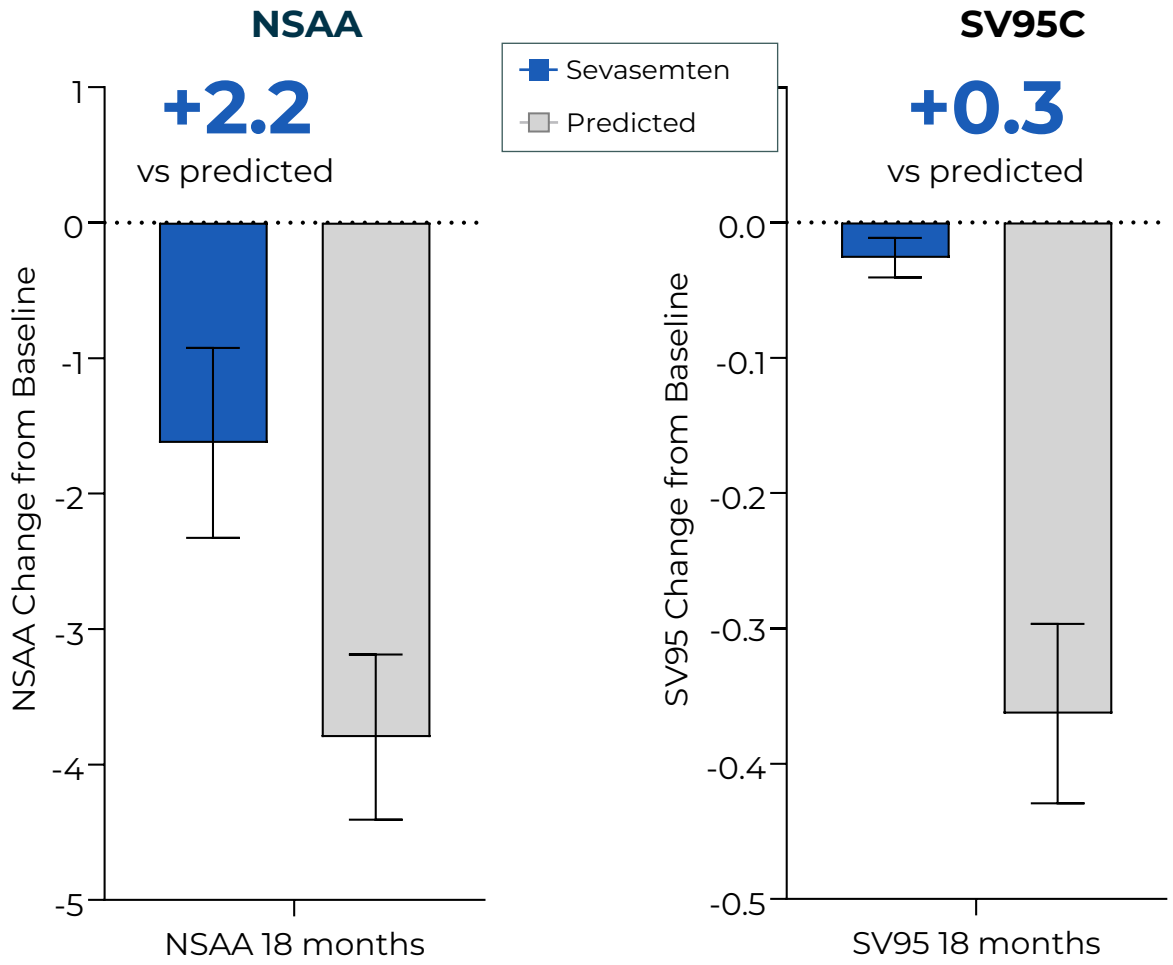
01MAY2025 interim data

Impressive Functional Outcomes Across NSAA and SV95C Following 18 Months Sevasemten Treatment (Cohorts 2 and 3)

- Sevasemten meaningfully reduced the rate of NSAA decline
- SV95C remained stable after 18 months
- 4SC also remained stable throughout the 18 months with mean change from baseline of 0.5 seconds

Comparing to Natural History

- **NSAA**: multivariate regression model provided in Muntoni 2022, based on baseline functional measures, age, height and weight
- **SV95C**: based on data in EMA qualification assessment



Note: Predicted change from Baseline values derived via DMD Prediction Model (Muntoni F, *et. al., Neuromuscul Disord*., 2022 Apr;32(4):271-283. doi: 10.1016/j.nmd.2022.02.009).
Qualification Opinion for Stride velocity 95th centile as primary endpoint in studies in ambulatory Duchenne Muscular Dystrophy studies (EMADOC-1700519818-1127132)
01May2025 interim data; Mean ± SEM
Abbreviations: NSAA, NorthStar ambulatory assessment; SV95C, stride velocity 95th centile

A 2-Part, Multi-Center, Randomized, Placebo-Controlled, Phase 2 Study in Duchenne Boys Post-Gene Therapy

PRIMARY ENDPOINT

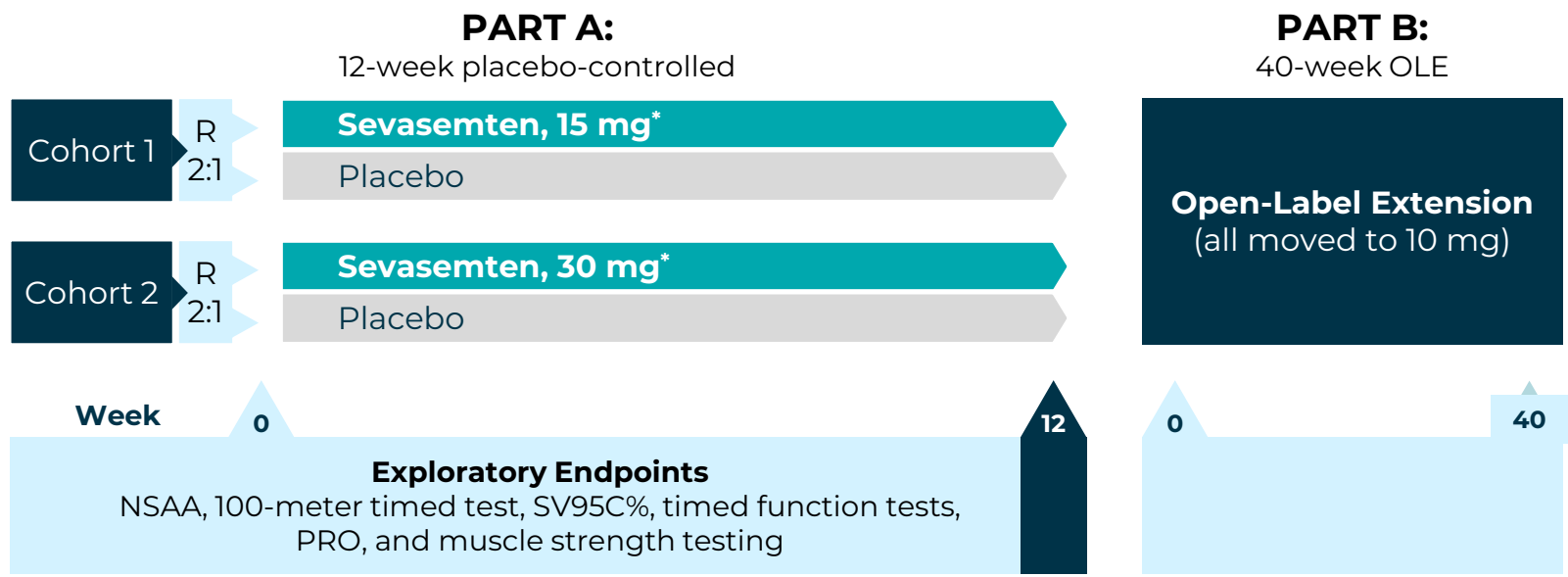
Safety after 24 months

KEY INCLUSION CRITERIA

Ambulatory, age 6-14, previously treated with gene therapy (>2 yrs after study drug admin), stable dose of steroids

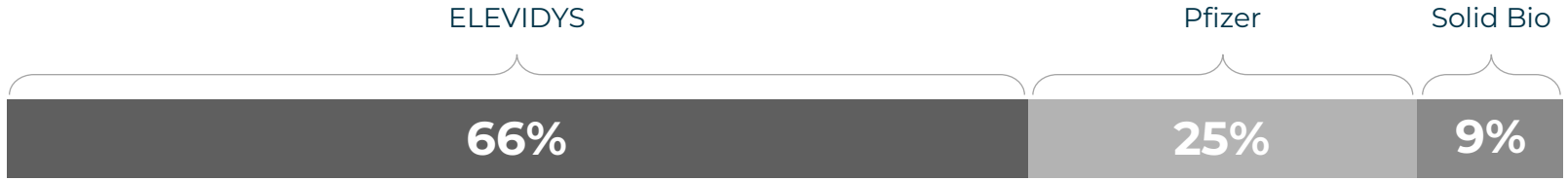
ENROLLMENT

32



* Cohorts 2 and 3 were dosed down to 10 mg during Part A

Gene Therapy Background of Participants (average 4 years out at study start)



Doses listed are starting doses. As trial continued, doses changed.
R, randomization; AE, adverse event; SAE, serious adverse event
1. ClinicalTrials.gov. NCT06100887. https://clinicaltrials.gov/ct2/show/NCT06100887. 2. Data on file

Sevasemten Safety During Placebo-Controlled Period

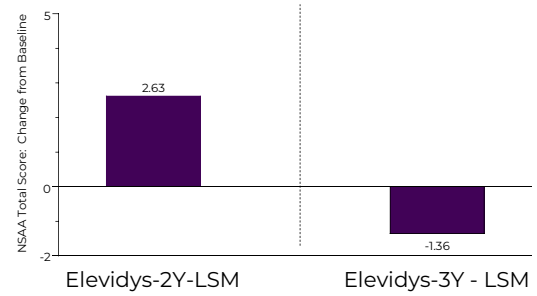
System Organ Class/Preferred Term ≥5% in Pooled Sevasemten	Placebo (N=11)	Sevasemten 15 mg (N=11%)	Sevasemten 30 mg (N=10)	Pooled Sevasemten (N=21)
Any TEAE	8 (73%)	9 (82%)	9 (90%)	18 (86%)
Gastrointestinal disorders				
Diarrhea	1 (9%)	1 (9%)	1 (10.0%)	2 (10%)
Nausea	0	0	3 (30%)	3 (14%)
Vomiting	1 (9%)	0	4 (40%)	4 (19%)
Infections and infestations				
Otitis externa	0	0	2 (20%)	2 (10%)
Injury, poisoning and procedural complications				
Fall	0	2 (18%)	3 (30%)	5 (24%)
Musculoskeletal and connective tissue disorders				
Muscular weakness	0	2 (18%)	3 (30%)	5 (24%)
Nervous system disorders				
Dizziness	0	3 (27%)	5 (50%)	8 (38%)
Headache	2 (18%)	1 (9%)	3 (30%)	4 (19%)
Somnolence	0	1 (9%)	3 (30%)	4 (19%)

Prior to 6 months of treatment, all participants were dose reduced to 10 mg, which was well-tolerated

01JUN25 interim data

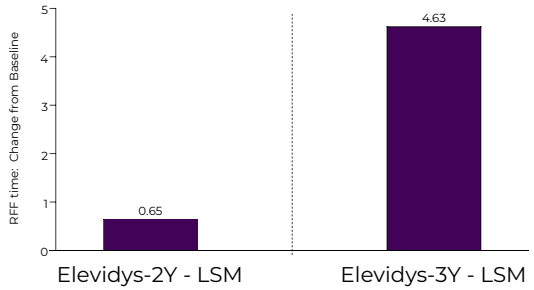
ELEVIDYS Natural History Data Provides Perspective on Observed Functional Changes with Sevasemten in FOX

