Leaders in Muscle Disease Science

Corporate Overview

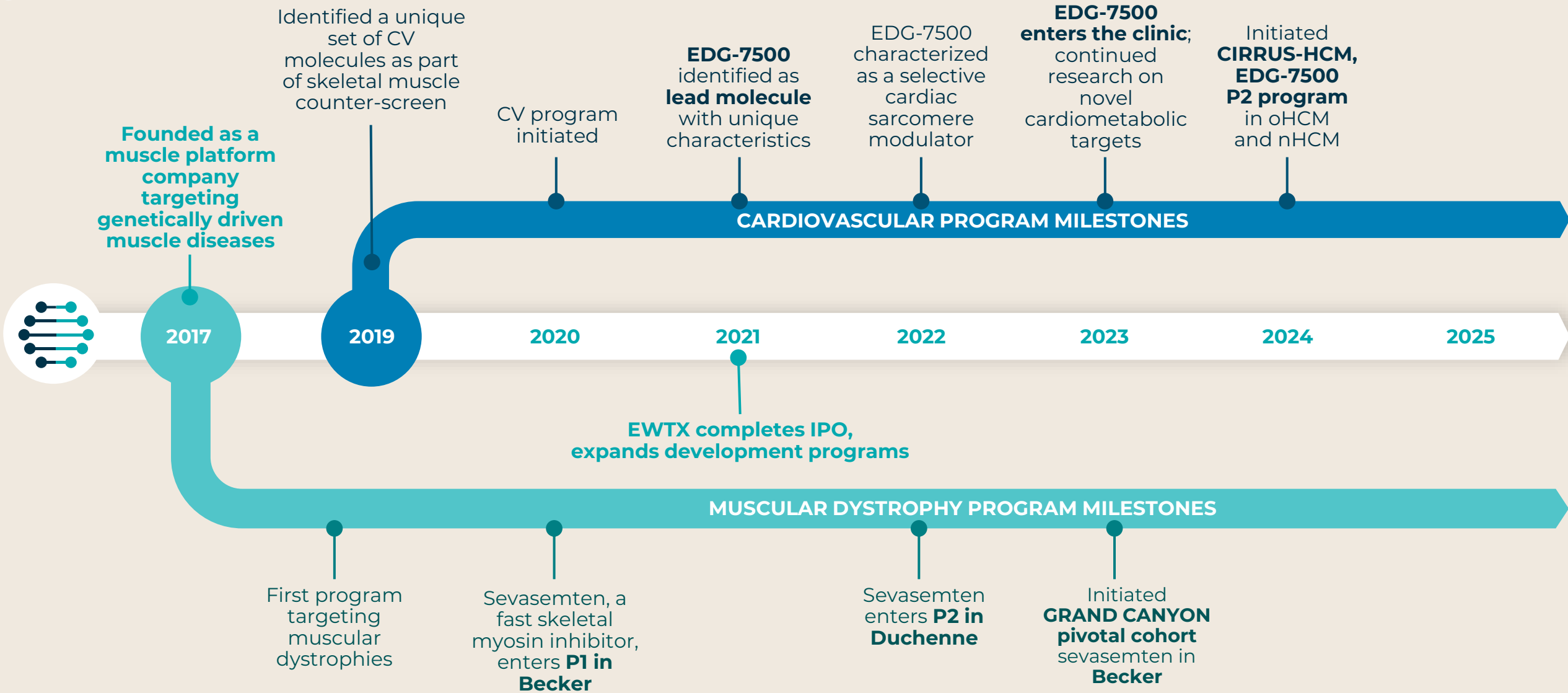
November 2024

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 expectations relating to its clinical trials and clinical development of sevasemten; statements regarding the potential of, and expectations regarding, Edgewise's product candidates and programs, including sevasemten and EDG-7500; statements regarding Edgewise's milestones, including timing of data from its CANYON trial; statements regarding whether data from GRAND CANYON could support a marketing application; and statements by Edgewise's 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; the potential that the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials; 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.

The Evolution of Edgewise



Edgewise® THERAPEUTICS

Focused on muscle science

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

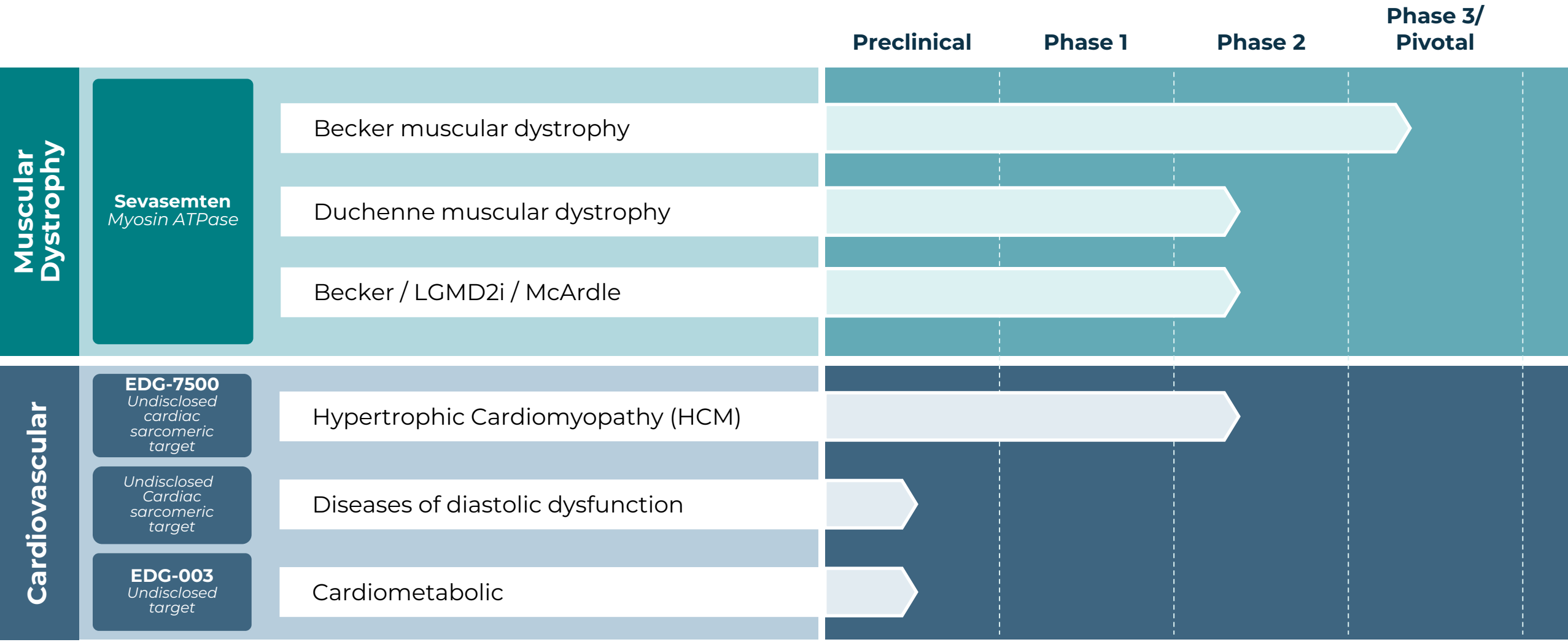
Rapidly advancing portfolio

- Advancing EDG-7500 in oHCM, nHCM, and other potential indications
- Moving sevasemten through a pivotal cohort as potential first therapy to treat Becker muscular dystrophy; advancing phase 2 program in Duchenne
- Additional 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 pipeline

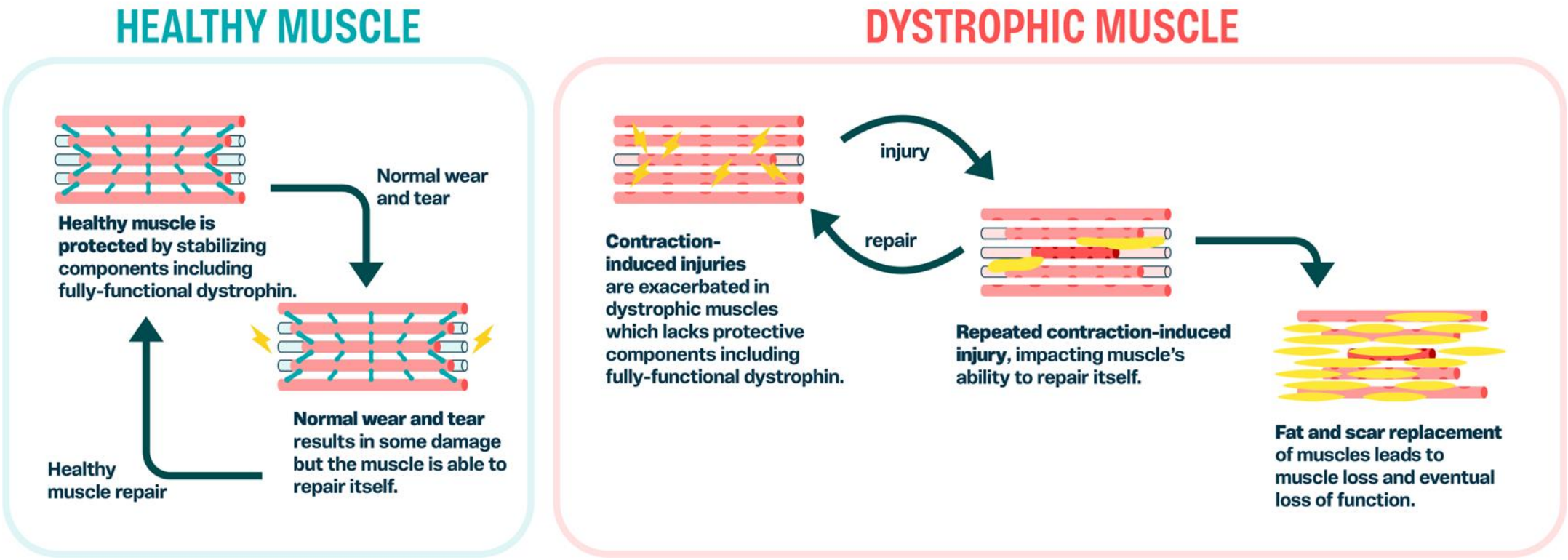


Abbreviations: Becker, Becker muscular dystrophy; Duchenne, Duchenne muscular dystrophy; Limb-Girdle LGMD2i

Contraction-induced muscle damage & sevasemten

The root driver of disease in muscular dystrophies

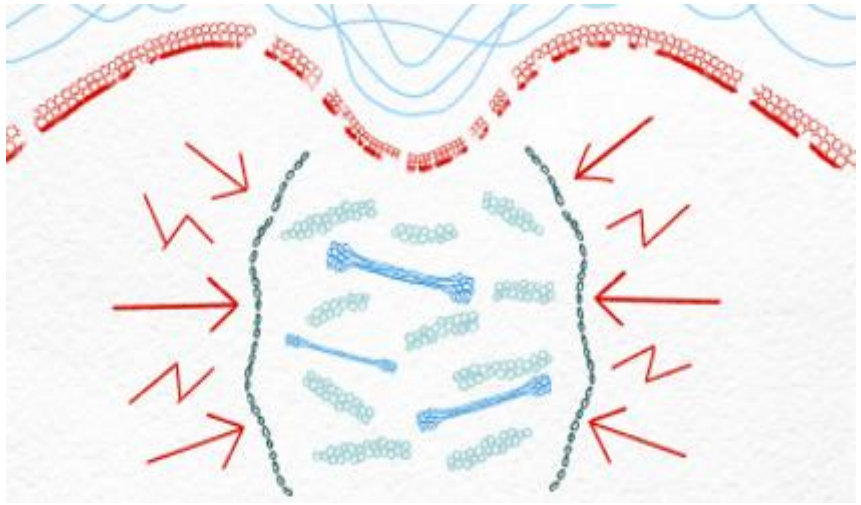
Contraction-Induced Muscle Damage in Muscular Dystrophies



