Cytokinetics

empowering

muscle

empowering

lives

Sarcomere directed therapies

Forward-Looking Statements

This Presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements express or implied related Cytokinetics' research and development and commercial readiness activities, including the initiation, conduct, design, enrollment, progress, continuation, completion, timing and results of clinical trials, projections regarding growing prevalence, low survival rates and market opportunity in heart failure, hypertrophic cardiomyopathy (HCM) or amyotrophic lateral sclerosis (ALS); projections regarding the size of the addressable patient population for *omecamtiv mecarbil, aficamten or reldesemtiv*; Cytokinetics' commercial readiness for *omecamtiv mecarbil*; the likelihood and/or timing of regulatory approval for our new drug application for *omecamtiv mecarbil* or any future new drug application for any of our other drug candidates; the timing of a second interim analysis of COURAGE-ALS, the timing of commencement of a second phase 3 clinical trial of *aficamten* as a monotherapy in patients with obstructive HCM, the timing of commencement of a phase 3 clinical trial of *aficamten* in nonobstructive HCM, our ability to fully enroll or to announce the results of any of our clinical trials by any particular date; Cytokinetics' cash expenditures or runway; the results of any of our interactions with the FDA or any other regulatory authority regarding *omecamtiv mecarbil* or any of our other drug candidates; the properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, *reldesemtiv* and Cytokinetics' other drug candidates. Such statements are based on management's current expectations; but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics may incur unanticipated research, development and other costs or be unable to obtain financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. These forward-looking statements speak only as of the date they are made, and Cytokinetics undertakes no obligation to subsequently update any such statement, except as required by law. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission (the "SEC").

Our Mission

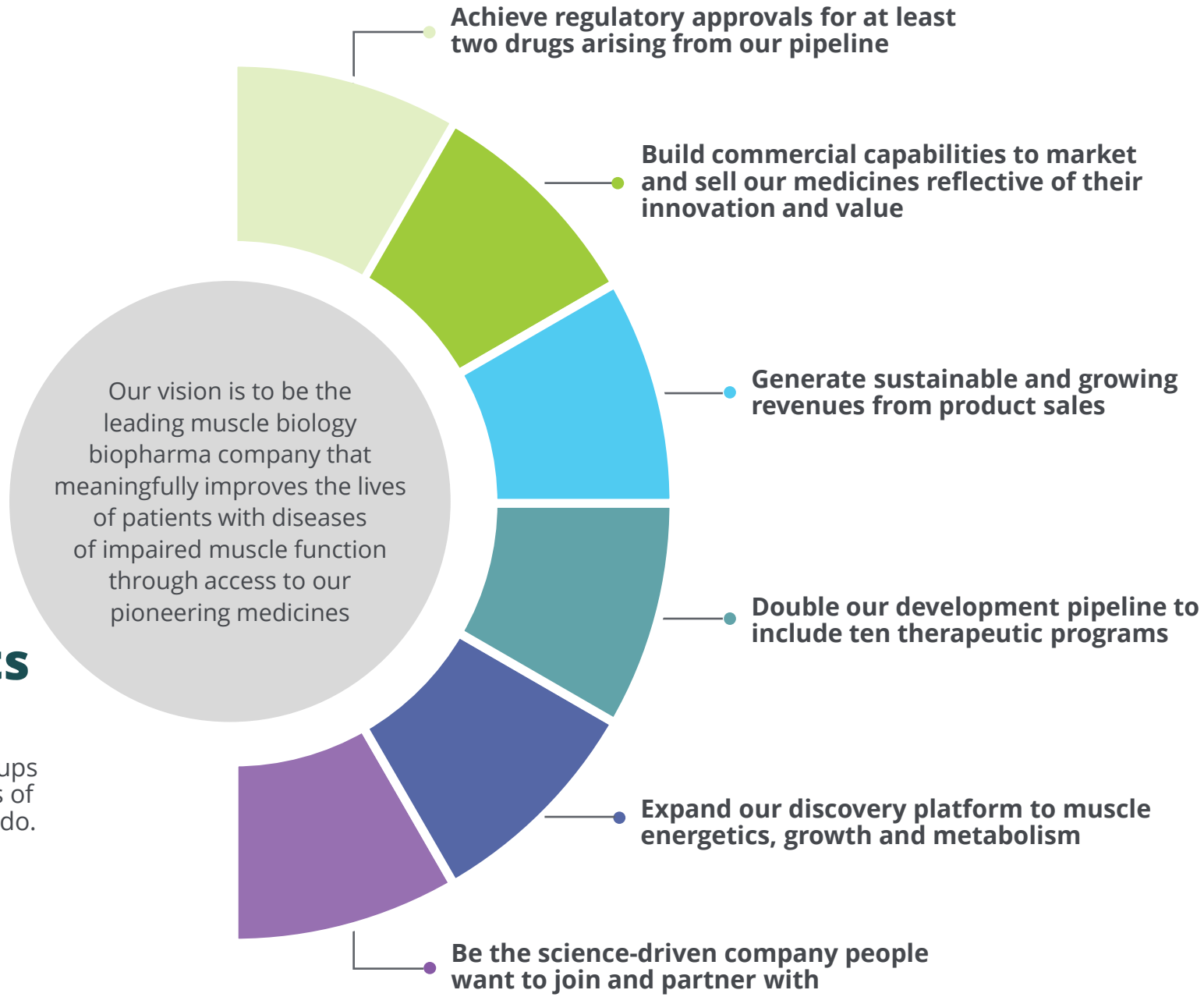
To bring forward new medicines to improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function.