Years: **0-2** **0-3**



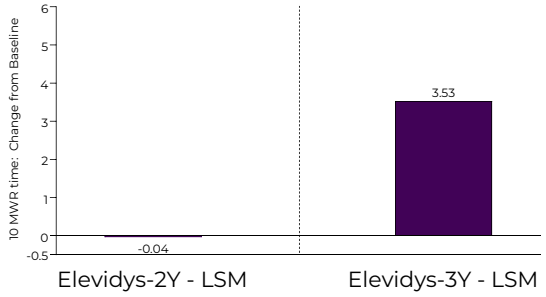
ELEVIDYS NSAA rate of decline:

-4.0 points



ELEVIDYS change in RFF:

+4.0 seconds



ELEVIDYS change in 10MWR time:

+3.6 seconds

Treated with ELEVIDYS ~4-5 years Prior

Sevasemten mean NSAA rate of decline:

-2.4 points

Sevasemten median change in RFF:

+0.7 seconds

Sevasemten median change in 10MWR time:

+0.8 second

References: 1.Mendell J, et al. Poster presented at MDA; March 16-19, 2025; Dallas, Texas. P167; 2. Proud C, et al. Oral presentation at MDA; March 16-19, 2025; Dallas, Texas

Discussions with Regulatory Agencies will Help Shape Path Forward in Phase 3 Including Target Population and Key Endpoints

LYNX

Phase 2 trial of sevasemten in children with Duchenne

FOX

Phase 2 trial of sevasemten in children and adolescents with Duchenne previously treated with gene therapy

- Sevasemten was found to be **well-tolerated**, with no new safety concerns identified
- Functional observations support **the 10mg dose** of sevasemten to move to a pivotal-stage program
- Phase 2 programs will continue with an **open-label extension** to collect longer term data
- Meetings are planned with regulatory agencies to receive input on **Phase 3** design

The Duchenne Community Remains In Great Need of New Therapeutic Options

~35,000 INDIVIDUALS LIVING WITH DUCHENNE IN US, EU-5 & JAPAN

SEVASEMTEN MUTATION AGNOSTIC MOA POTENTIAL FOUNDATIONAL THERAPY, ALONE OR IN COMBINATION, IN DUCHENNE

ONLY COMPANY RUNNING A TRIAL WITH BACKGROUND GENE THERAPY

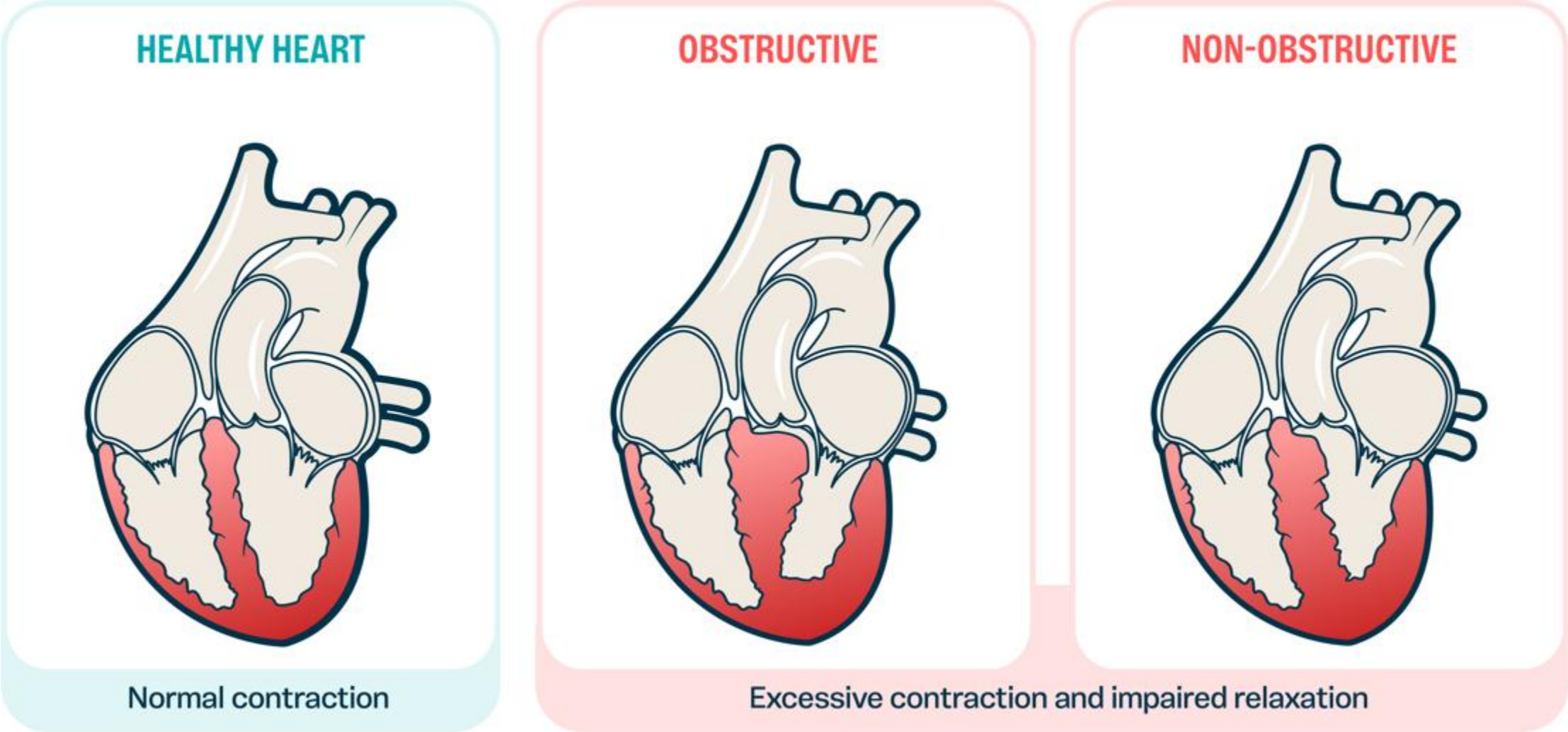
EDG-7500 for Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy (HCM): Chronic, Progressive and the Most Commonly Inherited Heart Disease

- HCM is characterized by diastolic dysfunction, left ventricular outflow tract obstruction (LVOTO), and atrial and ventricular arrhythmias
- The disease dramatically impairs overall quality of life - physical, emotional, social and financial
- There remains a significant unmet need for therapies that consistently and safely reduce LVOT gradient, improve symptoms and overall quality of life

> ***"I'll be walking down the street, going to the grocery store, and there will be the slightest incline in the sidewalk, and I can feel it, and I'll start getting completely winded and out of breath."***
>
> – Lindsay, living with HCM

HCM: Abnormalities in Heart Muscle Structure and Function Lead to Severe Abnormalities in Cardiac Performance



Treatments for HCM Have Key Limitations Leaving Substantial Unmet Need for Patients

LIMITED BENEFIT ACROSS THE SPECTRUM OF HCM

Efficacy & safety limitations with interventions in oHCM[1,3]

No approved therapies for nHCM

RISK OF HEART FAILURE[1,2]

Mavacamten **black box warning** for HF[3]

HF risk limits intervention[2]

SAFETY RISKS WORSEN PATIENT EXPERIENCE

Frequent **echo monitoring**[1-3]

Echo-based **dose titration for safety**[1-3]

HCM, hypertrophic cardiomyopathy; HF, heart failure; nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

1. Ommen SR et al. Circulation. 2024;149(23):e1239-e1311; 2. Maron MS et al. N Engl J Med. 2024;390:1846-61; 3. CAMZYOS [package insert]. Princeton, NJ: Bristol-Myers Squibb Company, 2023;

EDG-7500 is a *Selective Cardiac Sarcomere Modulator* Designed to Slow Acto-Myosin Engagement and Promote Faster Disengagement

Targeted MOA*

Slows rate of acto-myosin engagement and speed disengagement without inactivating myosin heads

EDG-7500 is targeted to address both obstructive and nonobstructive HCM

Minimal changes in LVEF*

EDG-7500 avoids excessive drops in systolic performance manifesting as reduced ejection fraction

Potential ease of administration

EDG-7500's novel MOA potentially eliminates the need for cumbersome and frequent echocardiographic assessments

EDG-7500 is well positioned to address unmet needs in HCM

* Based on preclinical and clincial data with EDG-7500
Abbreviations: HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; MOA, mechanism of action
References: Edgewise ACC presentation (https://edgewisetx.com/application/files/1616/7812/1221/EDG-7500_cat_HCM_ACC23-WCC_FInal.pdf)

CIRRUS
HCM

EDG-7500 Phase 2 in oHCM and nHCM

CIRRUS HCM Clinical Trial Design

PRIMARY OBJECTIVE

Safety & tolerability in adults with HCM

KEY INCLUSION CRITERIA

Male and female participants
≥ 18 years of age with HCM
LVEF ≥ 60%

TARGET ENROLLMENT

~70

KEY OUTCOME MEASURES

Cardiovascular PD, LVEF, Biomarkers, PK

PART A: Single Dose (oHCM)

ADULTS WITH oHCM → Single dose EDG-7500

PART B (4 Weeks): Multiple Dose (oHCM)

ADULTS WITH oHCM → Once-daily dose EDG-7500

PART C (4 Weeks): Multiple Dose (nHCM)

ADULTS WITH nHCM → Once-daily dose EDG-7500

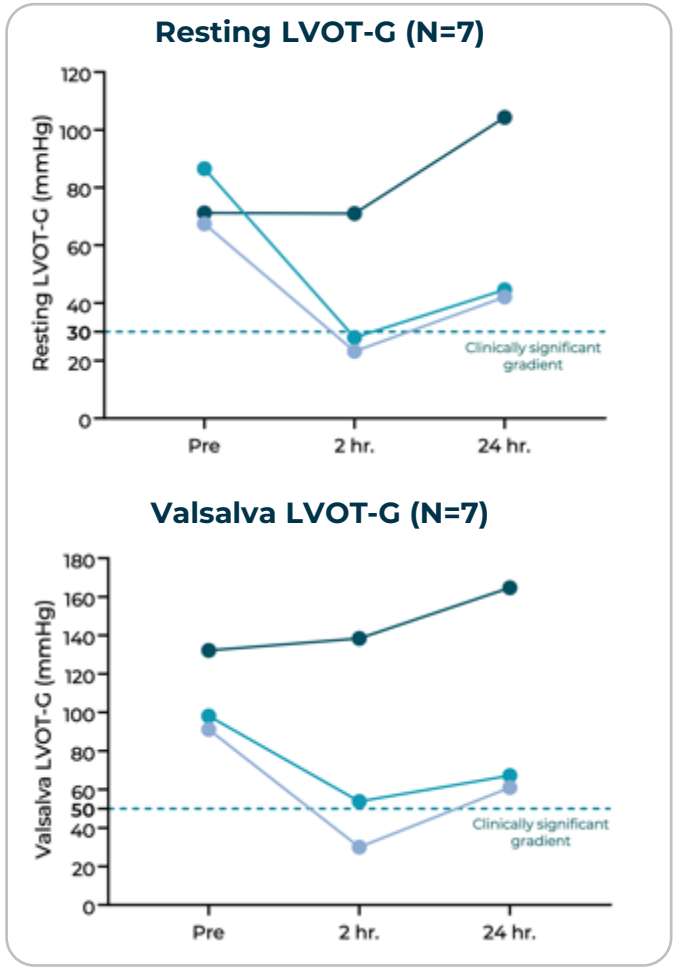
PART D (12 Weeks): Extended Dose (oHCM & nHCM)