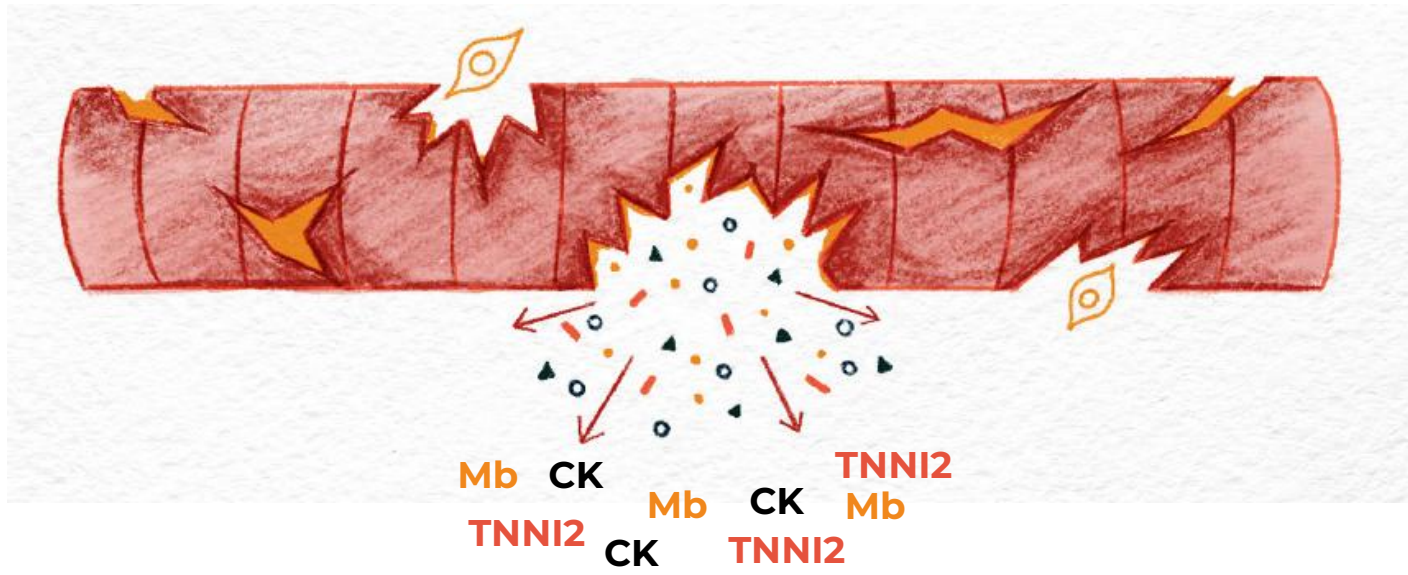
Muscle damage in muscular dystrophies causes leak of injury biomarkers, including CK, TNNI2 and myoglobin, into the circulation

Activity-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

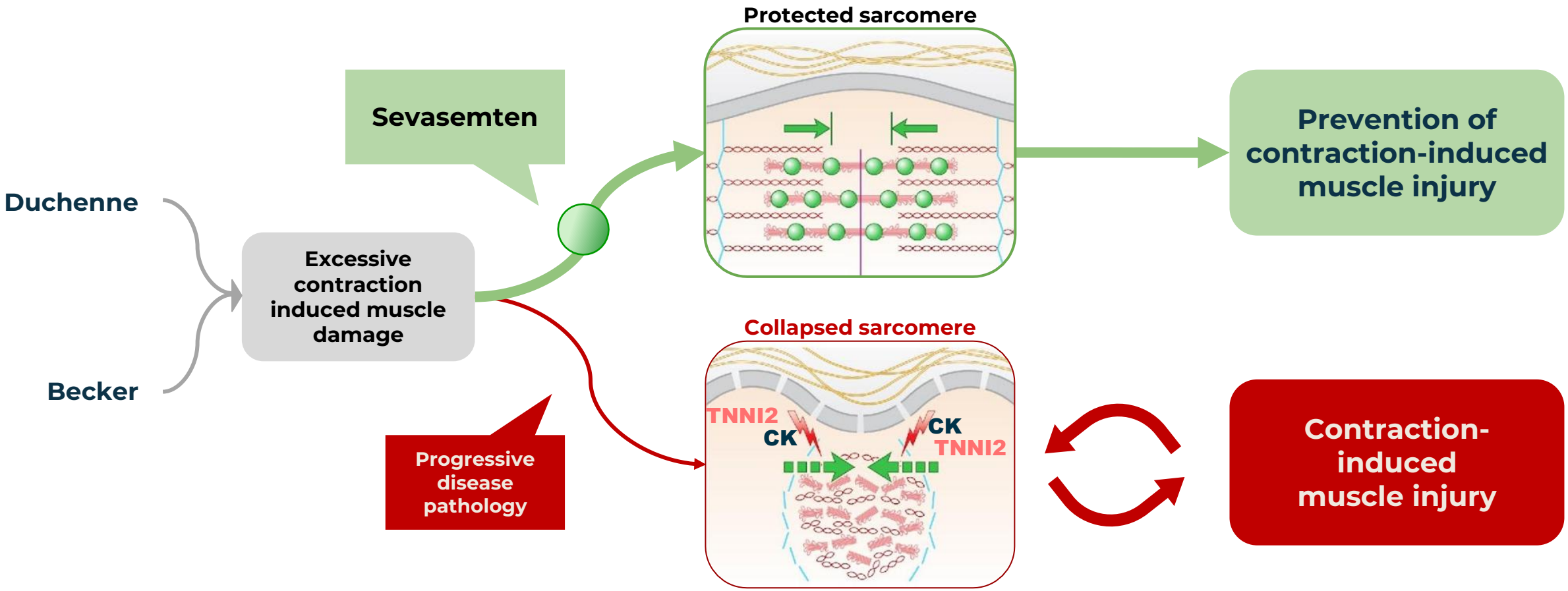


Legend: CK, Creatine Kinase; TNNI2, Fast Skeletal Muscle Troponin I; Mb, Myoglobin

Circulating levels of muscle injury biomarkers can be measured to determine ongoing muscle damage in muscular dystrophies

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.

Ongoing sevasemten clinical trials in muscular dystrophy

Becker

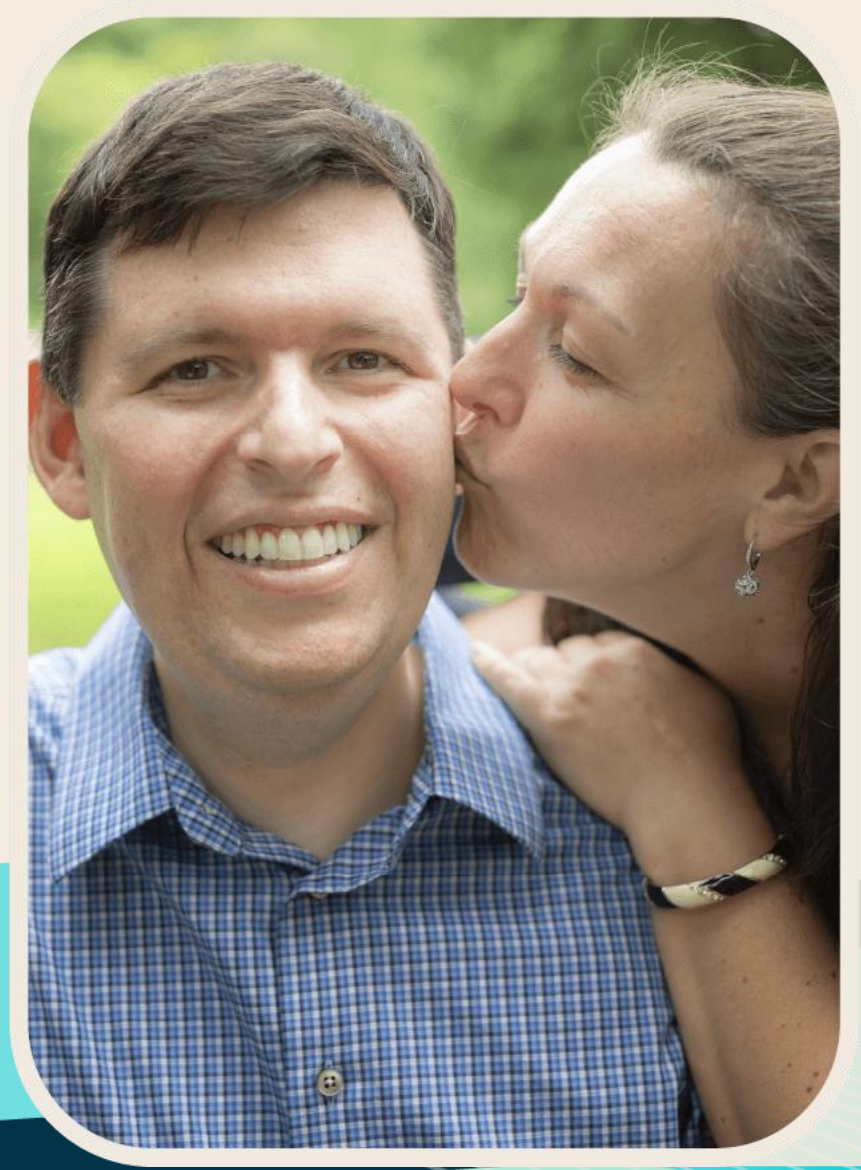
CANYON	**Ph 2 Becker** *(NCT05291091)*	*PK, biomarkers and longer-term safety* → *OLE*	***Fully Enrolled***
GRAND CANYON	**Pivotal Becker Cohort** *(NCT05291091)*	*Function (NSAA), PK, biomarkers and longer-term safety* → *OLE*	***Recruiting***
DUNE	**Ph 2 Becker, LGMD2i, & McArdle**	*Exercise challenge study* → *OLE*	***Complete***
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***

Duchenne

LYNX	**Ph 2 Duchenne Dose-Ranging** *(NCT05540860)*	*PK, biomarkers and safety* → *OLE*	***Recruiting***
FOX	**Ph 2 Duchenne Boys on Gene Tx** *(NCT06100887)*	*PK, biomarkers and safety* → *OLE*	***Recruiting***

Abbreviations: LGMD, limb-girdle muscular dystrophy; OLE, open label extension

Sevasemten program in Becker muscular dystrophy



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

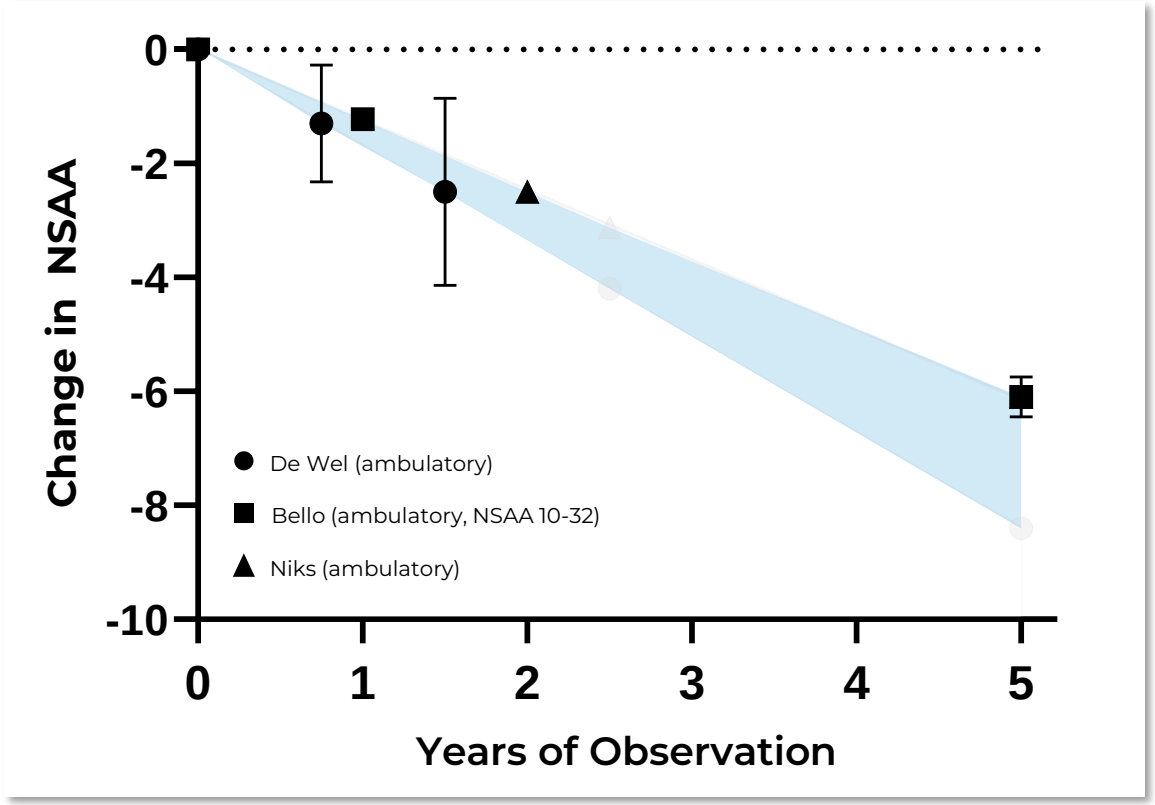
- Becker is a rare, genetic, life-shortening, debilitating and degenerative neuromuscular disorder
- The disease predominately affects males and imposes significant physical, emotional, financial and social impacts on the individuals and their caregivers
- Individuals with Becker lose mobility, function 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

Natural history data in Becker support that functional decline, measured by NSAA, is consistent and predictable

Natural history of Becker muscular dystrophy

- NSAA, a multi-item scale, is utilized in muscular dystrophy natural history studies to longitudinally assess functional measures
- Multiple natural history studies in individuals with Becker demonstrate a **NSAA average score decline of 1.2 to 1.8 points annually** .[1,2,3]



Reference: 1. Bello L, et al. Presented at MDA. 2022 and Bello L, et al. Sci Rep. 2016;6:32439. 2. De Wel B, et al. Eur J Neurol. 2024. 3. Van de Velde NM, et al. Neurology. 2021.; 95% CI shown

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

PRIMARY OBJECTIVE

Safety & tolerability

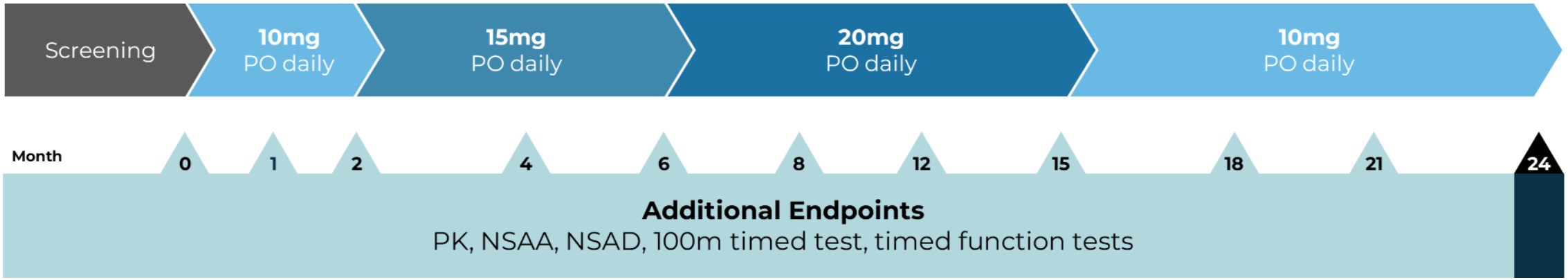
KEY INCLUSION CRITERIA

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

PATIENTS ENROLLED

12

Study design - 24 months



Reference: NCT05160415
Abbreviations: PO, by mouth; PK, pharmacokinetics; NSAD, North Star Assessment for limb-girdle type muscular dystrophies

ARCH

Becker participants had 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 Becker with similar baseline NSAA scores expected to decrease by 1.2[2,3] points per year

Abbreviations: DXA, dual energy x-ray absorptiometry; CK Creatine Kinase; SD standard deviation
Reference: 1. Data on file 2. Bello L, et al. Sci Rep. 2016. 3. Van de Velde NM, et al. Neurology. 2021.