Cytokinetics

VISION 2025

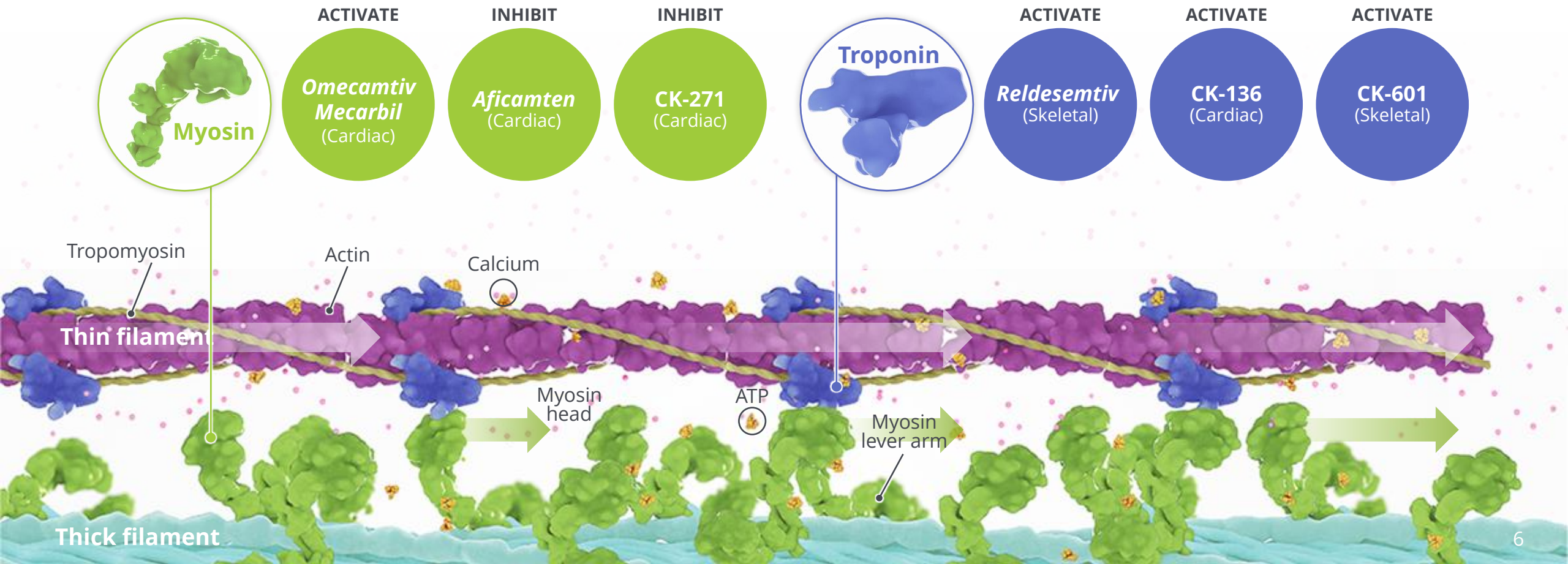
Leading with Science, **Delivering for Patients**

As always, we will support disease advocacy groups elevating the patient voice and live by our values of integrity, fairness and compassion in all that we do.