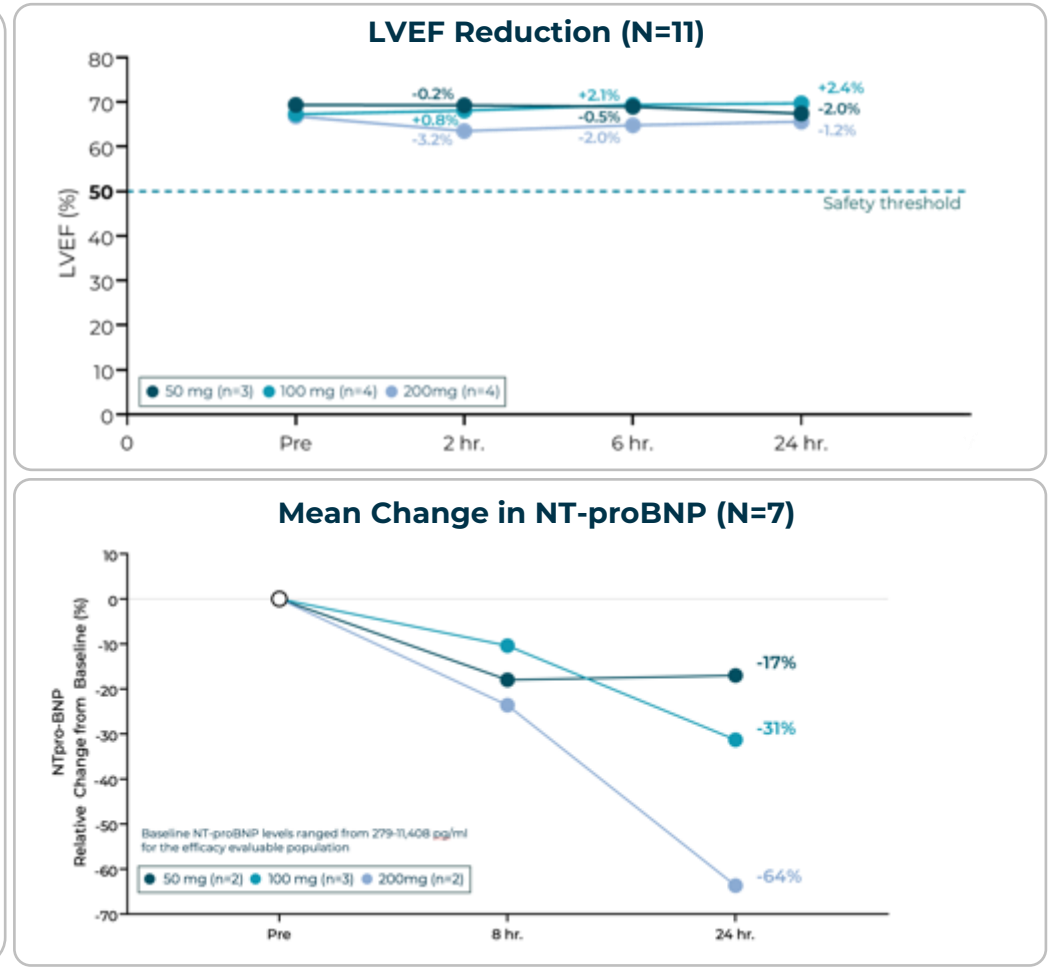
ADULTS WITH oHCM & nHCM → Once-daily dose EDG-7500

Abbreviations: PK, pharmacokinetics; PD, pharmacodynamics; EOS, end of study; oHCM, obstructive hypertrophic cardiomyopathy; nHCM, nonobstructive hypertrophic cardiomyopathy; LVEF, left ventricular ejection fracture

Observations from CIRRUS-HCM Single Dose Study (Part A) Highlighted EDG-7500's Potentially Differentiated Profile in HCM

- EDG-7500 was well tolerated across all doses studied in oHCM patients
- Reduction in resting LVOT-G of **67%** for the 100/200 mg cohorts combined
- Reduction in Valsalva LVOT-G of **55%** for the 100/200 mg cohorts combined
- LVOT-G relief was achieved **without reductions in LVEF**
- EDG-7500 administration led to a mean **31%** (100 mg) and **64%** (200 mg) decrease in NT-proBNP





Abbreviations: oHCM, obstructive hypertrophic cardiomyopathy; HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; LVOT-G, left ventricular outflow tract gradient; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Parts B and C: EDG-7500 Fixed Daily Dosing 4-Weeks in oHCM and nHCM Study Design

CIRRUS HCM

PRIMARY OBJECTIVE

Safety & tolerability in adults with HCM

KEY INCLUSION CRITERIA

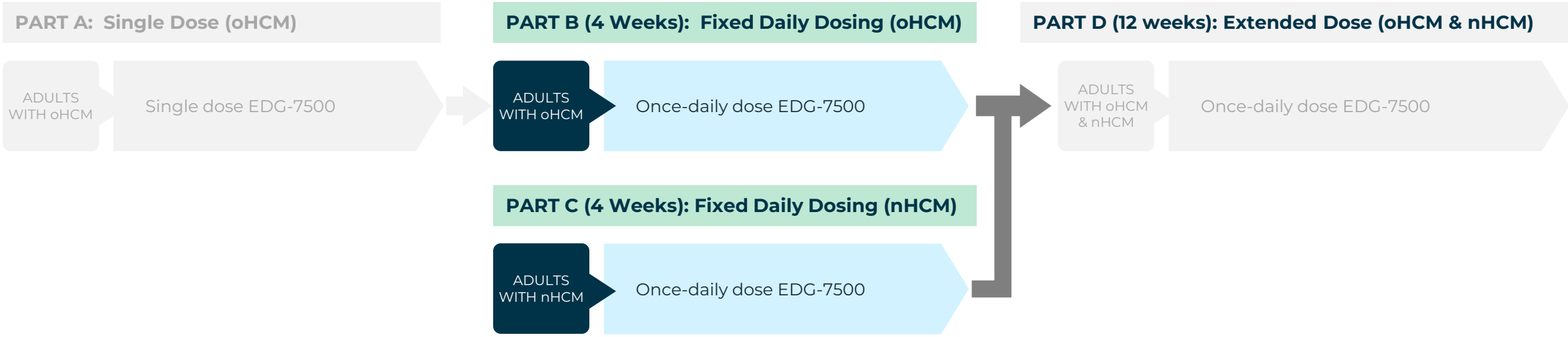
Male and female participants ≥18 yrs of age with HCM LVEF ≥60%

TOTAL CIRRUS TARGET ENROLLMENT

~70

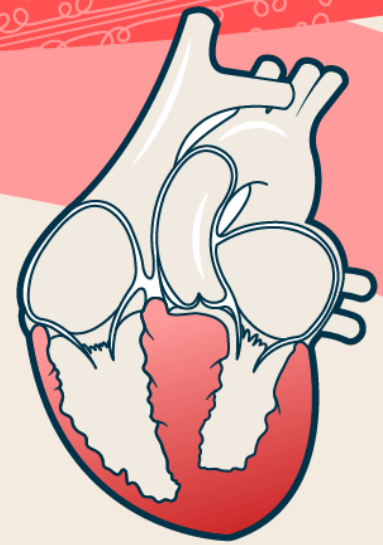
KEY OUTCOME MEASURES

Cardiovascular PD, LVEF, Biomarkers, PK



Abbreviations: oHCM, obstructive hypertrophic cardiomyopathy; nHCM, nonobstructive hypertrophic cardiomyopathy; LVEF, left ventricular ejection fracture; PD, pharmacodynamics; PK, pharmacokinetics

Part B – Obstructive HCM



CIRRUS
HCM

Obstructive HCM: Baseline Characteristics (N=17)

Demographics	
Age (yrs), mean (SD)	61 (13)
Female, n (%)	12 (71%)
BMI (kg/m²), mean (SD)	28 (4)
Pathogenic sarcomere variant, n (%)	4 (24%)
History of paroxysmal AF / flutter, n (%)	1 (6%)
ICD, n (%)	2 (12%)
Prior SRT, n (%)	1 (6%)
Hypertension, n (%)	11 (65%)
Diabetes, n (%)	1 (6%)
NYHA Class	
Class I, n (%)	1 (6%)
Class II, n (%)	10 (59%)
Class III, n (%)	6 (35%)

Echocardiographic Parameters	
LVEF (%), mean (SD)	65 (4)
LVOT-G (resting; mmHg), mean (SD)	59 (30)
LVOT-G (Valsalva; mmHg), mean (SD)	93 (32)
e' mean (cm/s), mean (SD)	6 (2)
Maximal LV wall thickness (mm), mean (SD)	18 (2)
LAVI (ml/m²), mean (SD)	37 (13)
Patient-Reported Outcome Measures	
KCCQ-OSS, mean (SD)	63 (16)
KCCQ-CSS, mean (SD)	69 (15)
Laboratory Measures	
NT-proBNP (geometric mean /median (IQR); pg/ml)	724 / 710 (381, 1074)

AF, atrial fibrillation; BMI, body mass index; e', early diastolic mitral annular velocity; CSS, clinical symptom score; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; KCCQ, Kansas City Cardiomyopathy Questionnaire; LAVI, left atrial volume index; LV, left ventricular; LVEF, LV ejection fraction; LVOT, LV outflow tract; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; oHCM, obstructive HCM; OSS, overall summary score; SRT, septal reduction therapy.

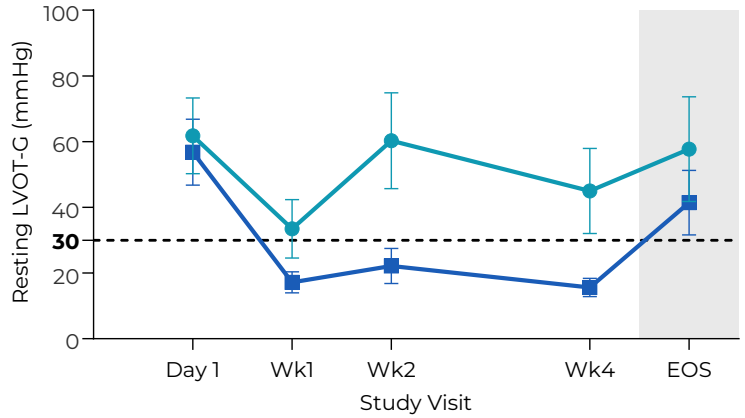
After Only 4 Weeks of Treatment, **~80%** of oHCM Participants in the Safety Population Showed a Complete LVOT-G Response

HEMODYNAMICS

Strong LVOT-G Responses (N=17**)

REST

Absolute Value

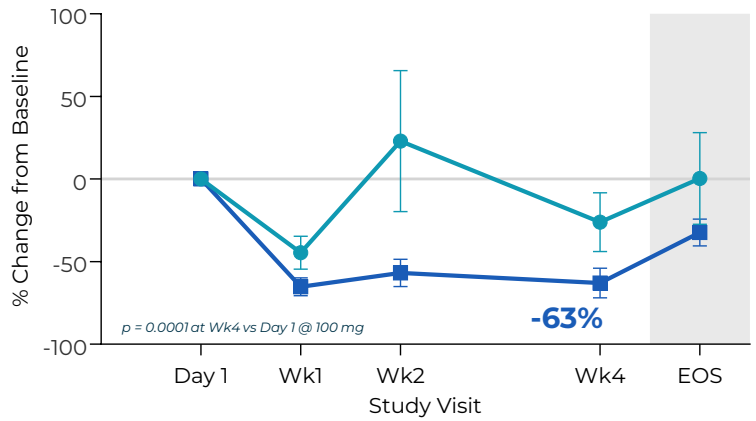


%* Reaching LVOT <30 mmHg (Week 4)