ARCH 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

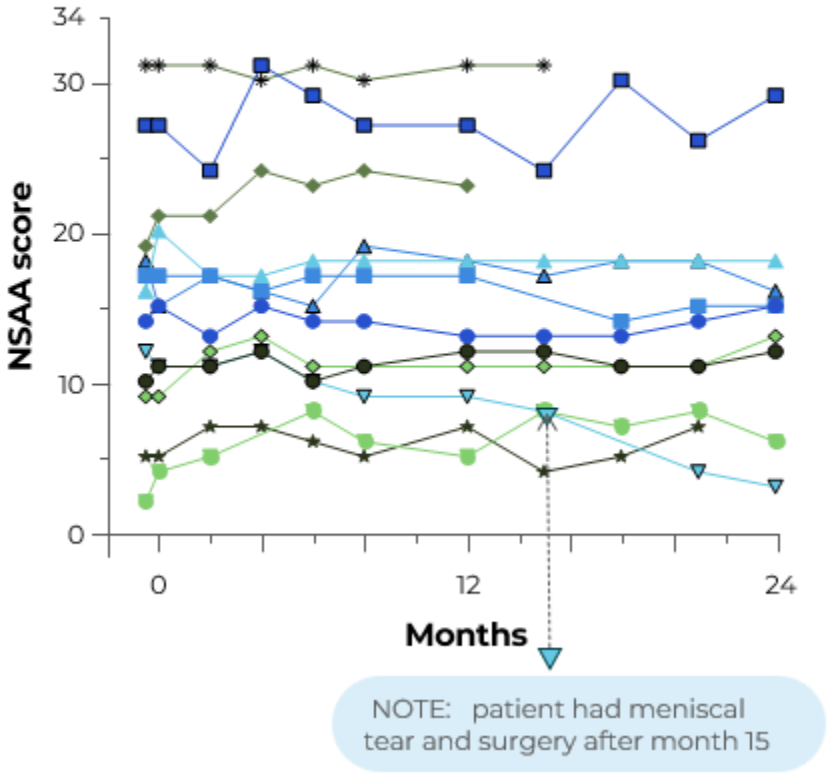
- No dose reductions or adjustments
- No treatment discontinuations due to AEs
- No SAE
- Withdrawals:
  - 3 (2 of whom are planning to enroll in separate open-label extensions)

*Falls are typical for Becker patients and are not related to dizziness
AEs, adverse events; SAE, serious adverse events; GERD gastroesophageal reflux disease; URI upper respiratory infection
Reference: Data on File

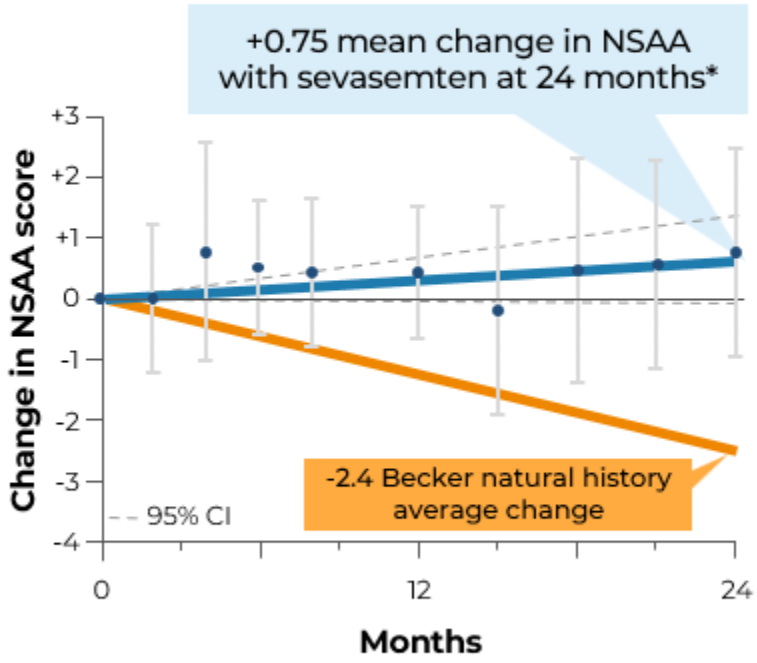
ARCH

After 2 years of treatment with sevasemten, NSAA functional scores predominantly stable or improved

NSAA scores stabilized

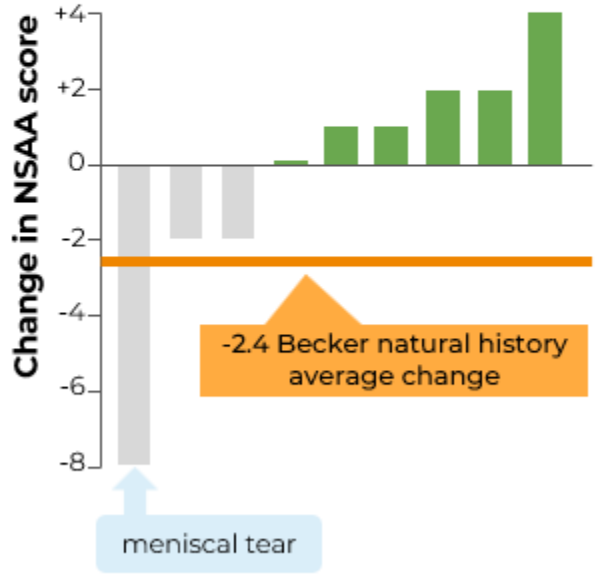


NSAA change diverges from natural history



*results exclude patient with meniscal tear

Individual NSAA responses at 24 months

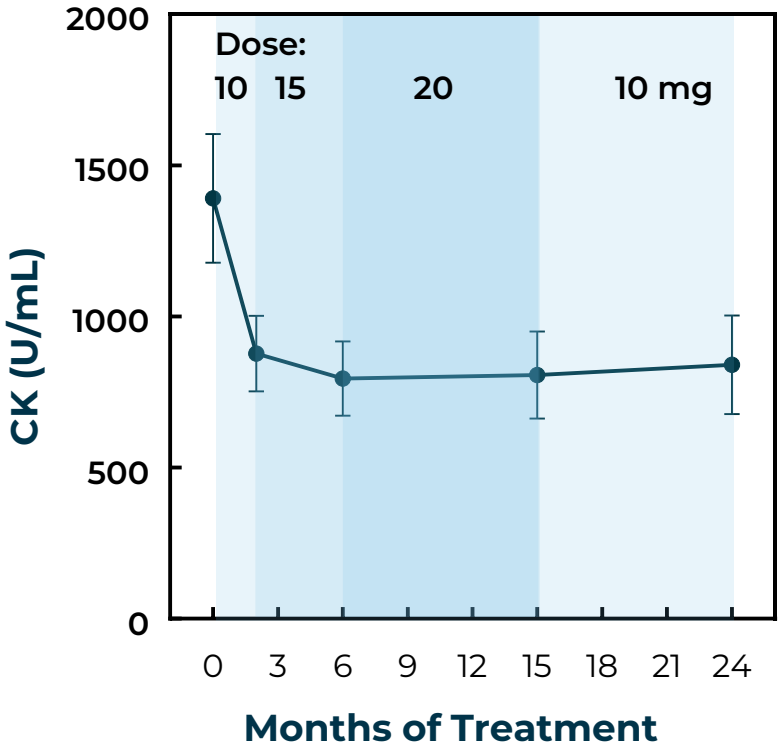


Natural history based on data presented by Bello at MDA (2022) and van de Velde NM et. al., Neurology, 2021
Mean ± 95% CI; Abbreviations: NSAA, North Star Ambulatory Assessment
Reference: Data on file

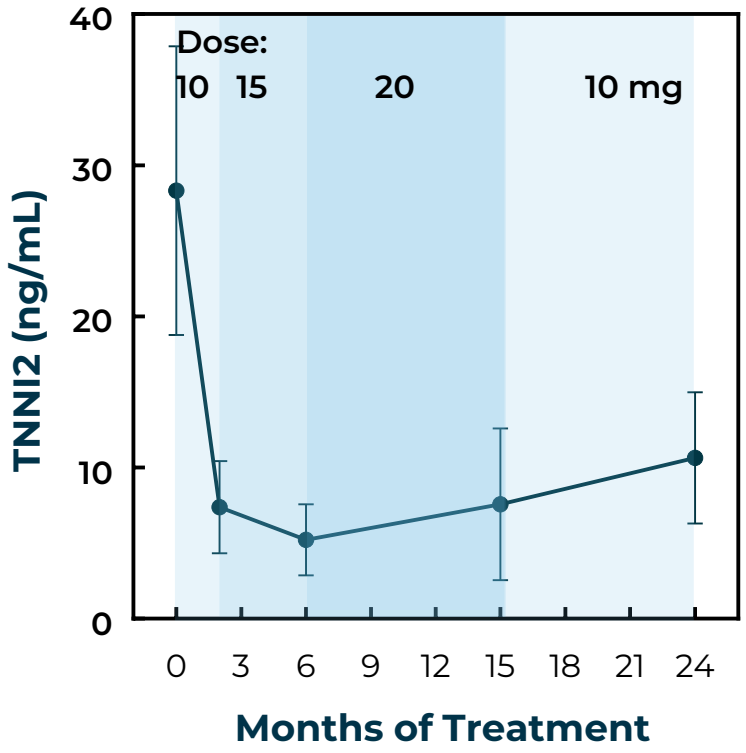
ARCH

Biomarkers of muscle damage show rapid & sustained decreases with sevasemten

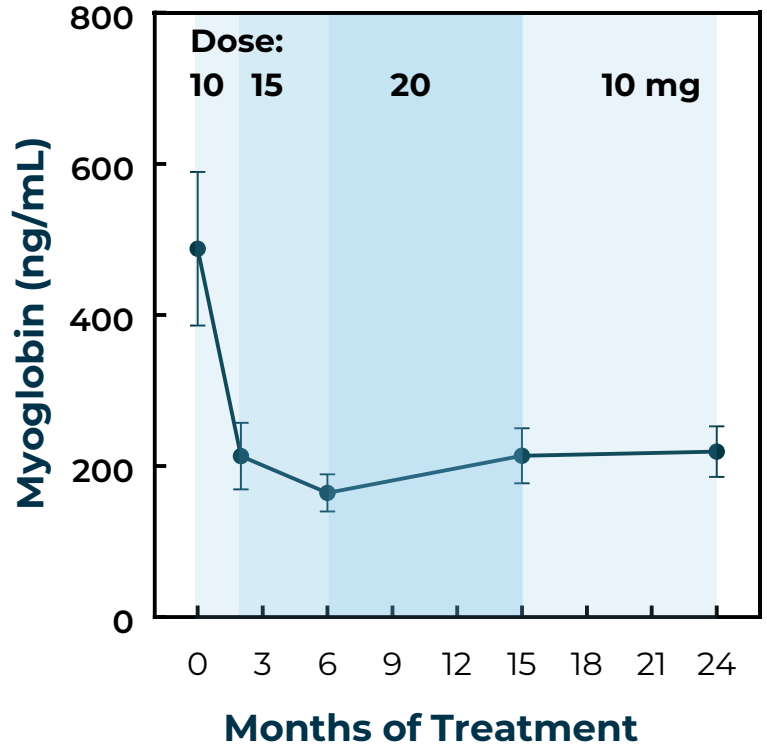
Creatine Kinase (CK)



Fast skeletal muscle troponin I (TNNI2)