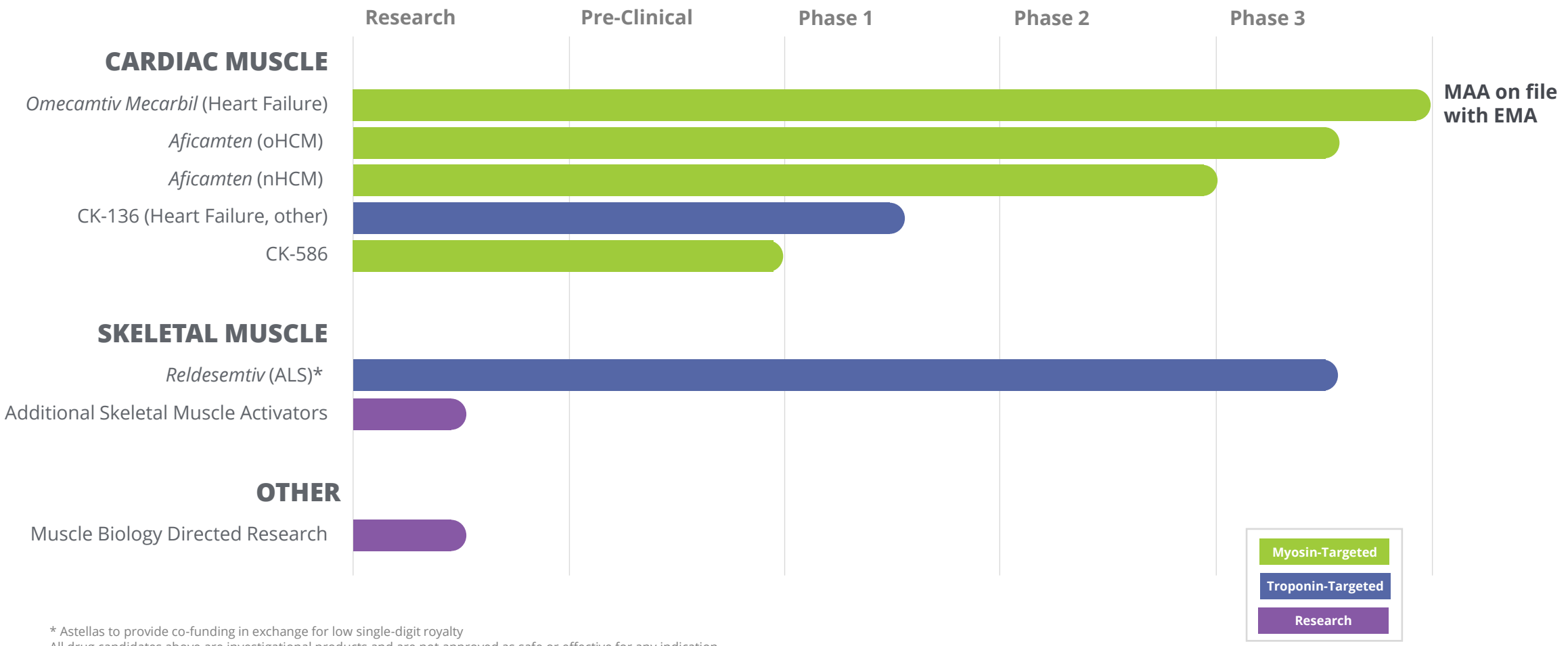


Sarcomere Directed Drug Development

The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables myocytes to contract and generate force



Pipeline of Novel Muscle-Directed Drug Candidates



* Astellas to provide co-funding in exchange for low single-digit royalty
All drug candidates above are investigational products and are not approved as safe or effective for any indication.

Key Priorities in 2023

Continue execution of SEQUOIA-HCM and advance **broad development program** and go-to-market strategy for *aficamten*

Request **meeting with FDA** regarding CRL for *omecamtiv mecarbil*

Continue execution of **COURAGE-ALS** and OLE

Advance development of **CK-586**

Expand research beyond contractility to muscle energetics, growth and metabolism

Sarcomere Directed Drug Development

Cardiac Muscle

Aficamten
Omecamtiv Mecarbil

Cytokinetics

Omecamtiv mecarbil and aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Aficamten