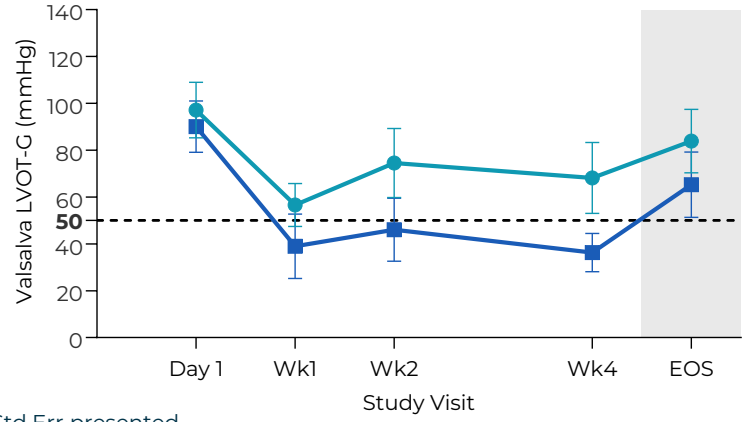
50 mg: **43%**

100 mg: **89%**

% Change from Baseline



VALSALVA

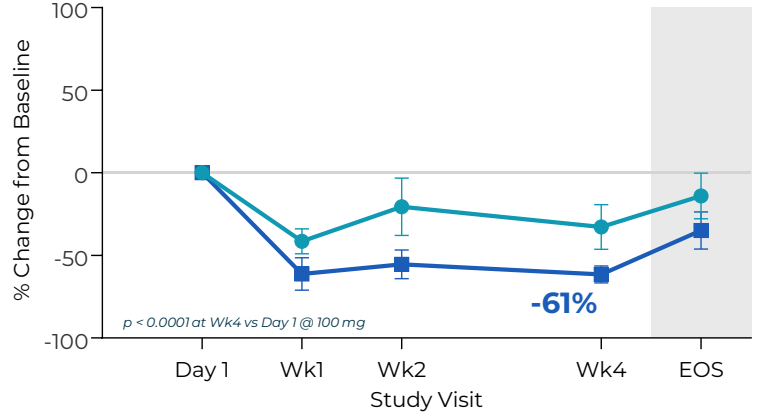


%* Reaching LVOT <50 mmHg (Week 4)

50 mg: **57%**

100 mg: **89%**

50 mg (N=8) 100 mg (N=9)



Means ± Std Err presented

Edgewise Therapeutics – Data on file. Complete LVOT-G response defined as resting and Valsalva gradients <30 mmHg and <50 mmHg, respectively

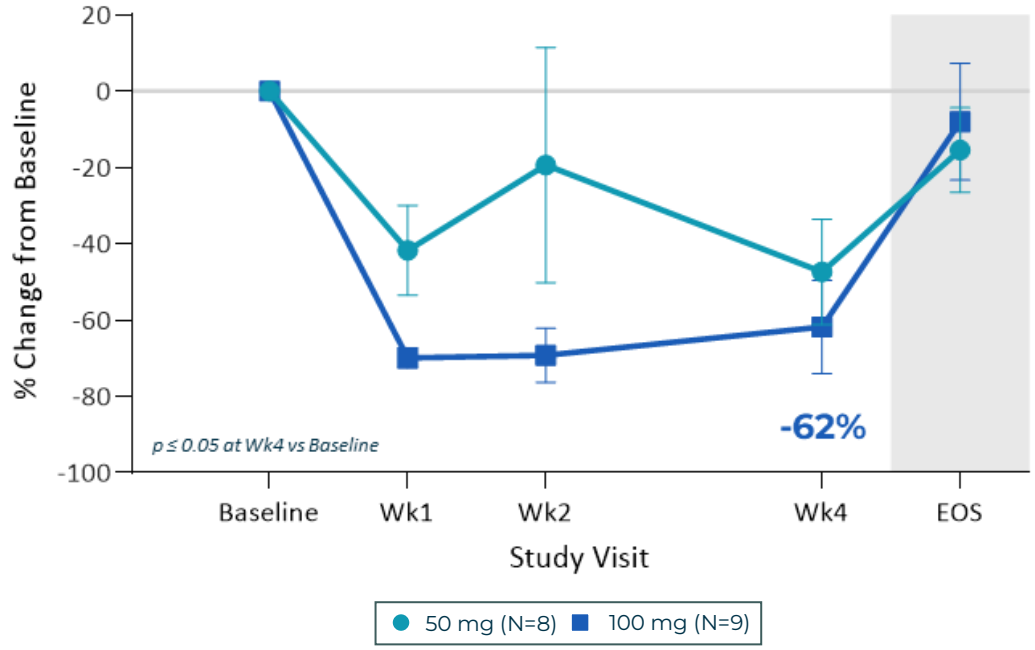
* % reaching LVOT criteria based on N=7 and N=9 participants with Week 4 data at 50 mg and 100 mg respectively.

** Five of the patients included in the Safety Population evaluation for LVOT had either resting or Valsalva gradients below clinical meaningful thresholds on Day 1

EDG-7500 Administration Resulted in Rapid and Robust Reductions in NT-proBNP, a Key Marker of Heart Failure in oHCM[1]

BIOMARKERS

5/9 (56%) Patients at 100 mg Achieved <150 pg/ml NT-proBNP, the Threshold for Normal



Improvements in NT-proBNP are Known to Show Strong Correlation to Improvements in pVO_2

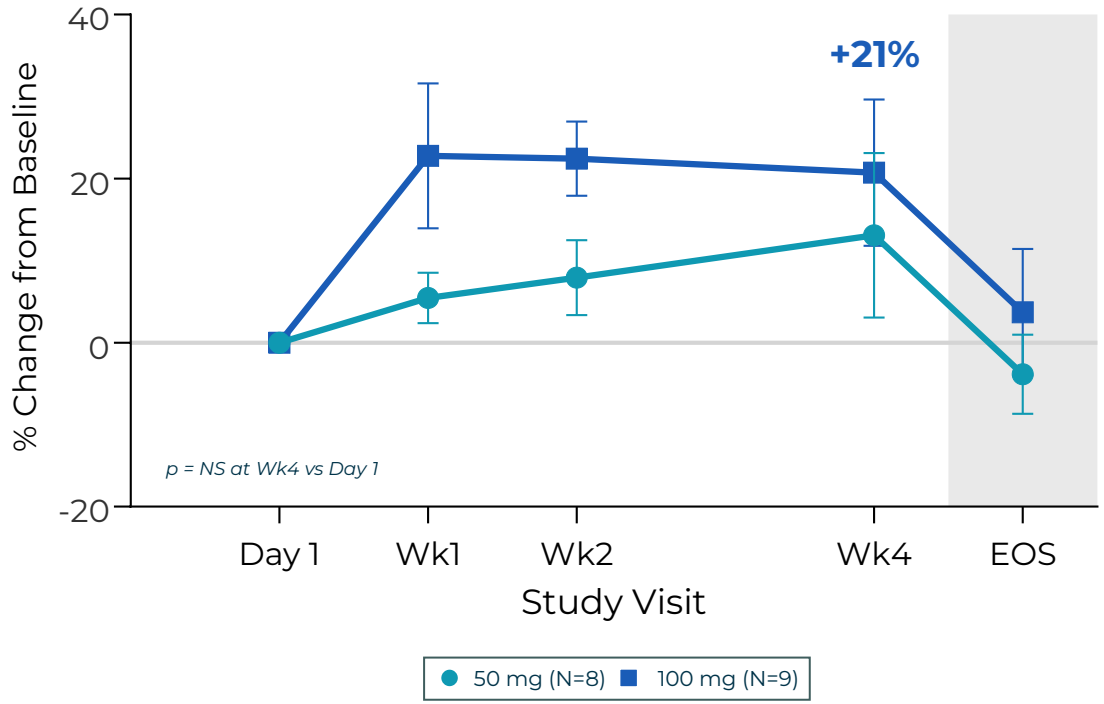
Geometric means ± Std Err for presented for values. Means ± Std Err for % Change from Baseline

[1]Coats C.J. et al. European Heart Journal. 2013; 34(32), 2529–2537; Cytokinetics Presentation at the European Society of Cardiology Congress, 2024; London, UK; September 1, 2024 (Clinical Application of Biomarkers in Obstructive HCM: Insights from SEQUOIA-HCM)
Edgewise Therapeutics – Data on file

Rapid and Sustained Increase in Early Diastolic Mitral Annulus Velocity (e') Suggesting an Improvement in Diastolic Function in oHCM[1]

DIASTOLOGY

Rapid Dose Responsive Improvements in Mean e' Observed as Early as 1 Week After Initiation of Treatment with EDG-7500

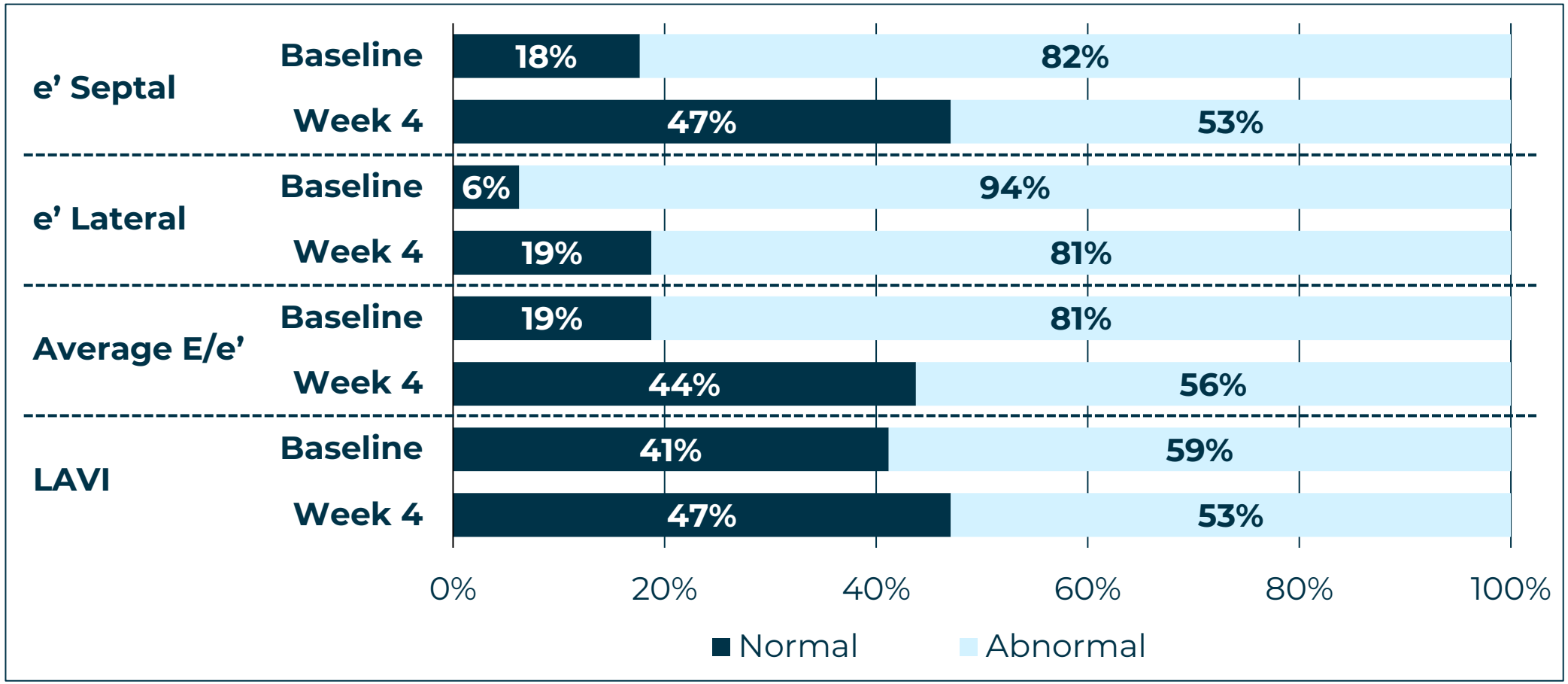


Means ± Std Err presented
Edgewise Therapeutics – Data on file

EDG-7500 Administration Led to Improvements in Left Ventricular Diastolic Function in Patients with oHCM