Myoglobin



Mean ± SEM
Reference: Data on File

Outcomes of the ARCH study informed the design of the GRAND CANYON pivotal cohort

Outcomes of the ARCH Study in Becker

Safety

Well-tolerated at all doses

Function

Stabilization of functional assessments with trends toward improvement

Biomarkers

Demonstration of **rapid, sustained & significant decreases** in multiple biomarkers of muscle damage

Pivotal Dose Identified

Maximal biomarker response at 10 mg dose

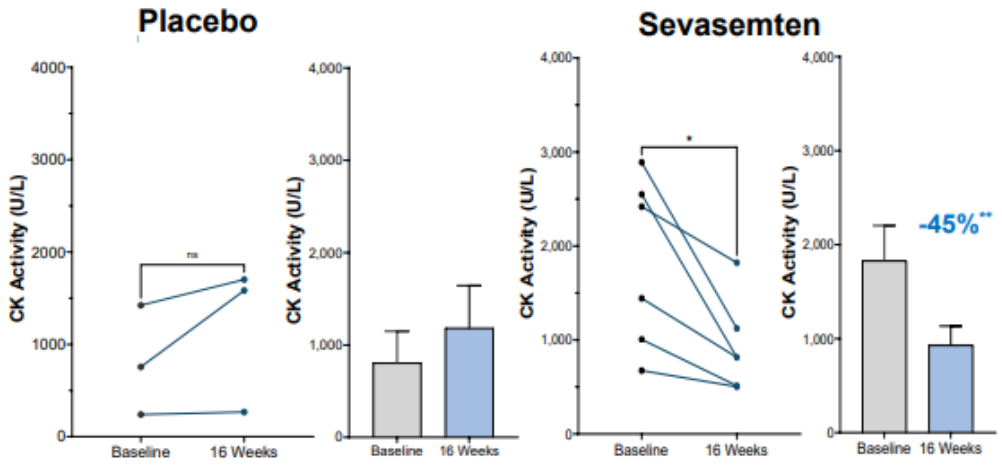
PK/PD supportive of **10 mg dose for pivotal cohort**

Exercise Challenge Study: Sevasemten shows significant reductions in biomarkers of muscle damage

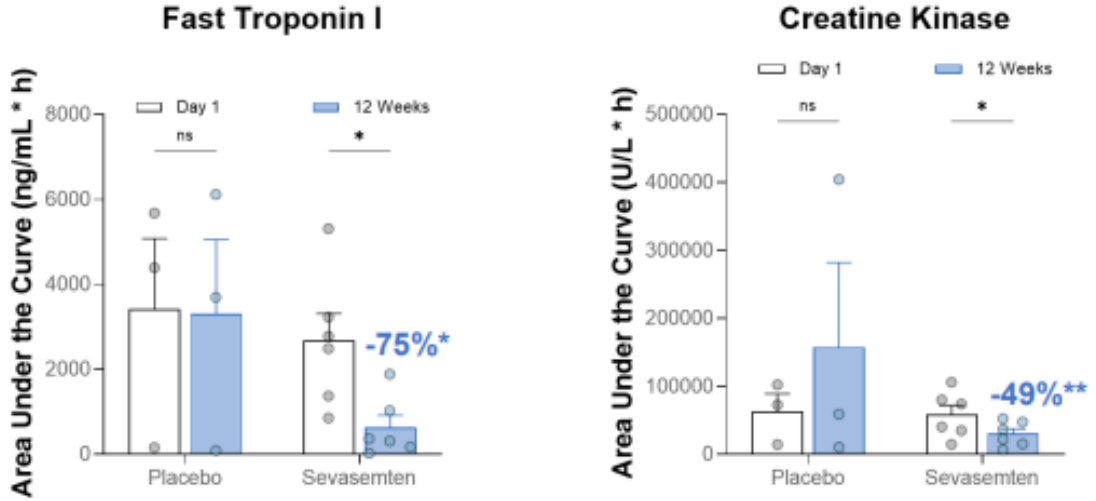
- A 16-week randomized, double-blind, placebo-controlled Phase 2 study assessing safety, PK and biomarker response to exercise in adults with Becker, LGMD2I or McArdle disease.
- Sevasemten was well tolerated across 21 participants: Becker (n=9), LGMD2I (n=9) and McArdle (n=3)

Becker Cohort Data

Primary endpoint: CK change from baseline after 16 weeks sevasemten vs. placebo



24 hours post exercise: Significant reductions in TNNI2 and CK



Reference: Stemmerik MG, et al. Presented at WMS 2024 Prague

CANYON Phase 2 trial in adults with Becker

Topline data from CANYON is anticipated in 4Q24

PRIMARY ENDPOINT

CK at 6, 9 & 12 months

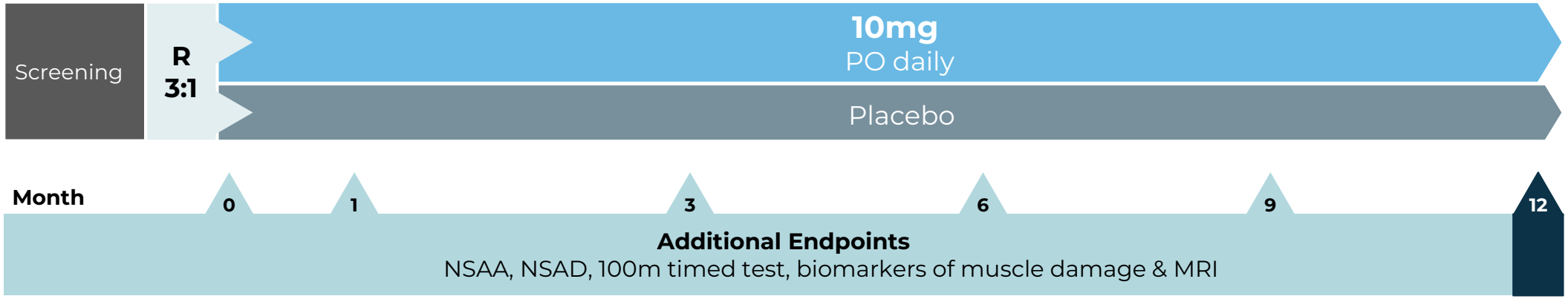
KEY INCLUSION CRITERIA

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

ENROLLMENT

40

Study design - 12 months



Abbreviations: PO, by mouth; NSAA, North Star Ambulatory Assessment; North Star Assessment for Muscular Dystrophies, CK, creatine kinase

GRAND CANYON

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

TARGET ENROLLMENT

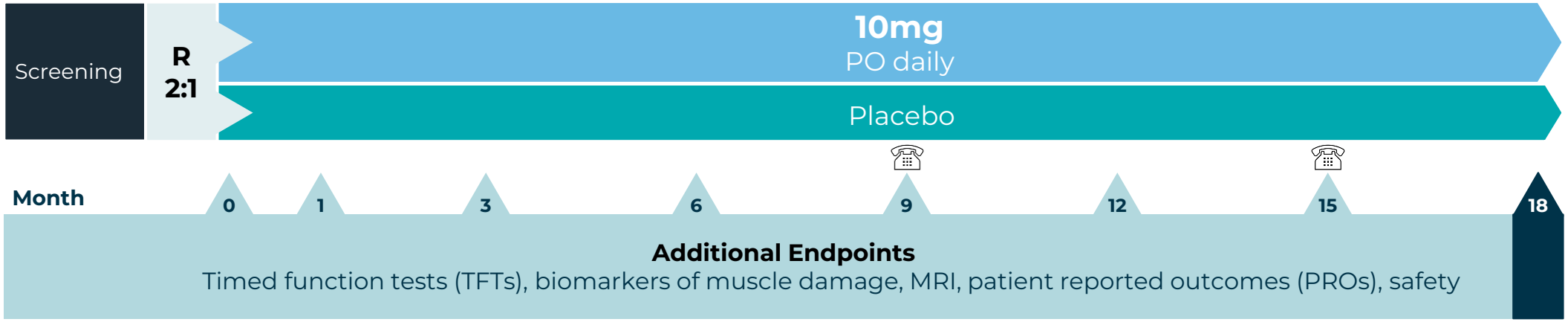
120

POWERED AT

>90%

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

Study design - 18 months



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

Edgewise THERAPEUTICS

CANYON has the potential to be a transformative trial for Edgewise

CANYON

Topline data anticipated in **4Q24**

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 fully enrolled at the time of filing)

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 in a market research study 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

Sevasemten program in Duchenne muscular dystrophy

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 mutation-agnostic MOA as potential foundational therapy—alone or in combination
- 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

A randomized, double-blind, placebo-controlled Phase 2 trial of sevasemten, followed by an OLE

PRIMARY ENDPOINT
Safety & tolerability

PATIENTS ENROLLED
>60
boys with Duchenne aged 4-9 years

NUMBER OF SITES
>12

Part A - 12 weeks
Sequentially enrolled, placebo-controlled dose-escalation (PO daily)

Part B - 21 months
OLE (may be dose-escalated based on an interim review)

Additional endpoints
PK, biomarkers of muscle damage, NSAA, SV95C, caregiver-reported outcomes

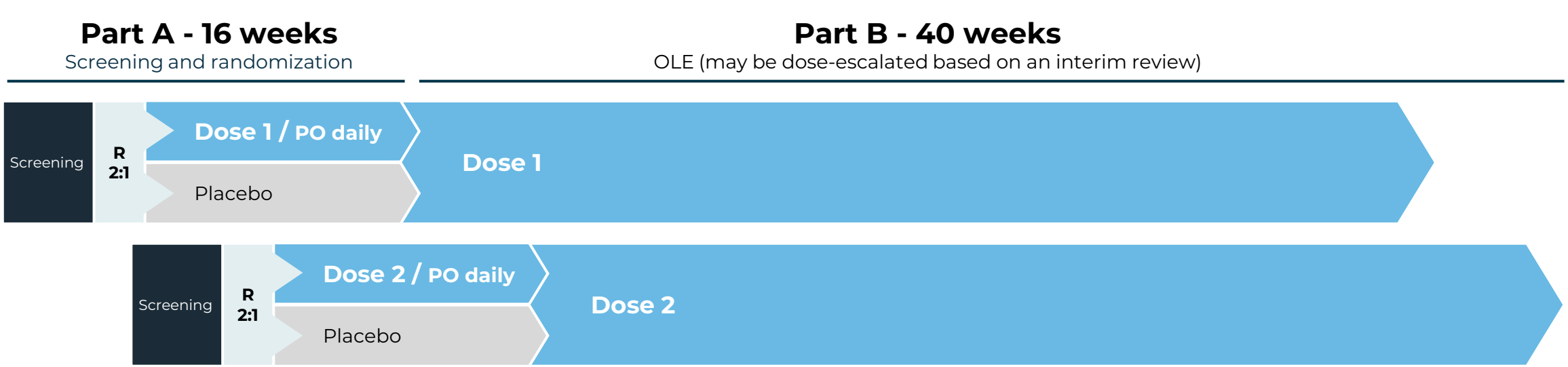
Abbreviations: OLE, open label extension; SV95C, Stride Velocity 95th Centile; R, randomization
Note: durations of timeline are not to scale

A Phase 2 study of sevasemten in Duchenne boys previously treated with gene therapy

PRIMARY ENDPOINT
Safety & tolerability

TARGET ENROLLMENT
>24
participants aged 6-17 years

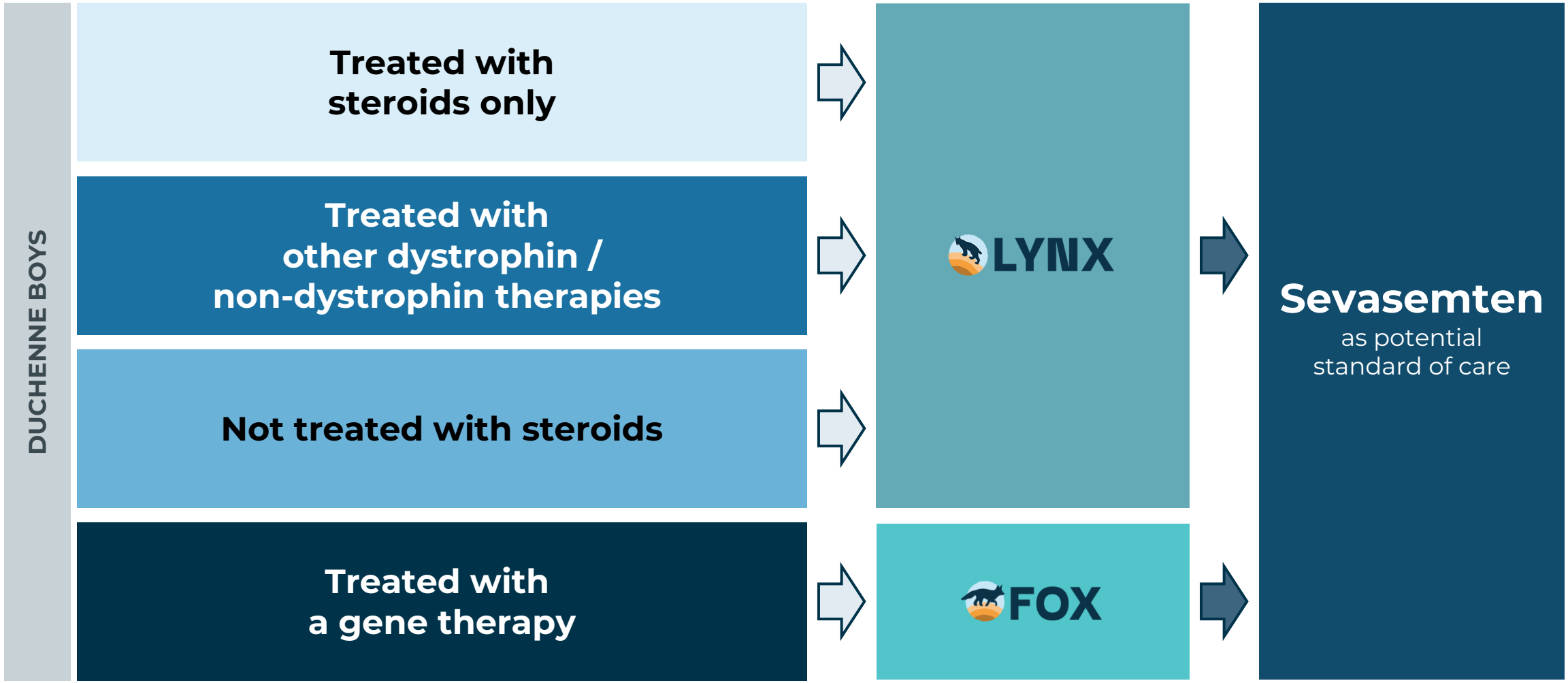
NUMBER OF SITES
7
in the US



Additional endpoints
PK, biomarkers of muscle damage, NSAA, SV95C, self-reported/caregiver-reported outcomes