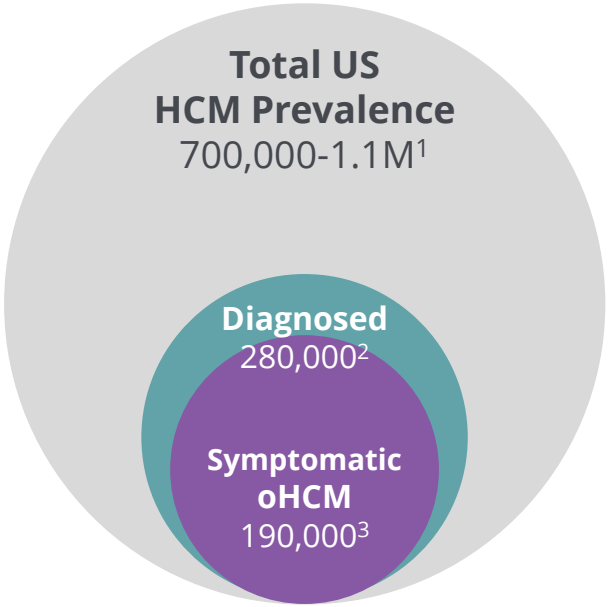
Cytokinetics

Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

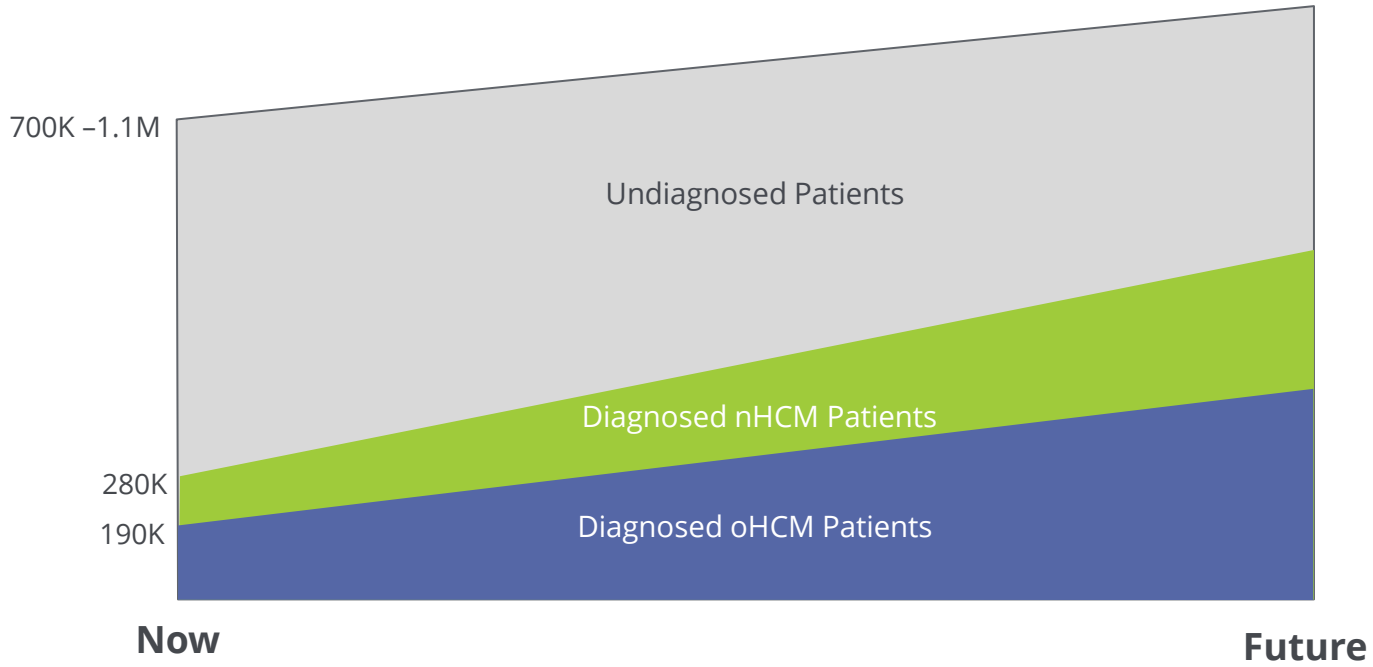
In US, Large HCM Population With Many Undiagnosed

280K Diagnosed HCM Patients; Estimated 400-800K Undiagnosed

Current US HCM Prevalence



Growing HCM Prevalence



nHCM: non-obstructive HCM; oHCM: obstructive HCM

1. CVrg: Heart Failure 2020-2029, p 44; Maron et al. 2013 DOI: 10.1016/S0140-6736(12)60397-3; Maron et al 2018 10.1056/NEJMra1710575
2. Symphony Health 2016-2021 Patient Claims Data DoF;
3. Maron MS, Hellawell JL, Lucove JC, Farzaneh-Far R, Olivotto I. Occurrence of Clinically Diagnosed Hypertrophic Cardiomyopathy in the United States. Am J Cardiol. 2016; 15;117(10):1651-1654.