DIASTOLOGY

More Patients Achieving Normal Diastolic Function Across a Number of Parameters



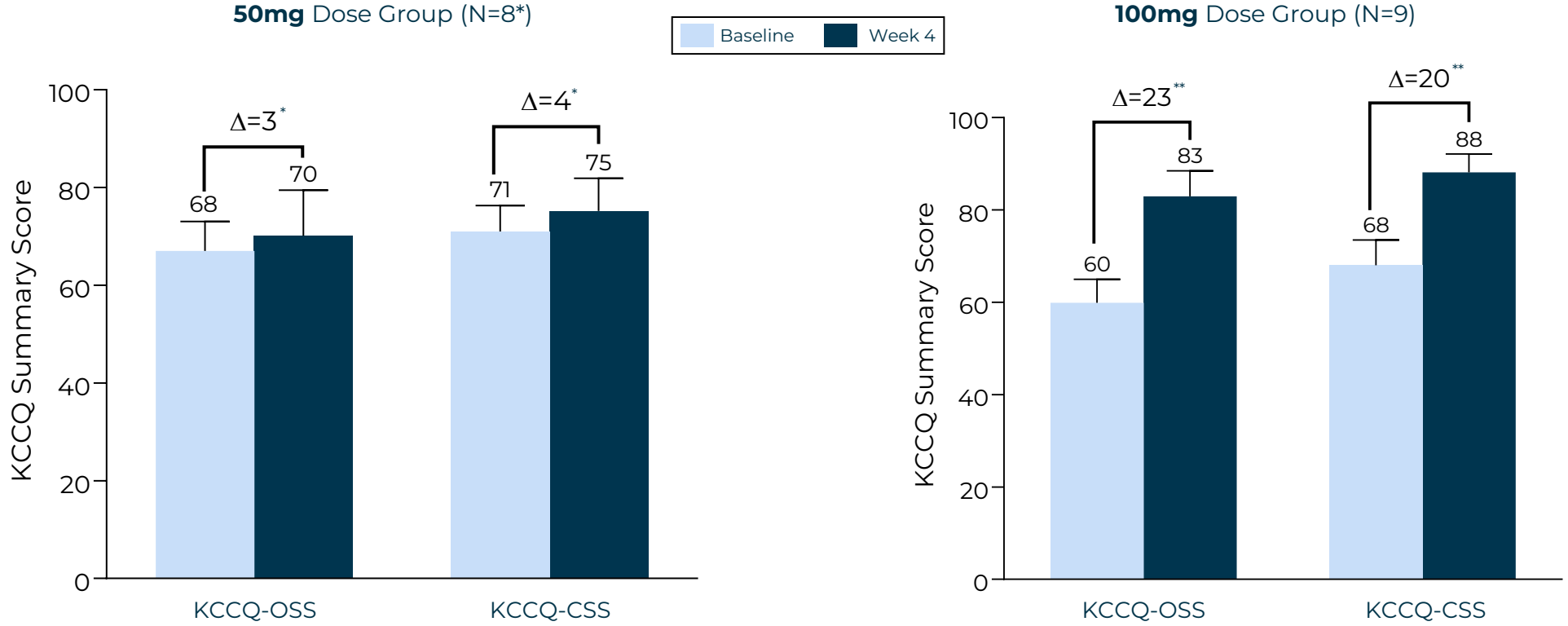
Abnormal Criteria: e' Septal < 7, e' Lateral < 10, E/e' mean >14, LAVI >34 (Criteria based on Hegde 2024)
Note: if a Week 4 value was missing, the last non-missing value in the treatment period was used (LOCF).

Edgewise Therapeutics – Data on file

Participants on 100 mg had Significant Improvements in Patient Reported Outcomes; Mean Increase in **KCCQ-OSS** of **23 points** in oHCM

SYMPTOMS

KCCQ Changes with EDG-7500 in oHCM after 4 Weeks vs. Baseline



Median KCCQ Improvement: **7 points** **2 points** **24 points** **18 points**

**p = NS at Wk4 vs Day 1*

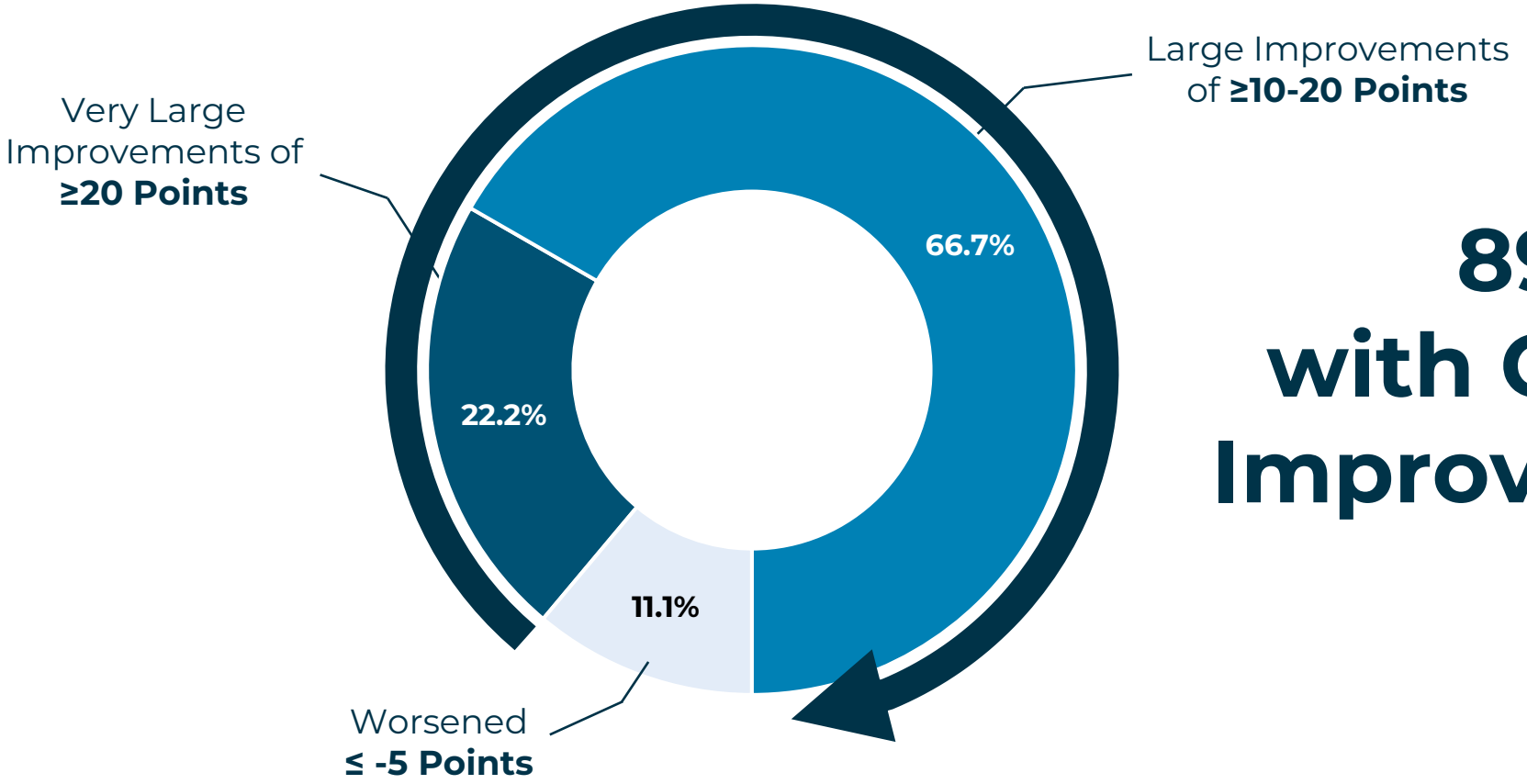
***p < 0.005 at Wk4 vs Day 1*

Means ± Std Err presented
Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; OSS, overall summary score; CSS, clinical summary score; oHCM, obstructive hypertrophic cardiomyopathy
Edgewise Therapeutics – Data on file
* Represents 7 individuals who were evaluated for KCCQ at week 4

89% of oHCM Participants Treated with 100 mg EDG-7500 Experienced Significant Clinical Improvements Shown in KCCQ-CSS

SYMPTOMS

KCCQ-CSS Changes with EDG-7500 Treatment in oHCM (100 mg) after 4 Weeks vs. Baseline



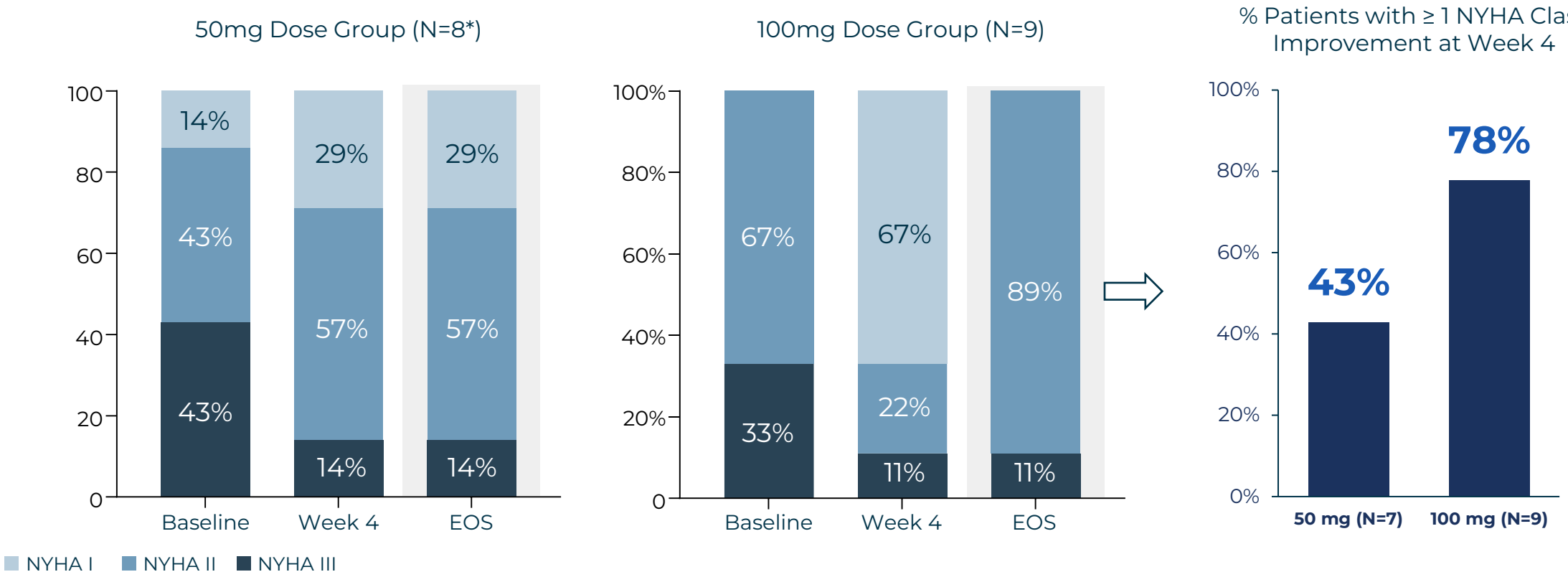
89% with Clinical Improvements

Abbreviation: KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire – Clinical Summary Score
Edgewise Therapeutics – Data on file

In oHCM, Administration of EDG-7500 100 mg Led to **78%** of Participants Achieving Improvements of ≥ 1 NYHA Class; **67%** Achieved NYHA Class I

SYMPTOMS

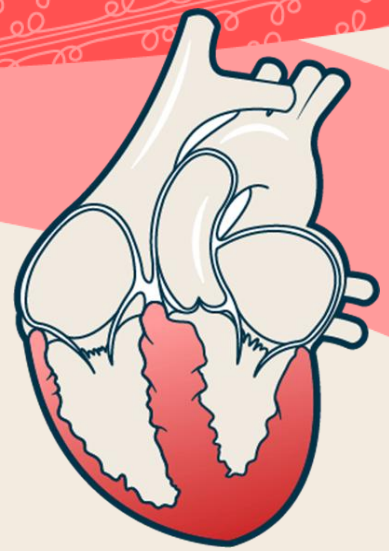
NYHA Functional Class Improvements with EDG-7500 in oHCM at 4 Weeks