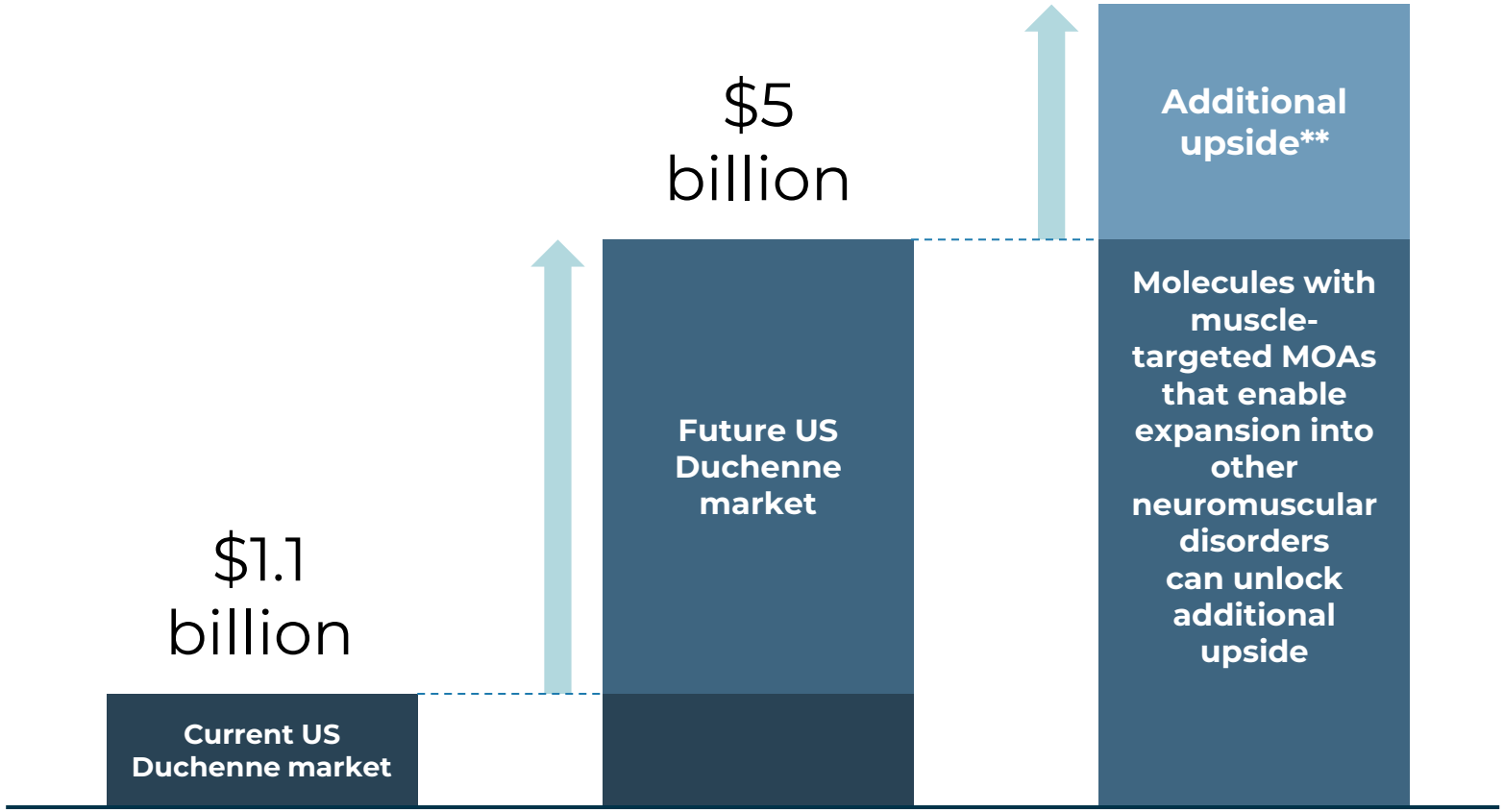
Abbreviations: OLE, open label extension; SV95C, Stride Velocity 95th Centile; R, randomization
Note: durations of timeline are not to scale

Our current clinical trials with sevasemten are designed to address all ambulatory boys living with Duchenne



Source: Edgewise analysis

Duchenne market has significant growth potential, with sevasemten uniquely positioned against the therapeutic backdrop



Reflects 2022 revenues for steroids and exon-skipping approaches for Duchenne only

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

~35,000

* Sources: Evaluate Pharma 2022 WW Market Value of top 6 products (sales data captured from company 2022 Q4 results and 10-K); 2028 forecasted global sales of top 10 Duchenne products; Edgewise market research
** there are currently no approved therapies for Becker and LGMD; global prevalence of LGMD as a group is estimated to be from 0.56 to 5.75 per 100,000 and there are an estimated 5,000-6,000 Becker in the US alone

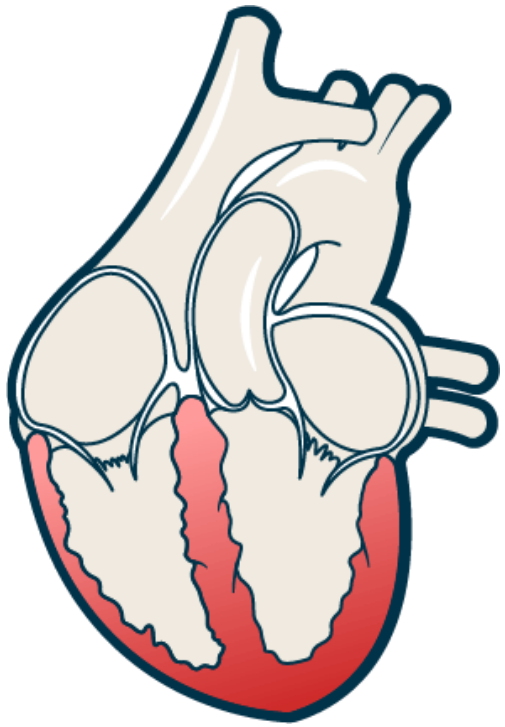
EDG-7500 program in Hypertrophic Cardiomyopathy (HCM)

Hypertrophic cardiomyopathy (HCM): Chronic, progressive & the most commonly inherited heart disease

- HCM impacts ~1 in 200-500 people in the US
  - Diagnosis at any age; mid-40s most common
  - Characterized by diastolic dysfunction, left ventricular outflow tract obstruction (LVOTO), & atrial & ventricular arrhythmias
- The disease dramatically impairs overall quality of life - physical, emotional & financial
- There remains a significant unmet need for therapies that consistently and safely reduce LVOT gradient, improve symptoms & overall quality of life

HCM: Abnormalities in heart muscle structure & function lead to severe abnormalities in cardiac performance

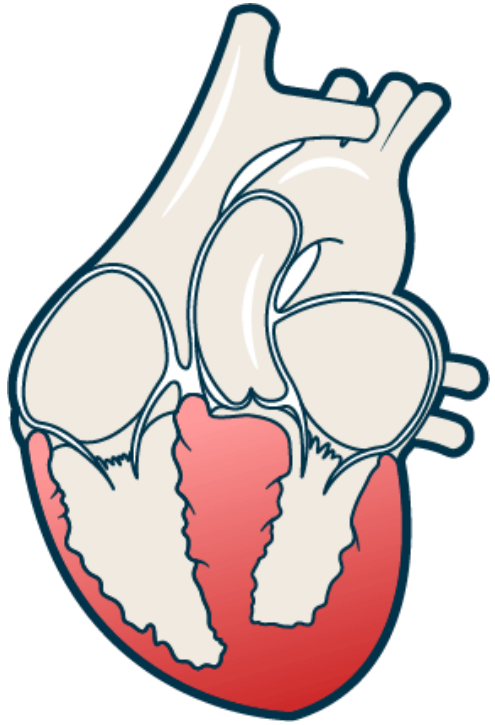
HEALTHY HEART



Normal contraction

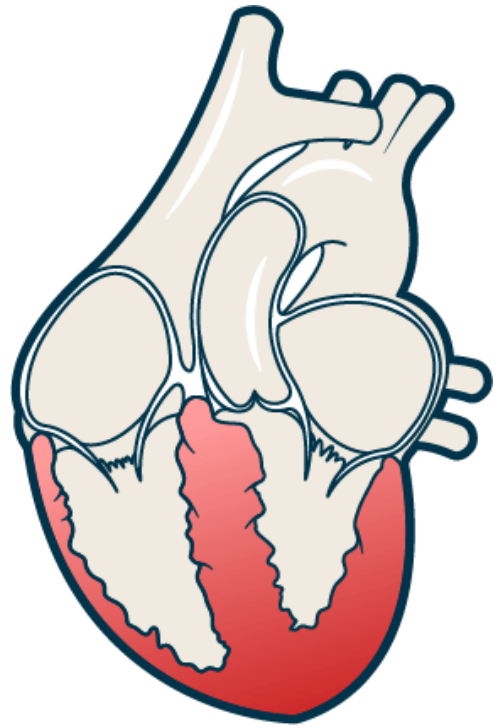
OBSTRUCTIVE HCM

(~65% OF PATIENT POPULATION)



NON-OBSTRUCTIVE HCM

(~35% OF PATIENT POPULATION)



Excessive contraction & impaired relaxation

Treatments for HCM have key limitations leaving substantial unmet needs for patients

LIMITED BENEFIT ACROSS THE SPECTRUM OF HCM

Efficacy and safety limitations with interventions in oHCM[4]

- BB and CCBs have **limited efficacy** and associated side effects
- SRT interventions are **highly invasive**
- CMI efficacy may be **limited by intrinsic mechanism** tied to LVEF changes and are not recommended for patients with LVEF <55%

No approved therapies for nHCM

- SOC for nHCM includes the need for heart transplant
- Limited efficacy of off-label therapies

RISK OF HEART FAILURE[1,2]

Mavacamten black box warning for HF[3]

- The US prescribing information for mavacamten contains a boxed warning regarding heart failure

HF risk limits intervention[2]

- Guidelines recommend an **interruption in treatment** for patients who develop **LVEF <50%**

SUBOPTIMAL PATIENT EXPERIENCE

Safety-driven frequent echo monitoring[1-3]