Aficamten: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor

Rapid Onset

Symptom relief as early as within 2 weeks initiation and dose adjustment possible biweekly if indicated

Precise Dosing

Echo guided dose titration allows both dose increases and decreases at the patient visit

Simplicity of Use

No off-target effects and use in combination with β-blockers, CCB, Disopyramide, and/or Ranolazine

Rapid Reversibility

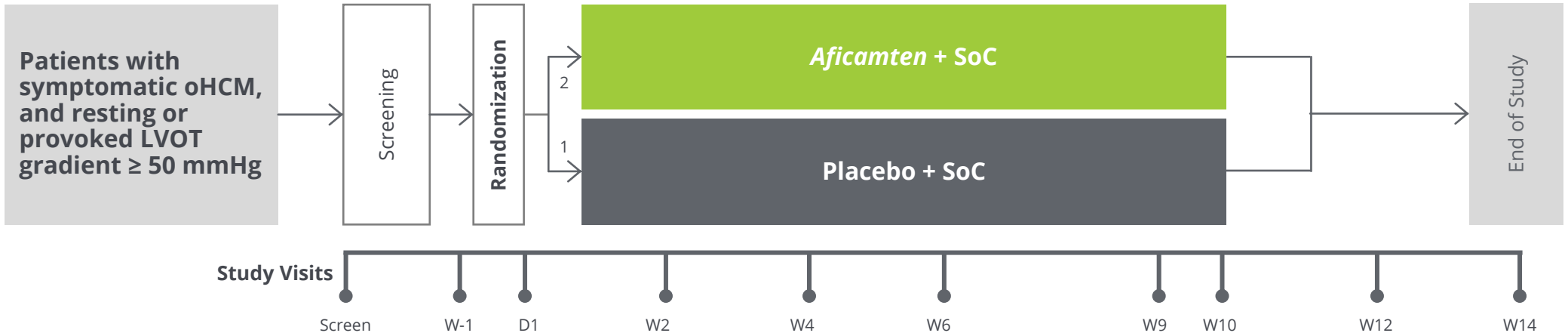
Washout of pharmacodynamic effect within 2 weeks

Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

REDWOOD-HCM: Cohorts 1 & 2

Patients with symptomatic oHCM on background therapy excluding *disopyramide*

Two sequential dose-finding cohorts



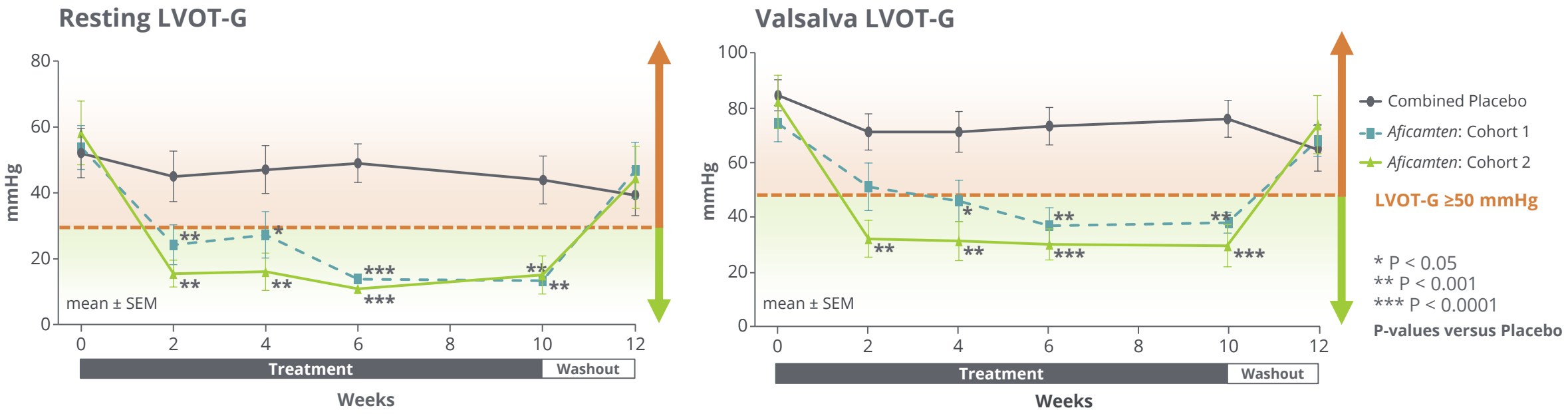
	Dose 1	Dose 2	Dose 3
Cohort 1	5 mg	10 mg	15 mg
Cohort 2	10 mg	20 mg	30 mg