- ~40% of patients treated with a CMI in Ph 3 did not observe a ≥1 NYHA Class change end of study (at 6 mos.) when patients were on maximally efficacious doses
  - Percent of pts who did not experience a ≥1 NYHA functional class improvement with mavacamten and aficamten were 35% and 42%, respectively

Abbreviation: NYHA, New York Heart Association Functional Classification
Maron M et al., N Engl J Med 2024;390:1849-1861; Olivotto I. et al. The Lancet 2020; 396(10253), 759–769.
Edgewise Therapeutics – Data on file
* Represents 7 individuals who were evaluated for NYHA at week 4

Part C – Nonobstructive HCM



CIRRUS HCM

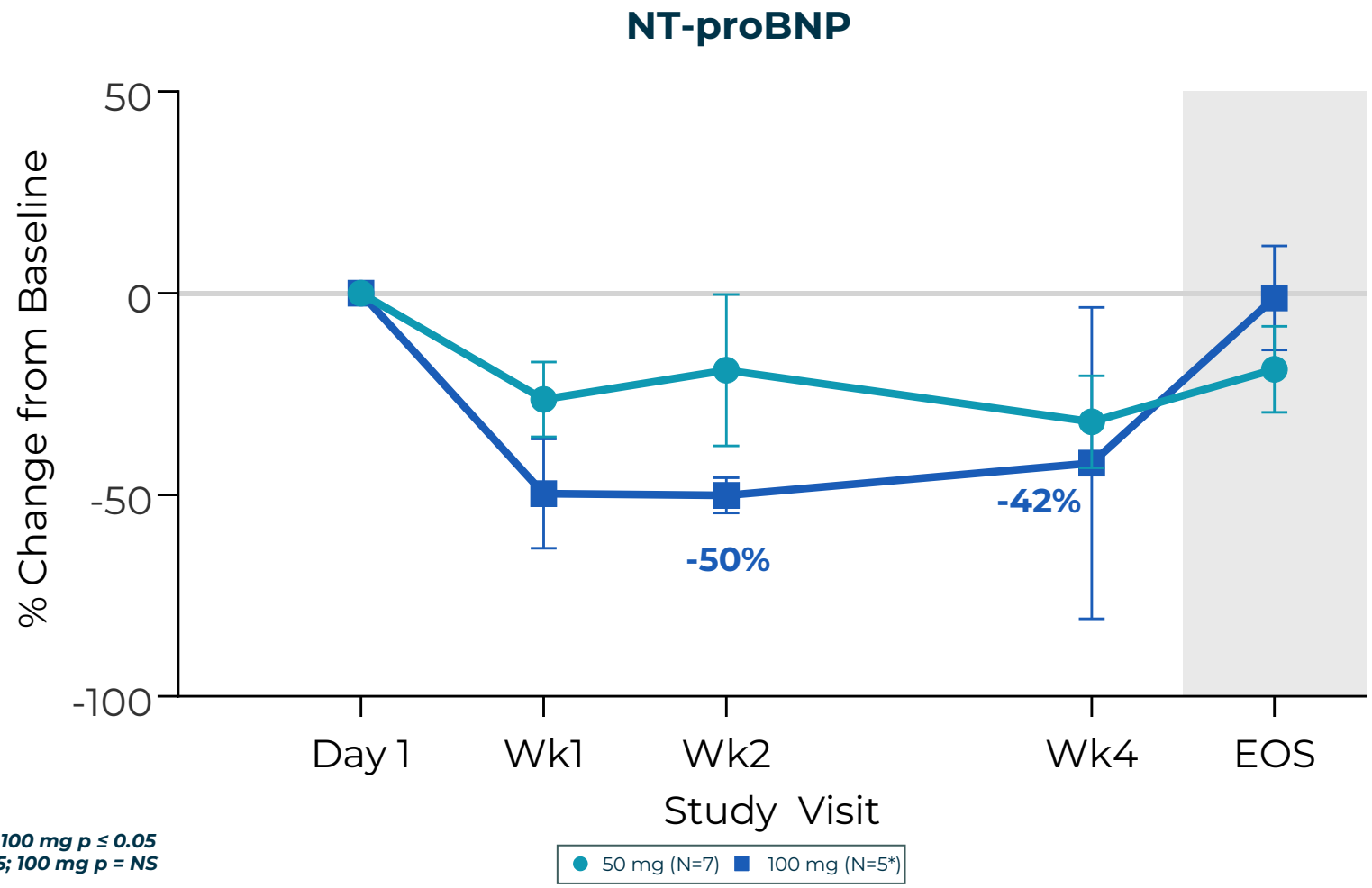
Nonobstructive HCM: Baseline Characteristics (N=12)

Demographics	
Age (yrs), mean (SD)	54 (19)
Female, n (%)	7 (58%)
BMI (kg/m²), mean (SD)	27 (4)
Pathogenic sarcomere variant, n (%)	4 (33%)
History of paroxysmal AF / flutter, n (%)	2 (17%)
ICD, n (%)	6 (50%)
Prior SRT, n (%)	0%
Hypertension, n (%)	2 (17%)
Diabetes, n (%)	2 (17%)
NYHA Class	
Class I, n (%)	0%
Class II, n (%)	6 (50%)
Class III, n (%)	6 (50%)

Echocardiographic Parameters	
LVEF (%), mean (SD)	61 (6)
LVOT-G (resting; mmHg), mean (SD)	9 (6)
LVOT-G (Valsalva; mmHg), mean (SD)	14 (10)
e' mean (cm/s), mean (SD)	7 (2)
Maximal LV wall thickness (mm), mean (SD)	18 (3)
LAVI (ml/m²), mean (SD)	31 (12)
KCCQ-OSS, mean (SD)	57 (22)
KCCQ-CSS, mean (SD)	63 (23)
NT-proBNP (geometric mean/median (IQR); pg/ml)	782 / 715 (546, 1231)

AF, atrial fibrillation; BMI, body mass index; e', early diastolic mitral annular velocity; CSS, clinical symptom score; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; KCCQ, Kansas City Cardiomyopathy Questionnaire; LAVI, left atrial volume index; LV, left ventricular; LVEF, LV ejection fraction; LVOT, LV outflow tract; nHCM, nonobstructive HCM; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; OSS, overall summary score; SRT, septal reduction therapy.

Administration of EDG-7500 Resulted in Rapid and Robust Reductions in NT-proBNP in Participants with nHCM

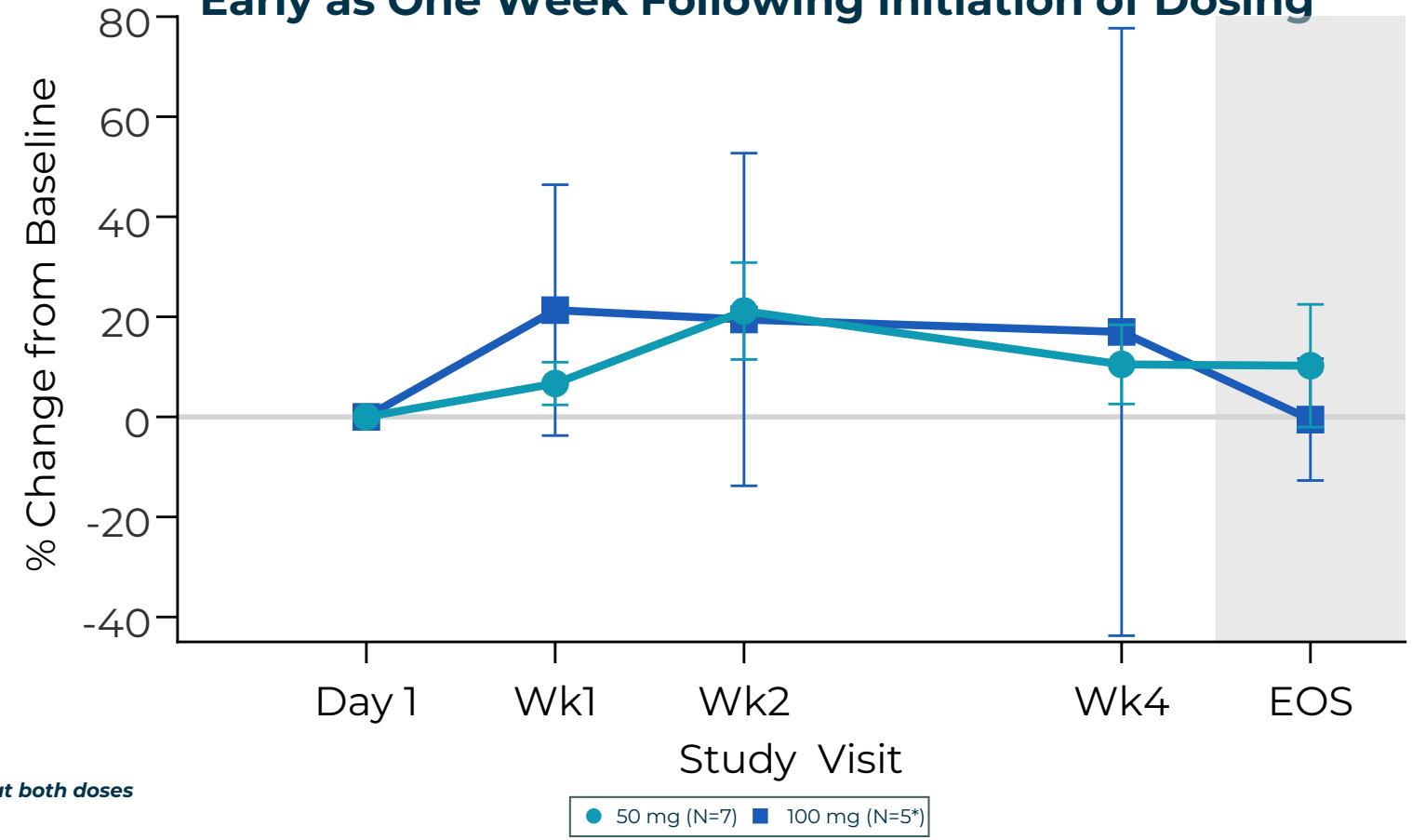


Wk2 vs Day 1: 50 mg p = NS; 100 mg p ≤ 0.05
Wk4 vs Day 1: 50 mg p ≤ 0.05; 100 mg p = NS

Means ± Std Err presented
* Two patients at week 4
Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; nHCM, nonobstructive hypertrophic cardiomyopathy
Edgewise Therapeutics – Data on file

Administration of EDG-7500 Led to Early and Rapid Signs of Diastolic Improvements in nHCM Participants after Only 4 Weeks

Treatment with EDG-7500 Led to Mean e' Changes in Participants with nHCM as Early as One Week Following Initiation of Dosing