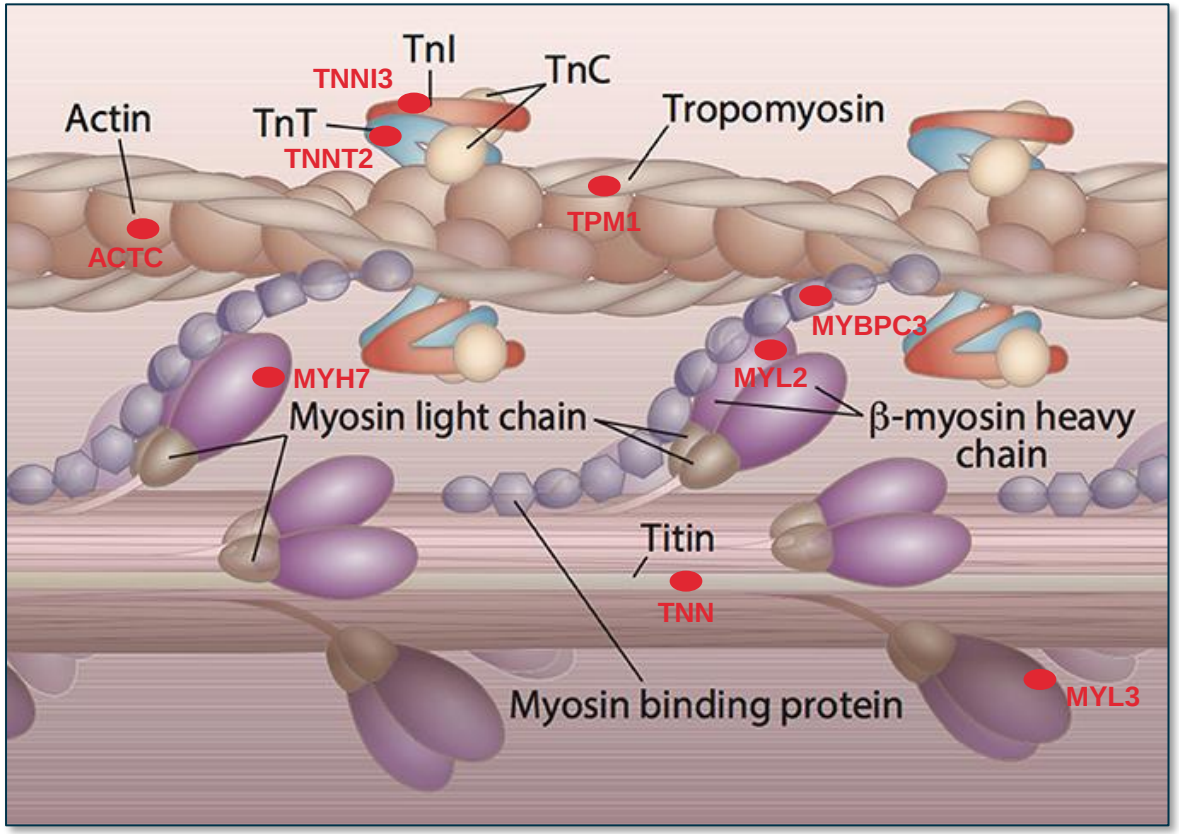
- Treatment with mavacamten requires **echocardiography monitoring** for both the initiation and maintenance phases
- **Extensive titration and adjustment of dosage** needed to find a safe window of efficacy avoiding EF drop risk

CMI, cardiac myosin inhibitor; LVEF, left ventricular ejection fraction; LVOT, left ventricle outflow tract; oHCM, obstructive hypertrophic cardiomyopathy; SOC, standard of care.

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;
4. Olivotto I et al. *Lancet*. 2020;396(10253):759-769.

EDG-7500: Designed to Slow Rate of Acto-Myosin Engagement and Speed Disengagement Without Inactivating Myosin Heads

The Sarcomere is the Molecular Unit in Cardiac Muscle Responsible for Heart Contraction and Relaxation



Protein	Gene Symbol	# of mutations to cause HCM
Cardiac β-MyHC	***MYH7***	**194**
Cardiac MyBP-C	***MYBPC3***	**197**
Cardiac TnT	*TNNT2*	31
Cardiac TnI	*TNNI3*	27
α-Tropomyosin	*TPM1*	11
Regulatory Light Chain	*MYL2*	10
Cardiac α-actin	*ACTC*	7
Essential Light Chain	*MYL3*	5
Titin	*TNN*	3

References: www.hypertrophiccardiomyopathy.com; https://sadayappanlab.org/hypertrophic_cardio.html; Kraker J, *et. al., Frontiers in Physiology*, 2016; Seidman CE & Seidman JG, *Circulation Research*, 2011

A compelling preclinical package supported initiation of clinical studies of EDG-7500 as a novel therapy for HCM

Preclinical model	Key result
In vitro: Myofibril systems[1]	✓ **Preserves myosin head motor function** ✓ **More potent at low calcium**
oHCM *In vivo*: *MYBPC3* A31P feline validated oHCM model[3]	✓ **Potent LVOT gradient reduction** ✓ **Well tolerated at supratherapeutic exposures**
nHCM *In vivo*: *MYH7* R403Q porcine validated nHCM model[4]	✓ **Improves diastolic function** ✓ **Positively impacts LA and LV remodeling** ✓ **Restores cardiac reserve**
HFrEF *In vivo*: Dogs with pacing induced left-ventricular systolic dysfunction	✓ **Improves diastolic performance in model of reduced systolic function** ✓ **No changes in systolic performance in a model of reduced LVEF**
In vivo: Systolic and diastolic function assessed in healthy dogs[2]	✓ **Increases ventricular diastolic compliance with limited effect on LVEF**

EDG-7500 has demonstrated potent LVOT gradient reduction & improvement in diastolic function with limited reduction in systolic performance, even at highest exposures, across multiple preclinical models

LA, left atrium; LV, left ventricle; LVEF, left ventricle ejection fraction, LVOT, left ventricle outflow tract; nHCM, non-obstructive hypertrophic cardiomyopathy; oHCM, obstructive hypertrophic cardiomyopathy.

1. Del Rio CL et al. 2023 American Heart Association Scientific Sessions. Philadelphia, PA. November 10–13, 2023. Abstract #15612; 2. Del Rio CL et al. 2023 American Heart Association Scientific Sessions. Philadelphia, PA. November 10–13, 2023. Abstract #15822; 3. Kaplan JL, et al. 2023 American College of Cardiology 72nd Annual Scientific Sessions. New Orleans LA. March 4–6, 2023. Poster #1066-13; 4. Evanchik M et al. 2024 American College of Cardiology 73nd Annual Scientific Sessions. Atlanta, GA. March 6–8, 2024. Poster #1087-05; 5. Evanchik M et. al., Poster Presentation at BCVS 2024

EDG-7500 is positioned to address unmet needs in HCM

Targeted MOA*

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

Slows acto-myosin engagement & promotes faster disengagement

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 supports investigating fixed dose regimens, potentially eliminates any need for cumbersome up-titration & frequent echocardiographic assessments

* Based on preclinical 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)

EDG-7500
Phase 1 Trial in Healthy Subjects

Study overview of EDG-7500 in healthy adults

PRIMARY OBJECTIVE

Safety & tolerability in healthy subjects

KEY INCLUSION CRITERIA

Healthy male, non-pregnant female 18 to <60 years of age

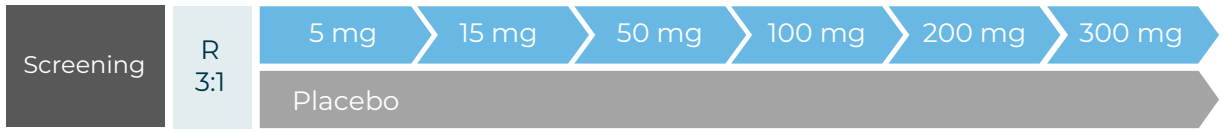
ENROLLMENT

72

KEY OUTCOME MEASURES

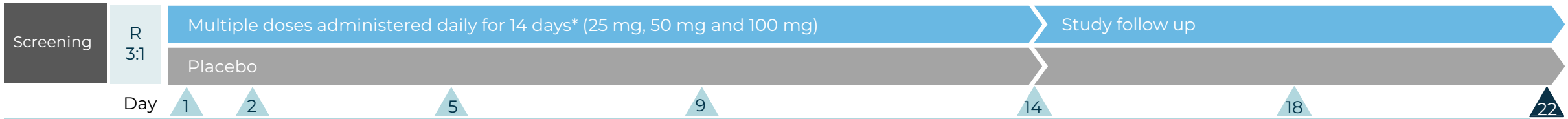
PK, LVEF

Part A (n=48)
Single Ascending Dose (SAD)



5 day follow up, EOS visit at day 9; 96-hour PK profile, echocardiography at 1.5, 6, 24, 96, and 192 hours post-dose

Part B (n=24)
Multiple Ascending Dose (MAD)



Once-daily dose for 14 days, 18-day follow-up, EOS visit at day 22;
24-hour PK profile on days 1 and 14; echocardiography at days 2, 5, 9, 15, 18 and 22

Abbreviations: EOS, end of study; LVEF, left ventricle ejection fraction; PK, pharmacokinetics
ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06011317

EDG-7500 was well tolerated across all doses in both the SAD & MAD healthy subject cohorts *(continued)*

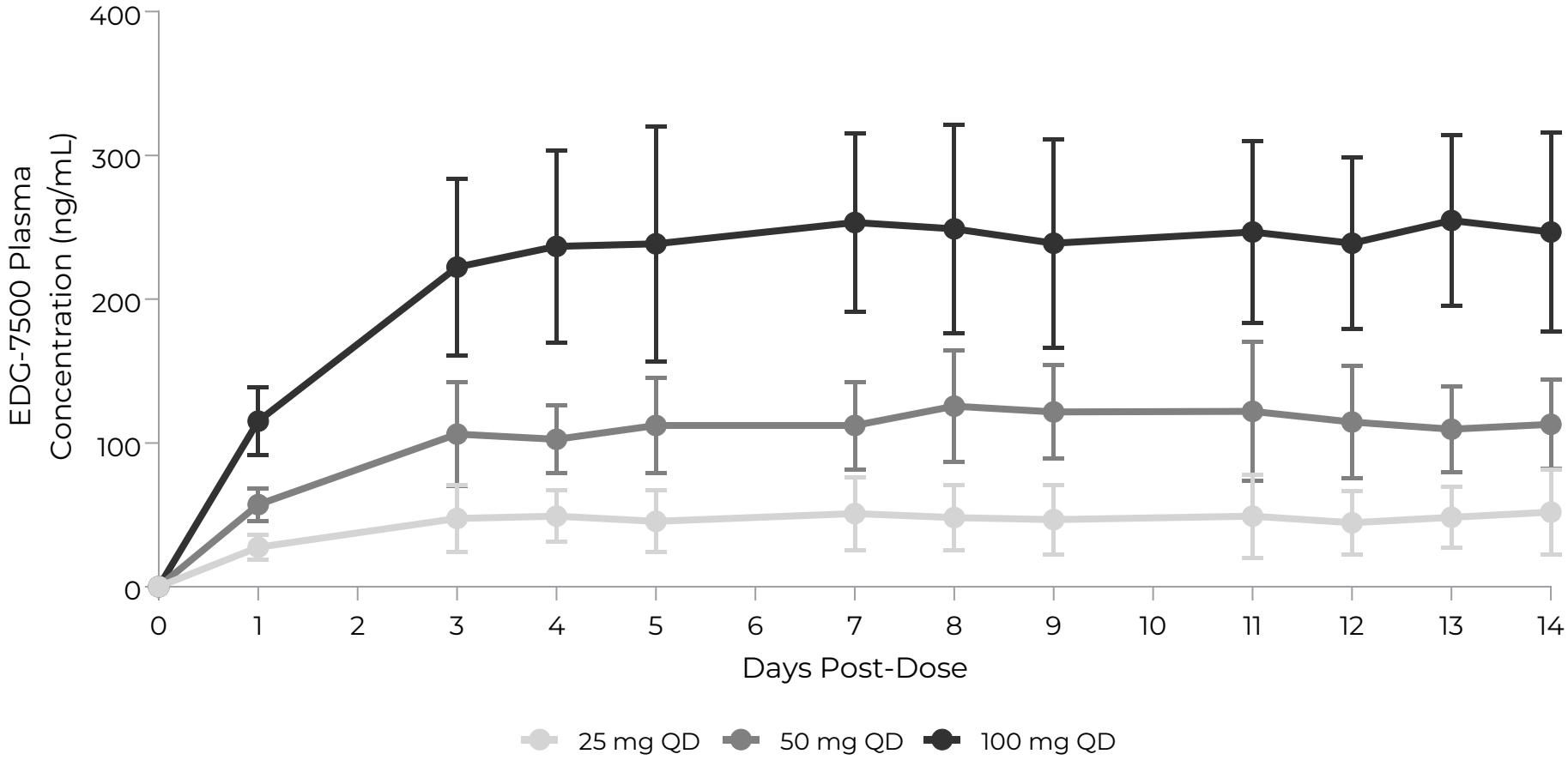
Across both the SAD and MAD cohorts:

- No significant changes in vital signs were observed
- Well-tolerated with no clinically significant changes or trends in clinical chemistry, hematology, or ECGs
- Incidence of treatment-emergent adverse events was similar compared to placebo
- LVEF remained within the normal range for all subjects at all time points; importantly, **none of the subjects** experienced a decrease in LVEF <50%