REDWOOD-HCM: Efficacy

Cohorts 1 & 2

REDWOOD HCM

Results published in *JACC* in January 2023

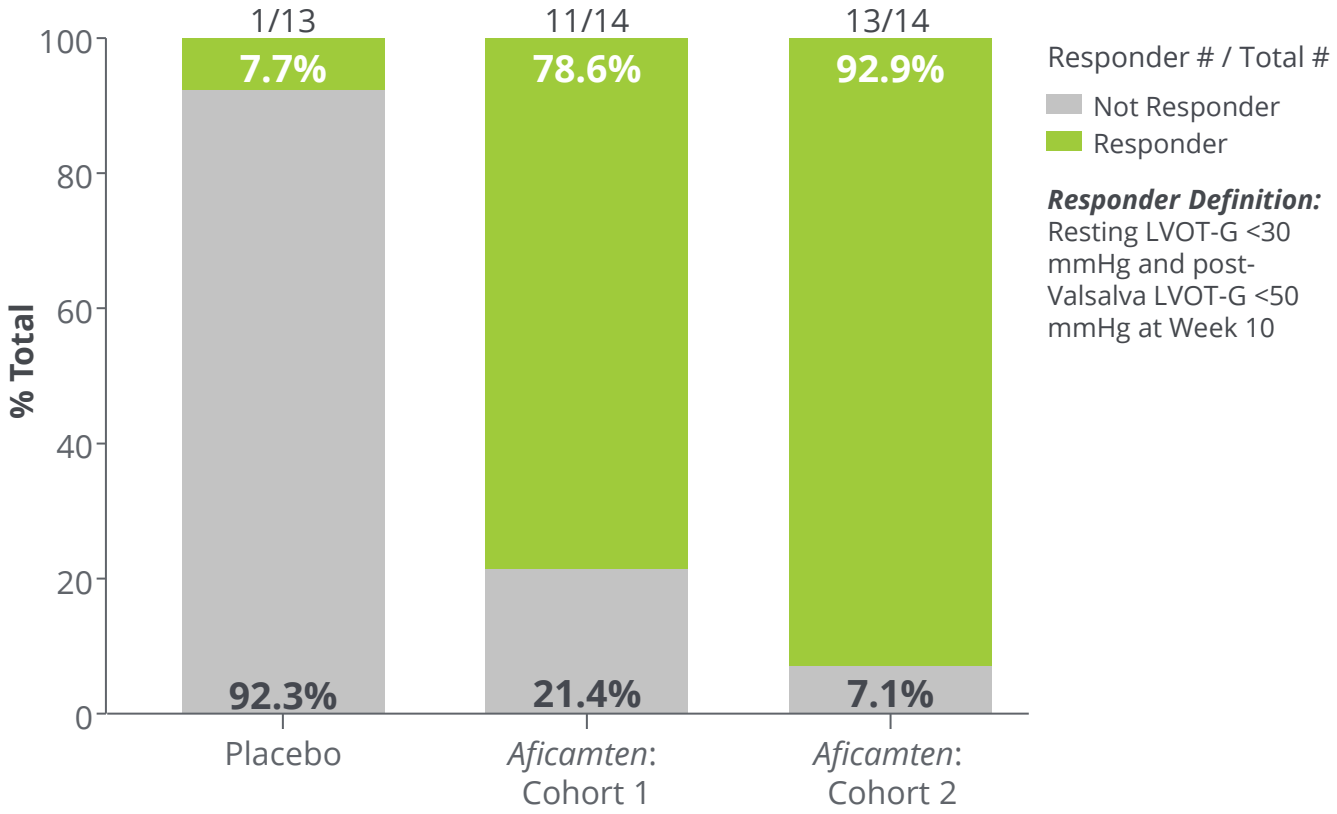


Dose finding study
Cohort 1 (n=21), Cohort 2 (n=20)

Maron M, et. al. Phase 2 Study of *Aficamten* in Patients With Obstructive Hypertrophic Cardiomyopathy. JACC. January 2023.