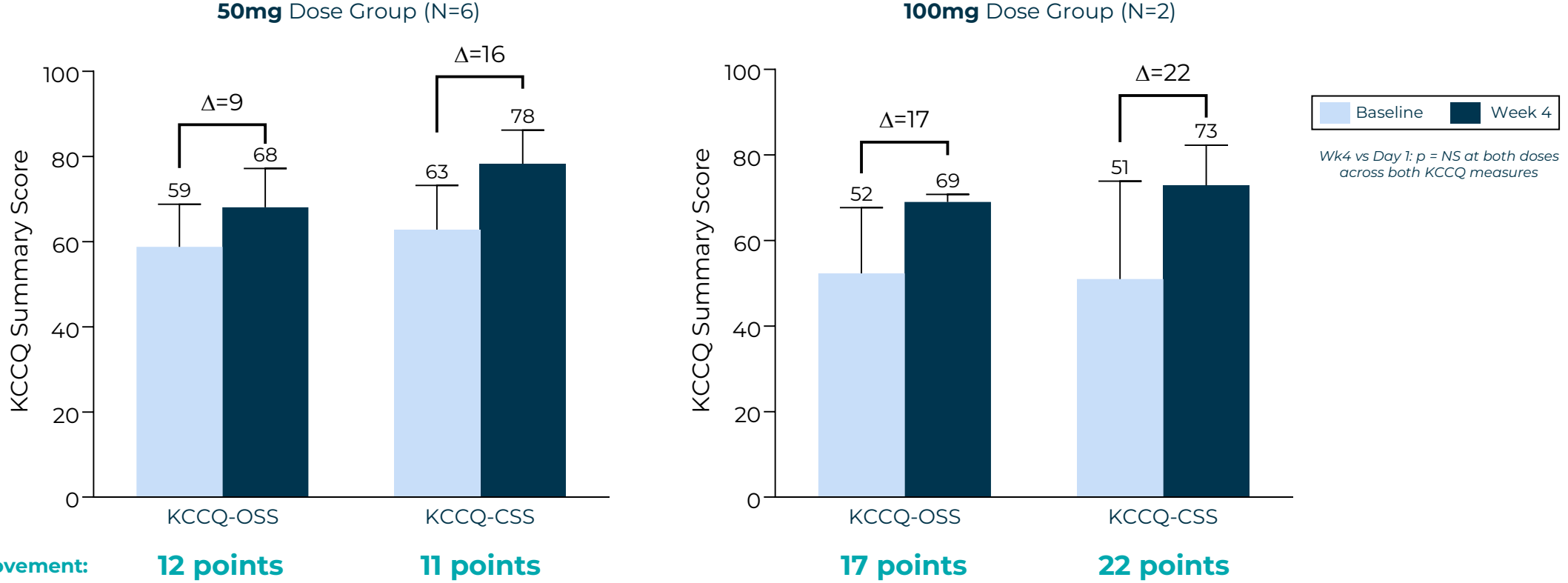


Wk2/Wk4 vs Day 1: p = 0.05 at both doses

Means ± Std Err presented
* Two patients at week 4
Abbreviations: nHCM, nonobstructive hypertrophic cardiomyopathy; EOS, end of study; e", E Prime
Edgewise Therapeutics – Data on file

Preliminary KCCQ Observations with EDG-7500 Suggest Improvements Beyond Those Observed in Other Therapeutic Clinical Trials in nHCM

KCCQ Changes with EDG-7500 in nHCM after 4 Weeks vs. Baseline

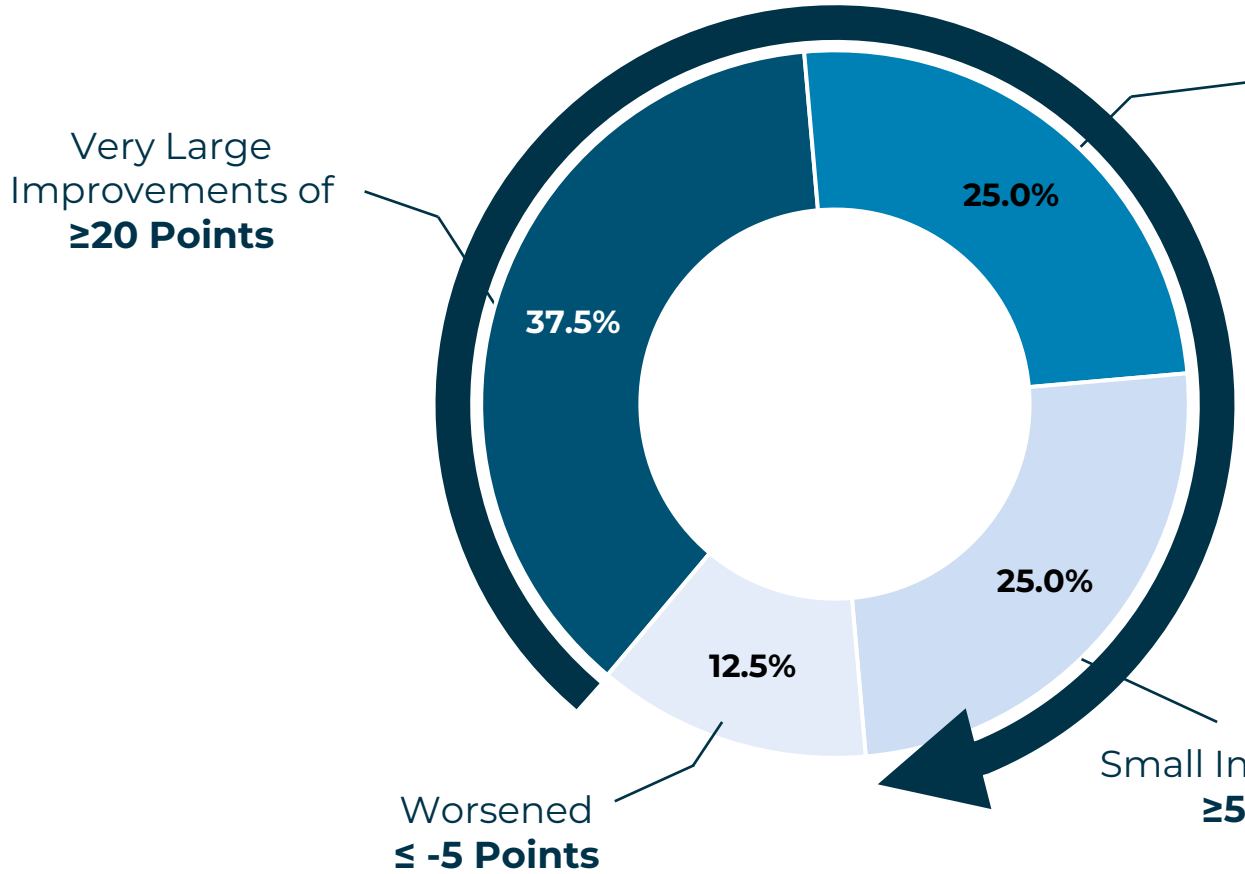


	50mg Dose Group (N=6)		100mg Dose Group (N=2)	
Median KCCQ Improvement:	**12 points**	**11 points**	**17 points**	**22 points**

Means ± Std Err presented
Note: To-date, no head-to-head comparisons of any other products to any of our product candidates in any clinical trial have been completed; results have been obtained from different trials with different designs, endpoints and patient populations; results may not be comparable.
Ahmad Masri Presentation at World Congress on Acute Heart Failure, 20 May 2023: Evaluation of Aficamten in Patients with Symptomatic N on obstructive Hypertrophic Cardiomyopathy: REDWOOD HCM Cohort 4; Ho C et al., JACC, Volume 75, Issue 21, 2 June 2020, Pages 2649-2660
Edgewise Therapeutics – Data on file

88% of nHCM Participants Treated with 100 mg EDG-7500 Experienced Significant Clinical Improvements Shown in KCCQ-CSS

KCCQ-CSS Changes with EDG-7500 Treatment in nHCM (50 mg and 100 mg) after 4 Weeks vs. Baseline



88% with Clinical Improvements

Abbreviation: KCCQ-OSS, Kansas City Cardiomyopathy Questionnaire – Clinical Summary Score
Edgewise Therapeutics – Data on file

EDG-7500 Safety in Parts B and C

CIRRUS
HCM

EDG-7500 was Generally Well Tolerated in oHCM Participants in Part B and nHCM Participants in Part C

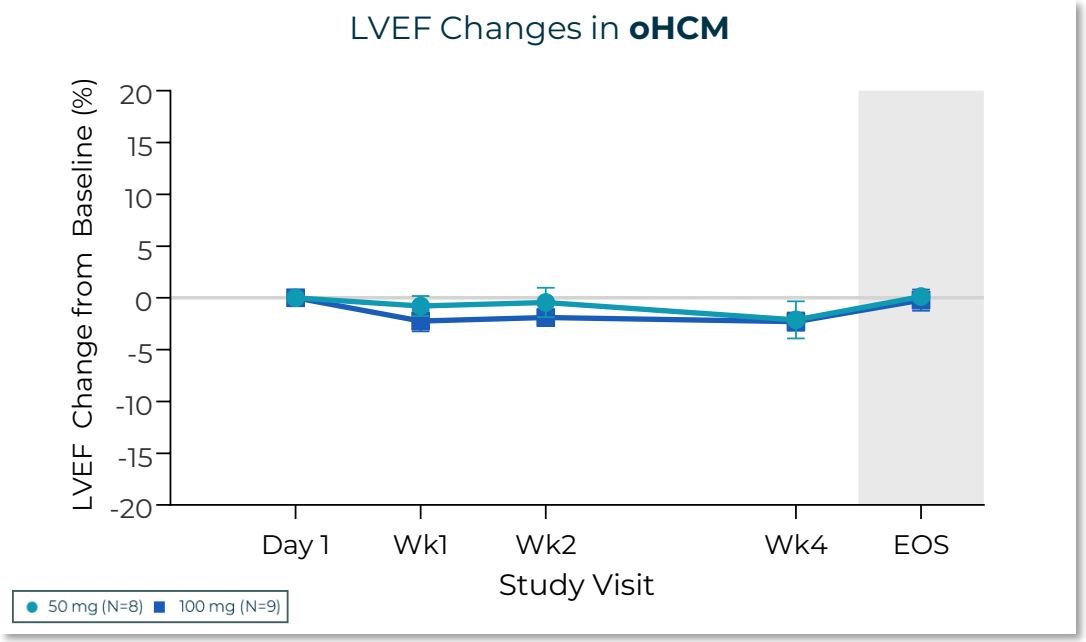
Treatment-Emergent Adverse Events (TEAE), n (%)	N=29
Dizziness (mostly mild and transient in duration)	8 (27.6%)
Upper respiratory tract infection	5 (17.2%)
Atrial fibrillation	4 (13.8%)
Influenza like illness	3 (10.3%)
Palpitations	3 (10.3%)
Constipation	2 (6.9%)
Diarrhea	2 (6.9%)
Headache	2 (6.9%)

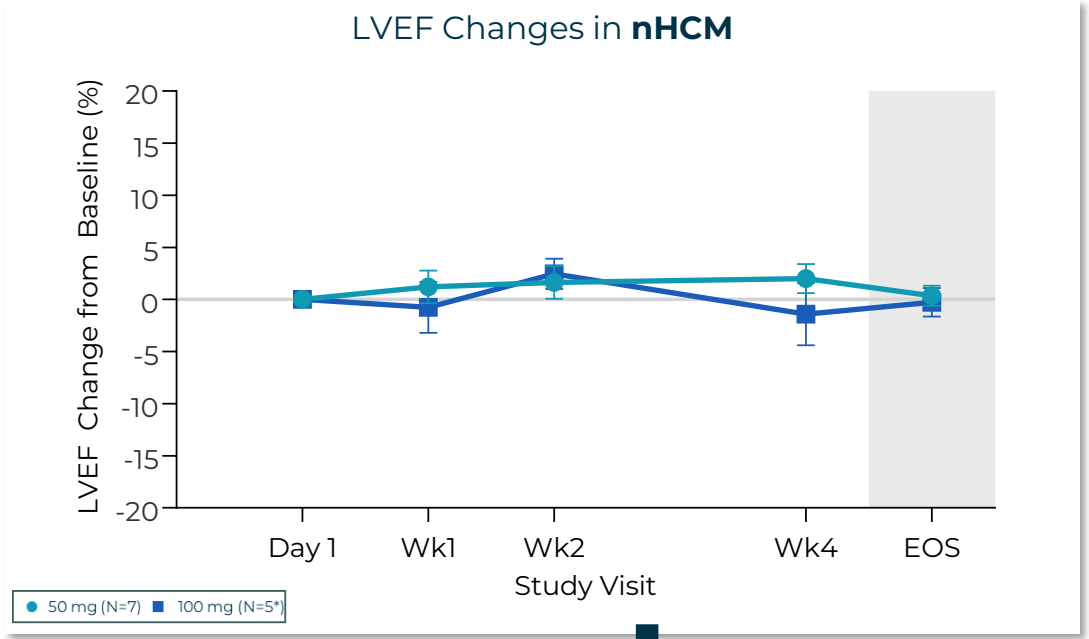
Treatment emergent adverse events in >1 participant in the combined oHCM and nHCM cohorts.