Source: Edgewise Therapeutics Data on File

Steady-state was achieved ~4 days after start of once-daily dosing with EDG-7500

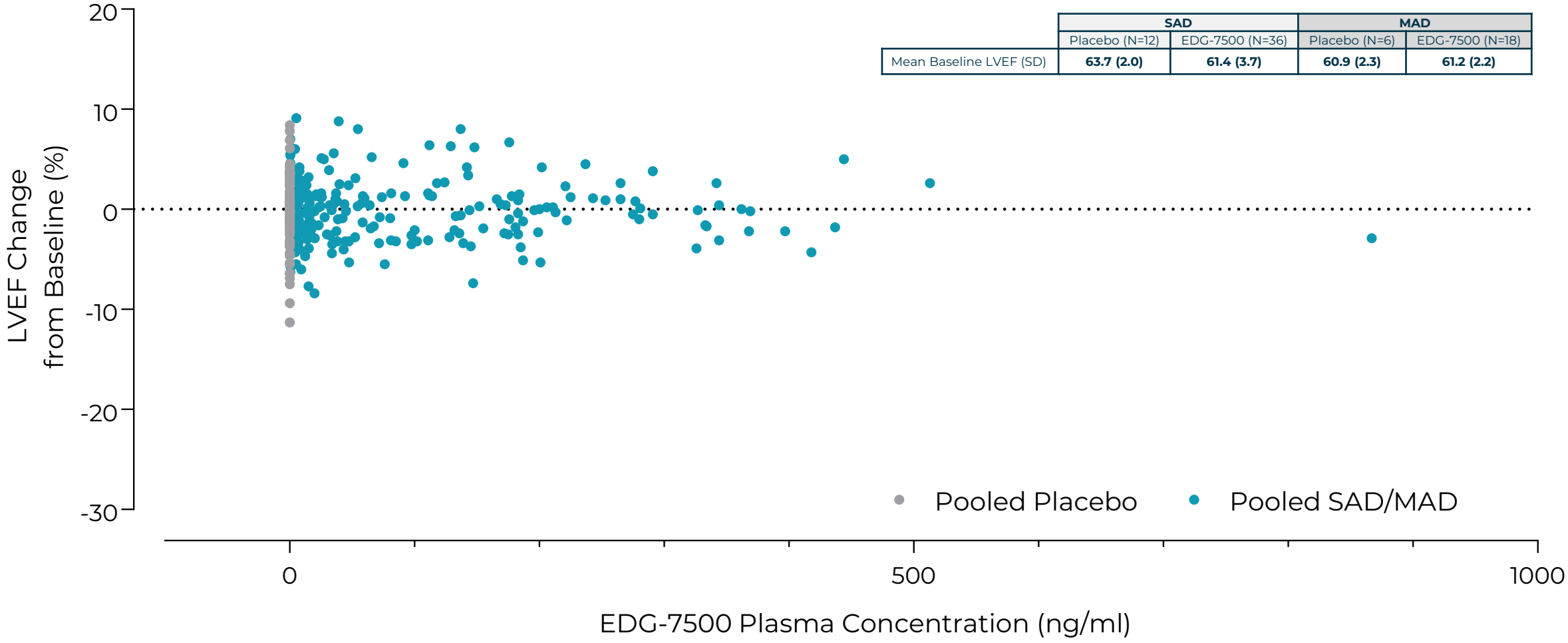
Plasma Concentration Over Time (mean ± SD) After 3 Ascending Doses of Daily EDG-7500 for 14 Days



Source: Edgewise Therapeutics Data on File

There was **no change in contractility** versus placebo & baseline with increasing doses of EDG-7500

	SAD		MAD	
	Placebo (N=12)	EDG-7500 (N=36)	Placebo (N=6)	EDG-7500 (N=18)
Mean Baseline LVEF (SD)	**63.7 (2.0)**	**61.4 (3.7)**	**60.9 (2.3)**	**61.2 (2.2)**



SAD: # Subjects = 48, # Observations = 238; MAD: # Subjects = 24, # Observations = 95
Source: Edgewise Therapeutics Data on File

Observations with EDG-7500 highlight a potentially unique mechanism to target HCM without **risk of reducing LVEF**

- EDG-7500 was **well-tolerated** with no clinically significant changes or trends in clinical chemistry, hematology or ECGs
- EDG-7500 showed optimal PK properties supporting **once-daily fixed-dose** administration, **reaching steady state ~4 days** after start of dosing
- **None of the subjects experienced a LVEF <50%** across both the SAD & MAD healthy subjects
- No meaningful drops in LVEF were observed within **a range of EDG-7500 plasma concentrations of up to 874 ng/ml**, above our predicted target therapeutic exposures

Healthy subject data with EDG-7500 support a differentiated MOA that does not rely on reductions in systolic performance

Phase 2 CIRRUS-HCM Trial in oHCM

Topline data: CIRRUS part A cohort of oHCM patients treated with a single dose of EDG-7500

PRIMARY OBJECTIVE

Safety & tolerability in adults with oHCM

KEY INCLUSION CRITERIA

- Healthy male, non-pregnant female ≥ 18 diagnosed with oHCM
- Resting LVOT-G ≥ 30 mmHg **AND** Valsalva LVOT-G ≥ 50 mmHg
  LVEF ≥ 60%
- NYHA I-III
- No previous CMI exposure

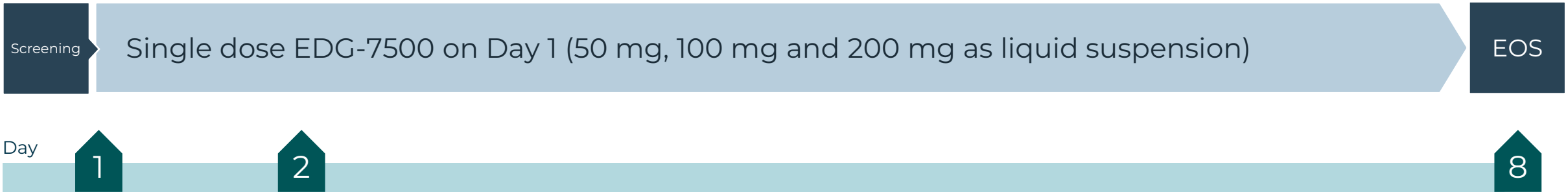
ENROLLMENT

11

KEY OUTCOME MEASURES

- Safety and tolerability
- LVOT-G (rest and during Valsalva)
- Cardiac biomarkers
- PK of EDG-7500

PART A (oHCM): Single Dose Administration (N=11)



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

CIRRUS HCM Pre-specified efficacy evaluable population

- 11 patients were eligible at screening and constituted the safety population
- 7 patients met the following criteria at baseline qualifying for efficacy evaluation:
  - Resting left ventricular outflow tract gradient (LVOT-G) ≥ 30 mmHg and Valsalva LVOT-G ≥ 50 mmHg determined by echocardiography
  - Good acoustic window and ability to obtain a high-quality transthoracic echocardiogram
  - No clinically significant cardiac structural abnormalities
- 4 patients did not meet the gradient eligibility at baseline but were evaluable for safety

Source: Edgewise Therapeutics Data on File

CIRRUS-HCM Part A: Baseline oHCM Patient Demographics and Characteristics

CHARACTERISTIC	oHCM PARTICIPANTS (n=11)
Age (Years), Mean (SD)	59 (15)
Sex – Female (%)	73
Race – Black/White (%)	9 / 91
BMI (kg/m^2)	28 (4)
NYHA Class (%)	
Class I	27
Class II	45
Class III	27
Time from HCM Diagnosis (years), Mean (SD)	5 (6)
Max End-Diastolic LV Wall Thickness (mm), Mean (SD)	20 (6)
LVOT-G Rest (mmHg), Mean (SD)*	60 (28)
LVOT-G Valsalva (mmHg), Mean (SD)*	88 (32)
LVEF (%), Mean (SD)*	68 (4)
Background Beta Blockers (%)	64

* Core read of Day 1 pre-dose baseline echocardiogram

Single doses of EDG-7500 were well tolerated across all 3 doses studied in oHCM patients

- EDG-7500 was well-tolerated by all oHCM patients
- No treatment emergent abnormalities in clinical hematology or chemistry laboratories
- No patients experienced a decrease in LVEF <50%

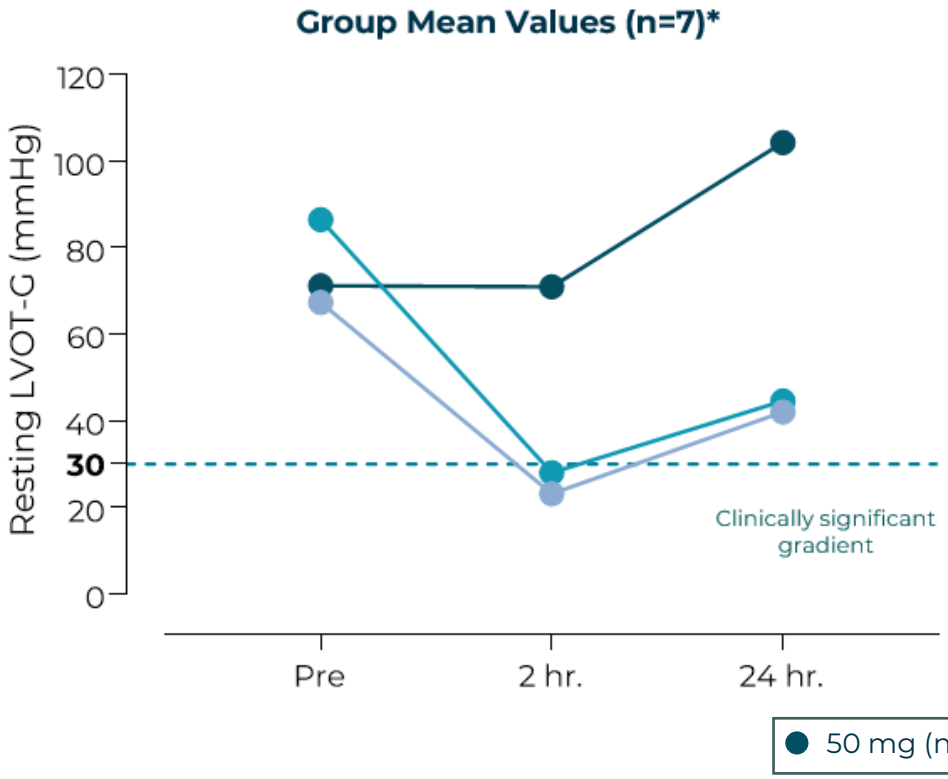
Summary of AEs

Dose	Term	Severity	Relatedness	Outcome	Serious	Comment
200 mg	Atrial Fibrillation (asymptomatic)	Mild	Not Related	Resolved	No	History of Paroxysmal AF; Patient on BB and NOAC
100 mg	Hypotension	Mild	Not Related	Resolved	No	History of Lightheadedness
50 mg	Parasomnia (nightmares)	Mild	Not Related	Resolved	No	History of PTSD, anxiety, depression
50 mg	Hypokalemia	Mild	Not Related	Resolved	No	3.9 → 3.1 mmol/L (LLN = 3.6)

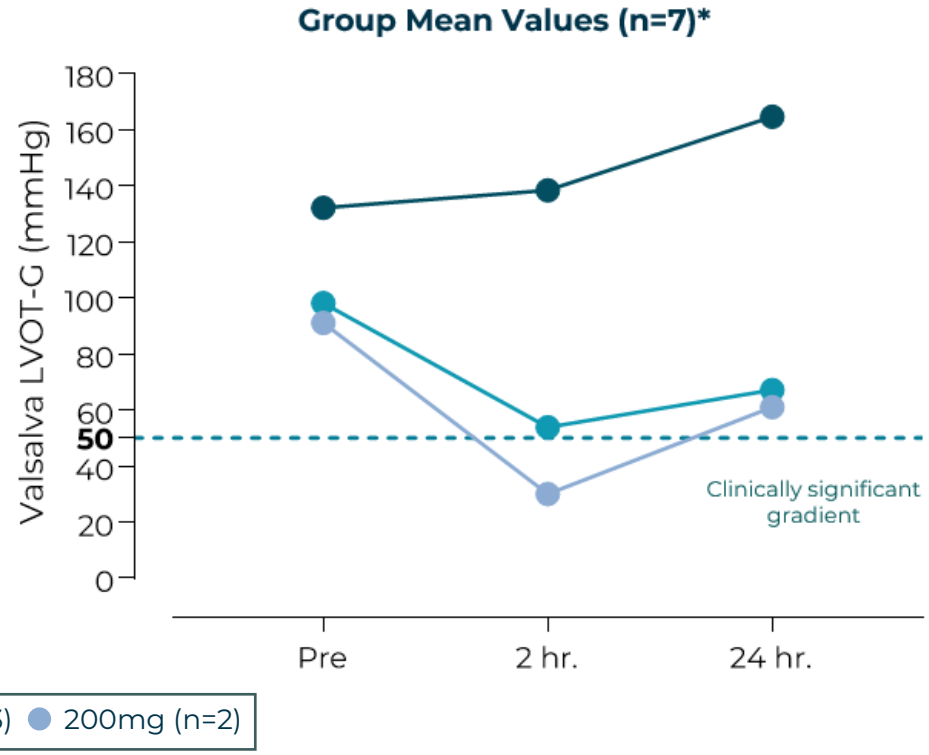
Source: Edgewise Therapeutics Data on File

EDG-7500 led to significant reductions of Resting and Valsalva LVOT-G in the combined 100/200 mg cohorts