Response Rates on Treatment with *Aficamten*

Cohorts 1 & 2



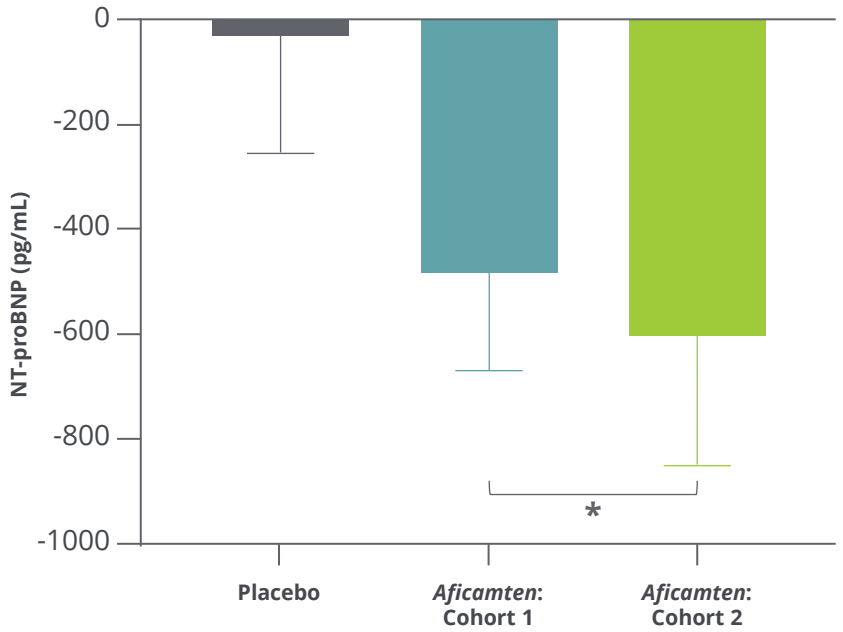
- Consistent, **clinically meaningful reductions in LVOT gradients** within two weeks
- **No treatment interruptions** or discontinuations
- No treatment-related SAEs
- **Reversibility of drug effect** demonstrated
- Statistically significant reductions in NT-proBNP
- Improvement in NYHA class

Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"
Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Change from Baseline in NT-proBNP & NYHA Class

Cohorts 1 & 2

Change from Baseline NT-proBNP to Week 10

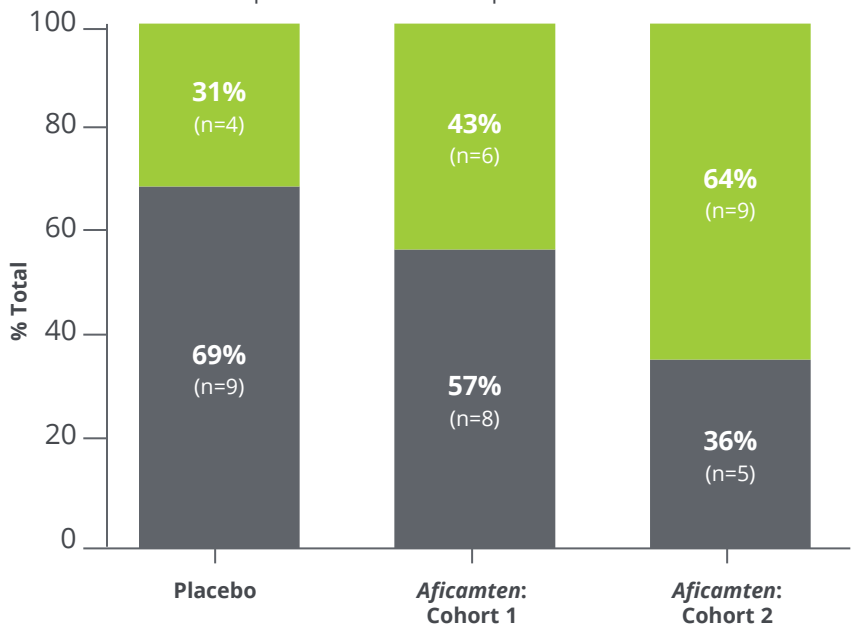


*** p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- Combined Placebo (N=13)
- *Aficamten*: Cohort 1 (N=14)
- *Aficamten*: Cohort 2 (N=14)