LVEF, left ventricular ejection fraction; nHCM, nonobstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

EDG-7500 Continues to Demonstrate No Meaningful Reductions in LVEF; No Participants had LVEF Drop to <50%

No Correlation Between EDG-7500 Plasma Concentration and LVEF Change



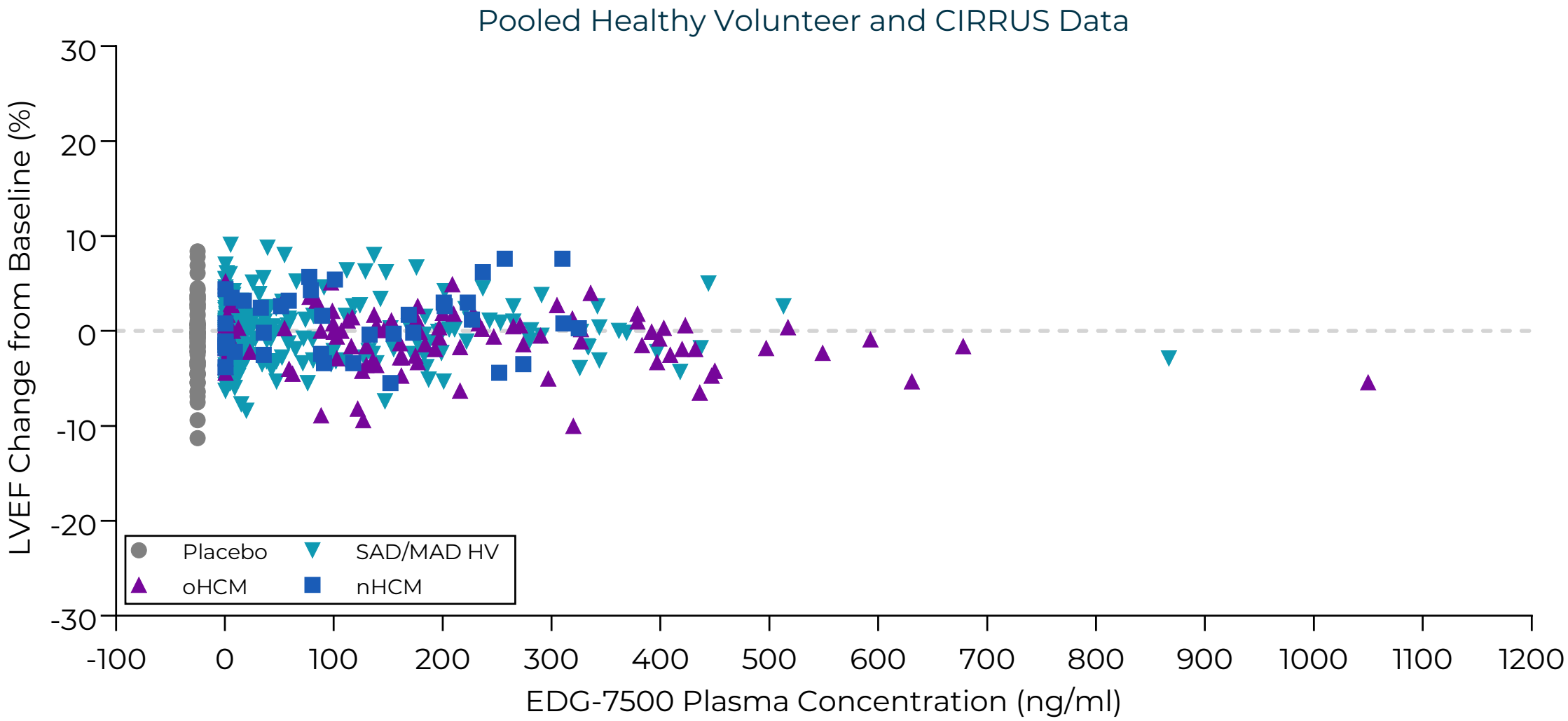


- 4/12 (33%) nHCM patients had a baseline LVEF <60% by core lab; all 4 remained stable throughout the treatment period
- No LVEF drops below 50%; mean change from baseline was +2.5% for the 4 nHCM subjects

Subject	Dose (mg)	Baseline	Week 4	Change
1	100	56.0%	57.6%	1.60%
2	50	53.4%	56.0%	2.60%
3	50	55.8%	55.5%	-0.30%
4	50	52.4%	58.6%	6.20%

Means ± Std Err presented
* Only two patients at week 4
Edgewise Therapeutics – Data on file

No Meaningful Reductions in LVEF or LVEF<50% Across a Broad Exposure Range Observed After EDG-7500



Abbreviations: LVEF, left ventricular ejection fraction; HV, healthy volunteers

Edgewise is Committed to Delivering a Novel and Differentiated Therapy for Individuals with HCM

Aspirational Target Product Profile for EDG-7500 in the Treatment of HCM

Safety	Based on Observations to Date, No Meaningful Change in LVEF; Potential to Eliminate Safety Echoes
Efficacy	Ability to Deepen Functional, Symptom and QoL Improvements Without Concerns of LVEF Drops < 50%
Monitoring	No Excessive Monitoring Requirements Outside of Standard of Care in HCM; Opens Potential for Use Outside of CoEs
Superior Patient Experience	Overcomes the Need for Cumbersome Safety Echoes, Easing the Burden on Patients
Diastolic Effect	Ability to Resolve Diastolic Dysfunction in Patients with Nonobstructive HCM
Dosing	Optimized to Support Intra-Patient Dosing Using SOC Assessments (Biomarkers, Feel-and-Function and Echo at Physician's Discretion)

Abbreviations: CoE, centers of excellence; HCM, hypertrophic cardiomyopathy; LVEF, left ventricular ejection fraction; SOC, standard of care

Part D: 12-Week Extended Dose in oHCM and nHCM will Inform EDG-7500 Phase 3 Design

PRIMARY OBJECTIVE

Safety & tolerability in adults with HCM

KEY INCLUSION CRITERIA

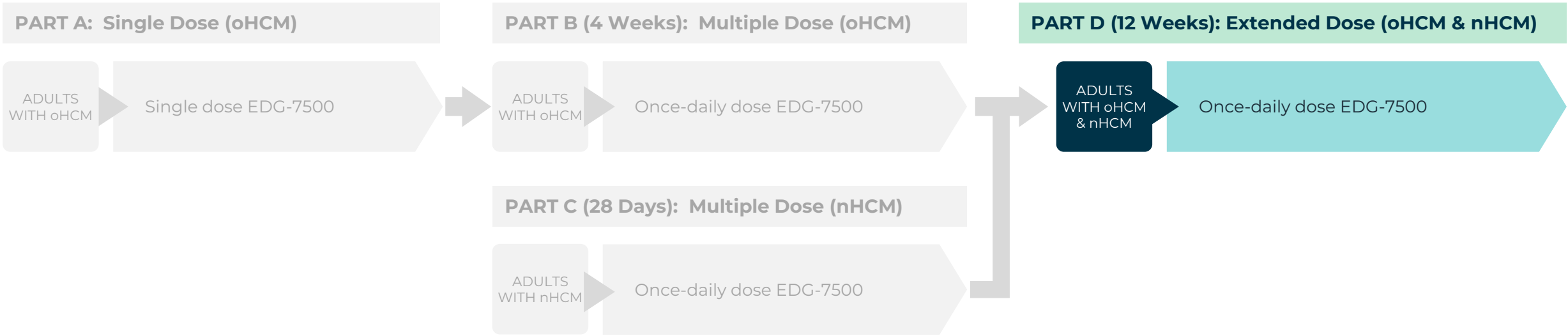
Male and female participants ≥ 18 years of age with HCM
LVEF ≥ 60%

TARGET ENROLLMENT

~70

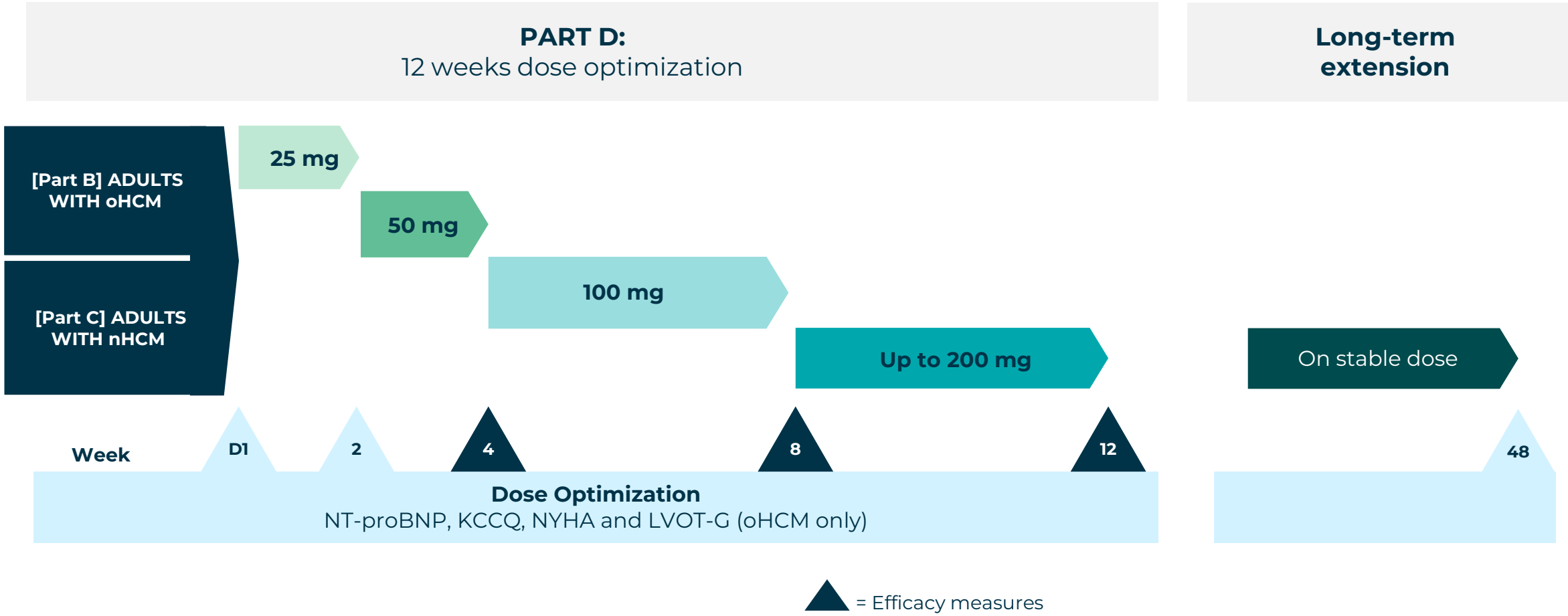
KEY OUTCOME MEASURES

Cardiovascular PD, LVEF, Biomarkers, PK



Abbreviations: PK, pharmacokinetics; PD, pharmacodynamics; EOS, end of study

Positive Observations from Part B and C Used to Inform Intra-Patient Dose Optimization in Part D



Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVOT-G, left ventricle outflow tract gradient; oHCM, obstructive hypertrophic cardiomyopathy; nHCM, nonobstructive hypertrophic cardiomyopathy

High Unmet Need in Obstructive and Nonobstructive HCM

~1 in 500 People impacted by HCM

≥5 years Diagnostic journey in majority of patients

Significant limitations in current HCM therapies

Edgewise: Well-Capitalized to Execute Important Milestones Across Both Sevasemten and EDG-7500

CASH, CASH EQUIVALENTS & MARKETABLE SECURITIES*

~$624M

DEBT

$0

COMMON SHARES OUTSTANDING (NASDAQ: EWTX)

~105M

CASH RUNWAY THROUGH 2028*

*Pro forma cash, including cash, cash, equivalence and marketable securities as of March 31, 2025

Leaders in muscle disease science

Headquartered in beautiful **Boulder, Colorado,** with expert teams spanning the globe, we are dedicated to our mission: changing the lives of patients and families affected by serious muscle diseases