Reduction in Resting LVOT-G of 67%



Reduction in Valsalva LVOT-G of 55%

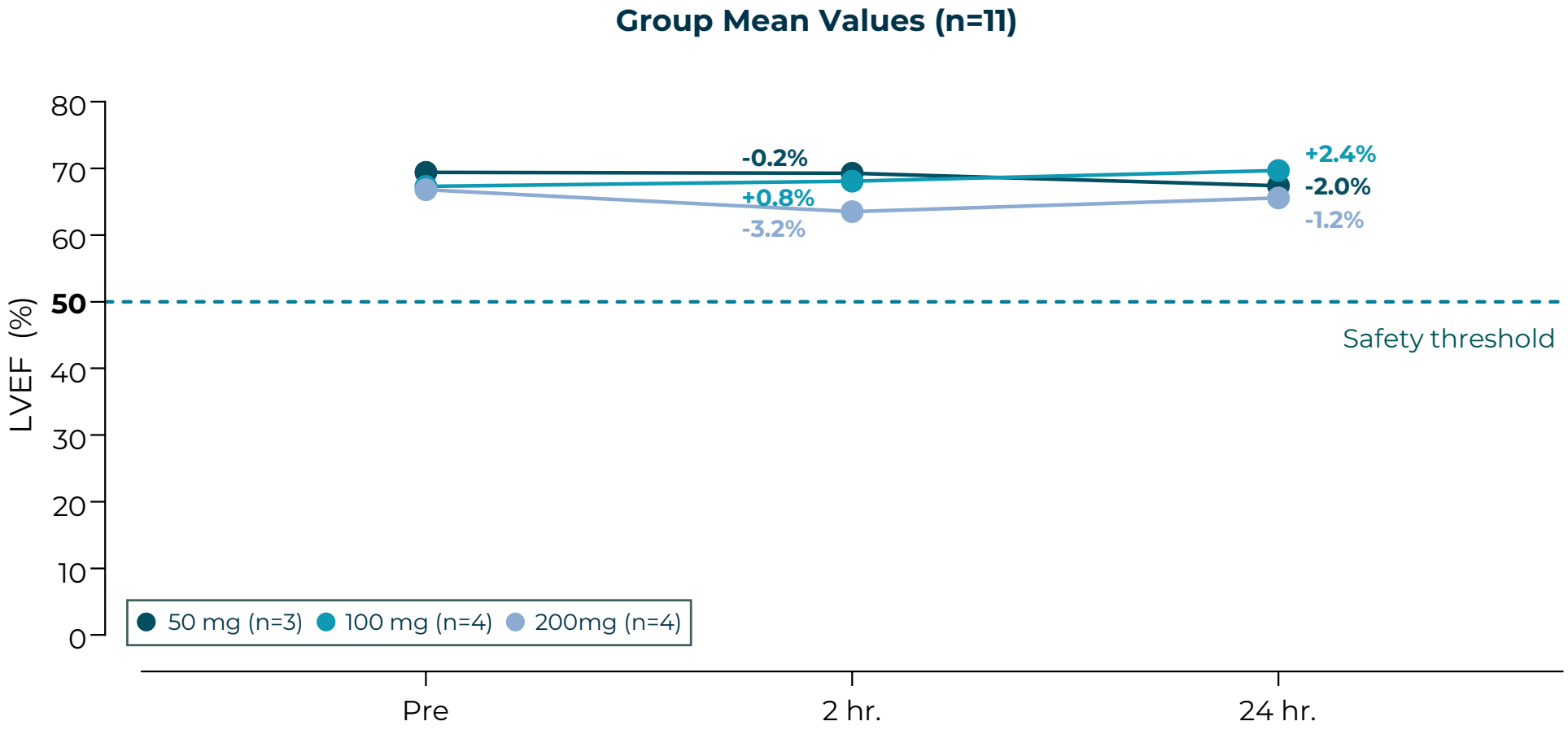


50 mg (n=2) 100 mg (n=3) 200mg (n=2)

3 of 5 Patients (100 mg and 200 mg Cohorts) Had a Resting LVOT-G of <30 mmHg & a Valsalva LVOT-G of <50 mmHg After a Single Dose of EDG-7500

* Efficacy evaluable population
Source: Edgewise Therapeutics Data on File

Gradient relief in oHCM patients was achieved without a meaningful reduction in LVEF

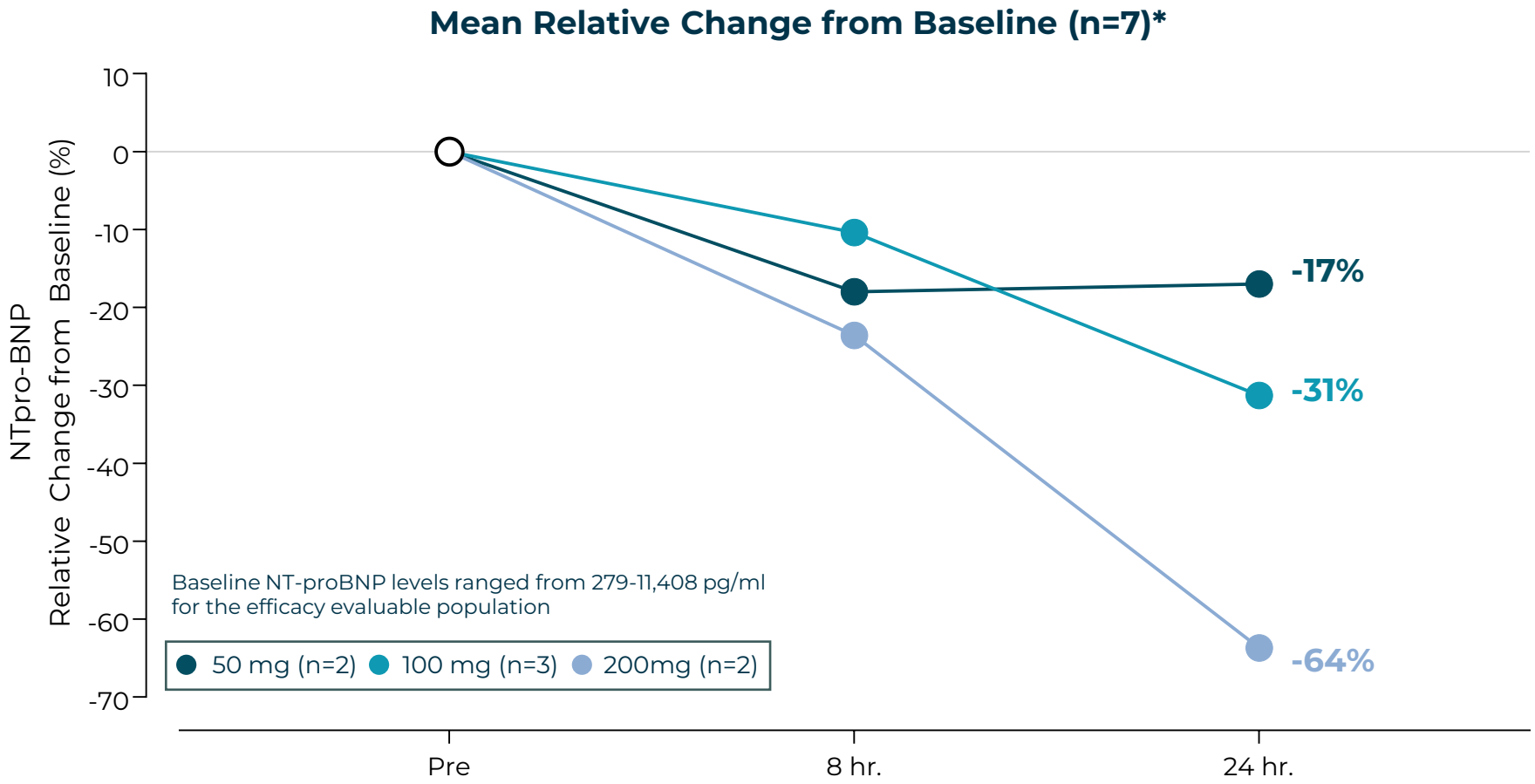


There was no correlation between EDG-7500 plasma concentration and LVEF change

Source: Edgewise Therapeutics Data on File

CIRRUS HCM

EDG-7500 administration resulted in robust reductions in NT-proBNP, a key marker of heart failure in HCM[1]



NT-proBNP is a marker of diastolic function, & reductions have been associated with increased pVO_2 the primary endpoint in oHCM Phase 3 trials

* Efficacy evaluable population
Source: Edgewise Therapeutics Data on File
[1]Coats C.J. et al. European Heart Journal. 2013; 34(32), 2529–2537

Edgewise THERAPEUTICS

EDG-7500 in oHCM patients relieved LVOT-G without reductions in LVEF

- EDG-7500 administration was **well tolerated** across all doses studied in oHCM patients
- EDG-7500 administration led to a reduction in **resting LVOT-G of 67%** for the 100/200 mg cohorts combined with multiple individuals achieving gradients <30 mmHg
- EDG-7500 administration led to a reduction in **Valsalva LVOT-G of 55%** for the 100/ 200 mg cohorts combined with multiple individuals achieving gradients <50 mm Hg
- LVOT-G relief was achieved without reductions in LVEF
- EDG-7500 administration also led to a mean **31%** (100 mg) and **64%** (200 mg) drop in NT-proBNP, an independent predictor of heart failure

Positive data from CIRRUS-HCM part A supported the initiation of parts B and C in oHCM and nHCM, respectively

- Edgewise initiated enrollment of patients in the **28 Day study** of EDG-7500 for both obstructive and non-obstructive HCM
  - *Part B*: designed to demonstrate continued safety and deepening of efficacy response after 28-days of dosing with EDG-7500 in patients with **obstructive HCM**
  - *Part C*: designed to demonstrate improvements in diastolic function after 28-days of dosing with EDG-7500 in patients with **non-obstructive HCM**
  - Solid dosage form enables **outpatient administration** of EDG-7500
- Upon completion of Parts B and C, patients have the opportunity to enroll in Part D, the extended dose portion of CIRRUS-HCM

Initial readout of EDG-7500 Phase 2 28-Day study anticipated 1H 2025

CIRRUS-HCM: Clinical Trial Design

PRIMARY OBJECTIVE

Safety & tolerability in adults with HCM

KEY INCLUSION CRITERIA

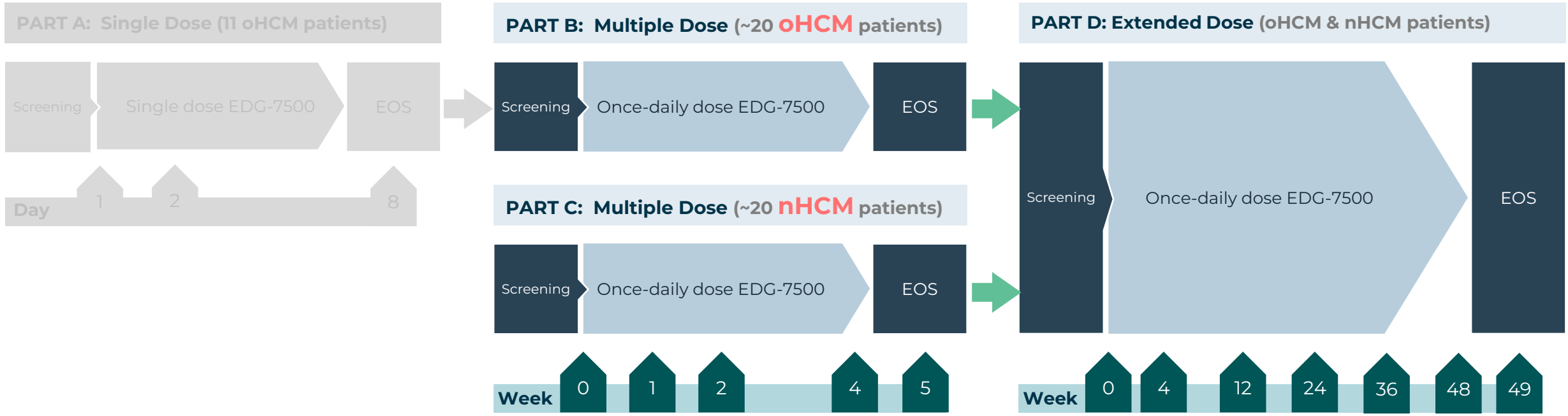
Male and female patients ≥ 18 years of age with HCM
LVEF ≥ 60%

TARGET ENROLLMENT

~50

KEY OUTCOME MEASURES

Cardiovascular PD, LVEF, Biomarkers, PK



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

Aspirational target product profile for EDG-7500 in the treatment of HCM

Safety	**Based on observations to date, no concerns of LVEF drops**
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**
Diastolic Effect	**Ability to resolve diastolic dysfunction in patients with non-obstructive HCM**
Dosing	**Fixed once-daily dosing without the need for a complicated titration**

Edgewise upcoming value-generating milestones

		H1 2024	H2 2024	H1 2025
Cardiac **EDG-7500**	**Hypertrophic Cardiomyopathy**	**Phase 2 CIRRUS-HCM** Initiation ✓	**Phase 1/Phase 2** EDG-7500 data in HVs & oHCM** ✓	
			Phase 2 28-day study Initiate in oHCM & nHCM** ✓	**Phase 2 28-day study** Initial Data readout
Muscular Dystrophy **sevasemten**	**Becker**	**ARCH** 24-month data ✓	**Phase 2 CANYON** 1-year placebo-controlled data	**GRAND CANYON** Recruitment complete (Q1)
	Duchenne	**Phase 2 DUNE** Exercise challenge data* ✓	**Phase 2 LYNX & FOX** Controlled dose-ranging data	**Phase 3 trial** Initiation

*includes Limb-Girdle & McArdle

**HV, healthy volunteers, oHCM, obstructive hypertrophic cardiomyopathy nHCM, non obstructive hypertrophic cardiomyopathy

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