Improvement in Heart Failure Symptoms (NYHA Class)

Week 10 Responder Definition: Improvement in NYHA Class ≥1



Cohort 1 vs Placebo: p > 0.1
Cohort 2 vs Placebo: p = 0.08

- No Improvement in NYHA Class
- ≥1 NYHA Class Improvement

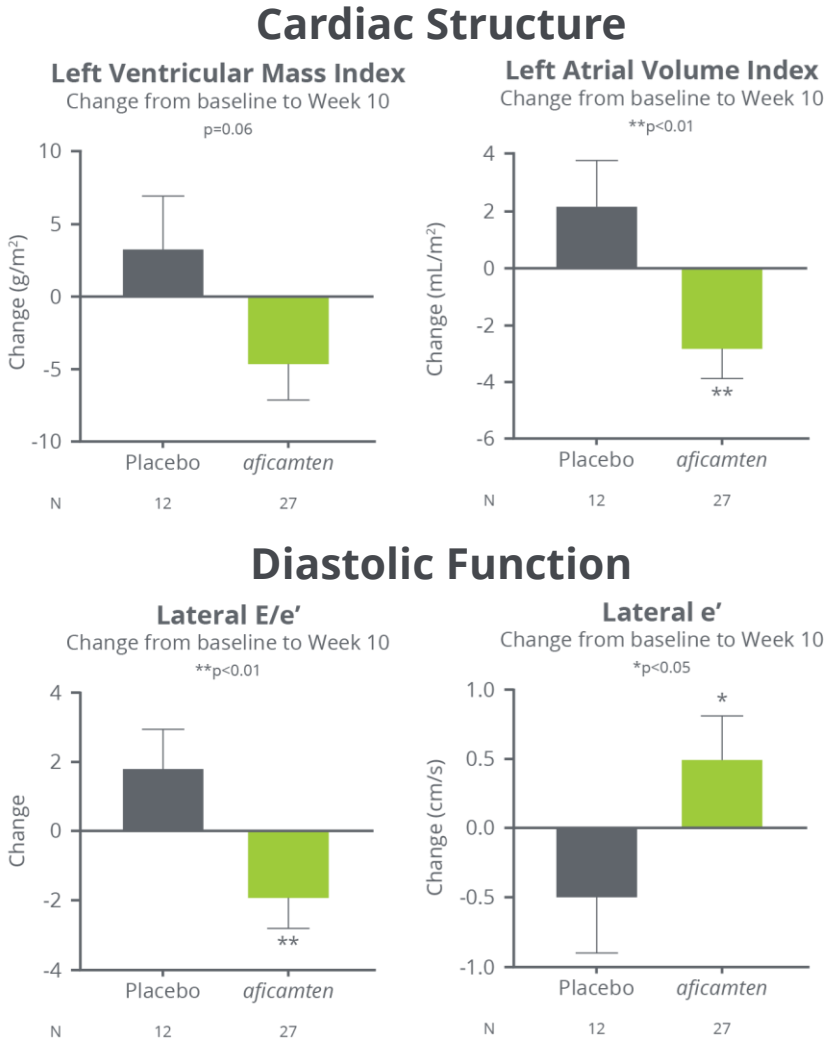
Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, *Aficamten*, In Obstructive Hypertrophic Cardiomyopathy"

Improved Cardiac Structure and Diastolic Function

Cohorts 1 & 2: Early signs of improvement in cardiac structure and myocardial relaxation

Treatment with *aficamten* for 10 weeks resulted in:

- **Significant reduction in left atrial volume index**
- Trend towards a **reduction in LV mass index**
- **Improved diastolic function**
  - reduction in lateral E/e' ($p<0.01$)
  - increase in lateral e' ($p<0.05$))



Abraham T. et al. "Early Cardiac Structural and Functional Reverse Remodeling in Obstructive Hypertrophic Cardiomyopathy after 10 Weeks of *Aficamten* Therapy: Analyses from REDWOOD-HCM"

REDWOOD-HCM: Cohort 4

Patients with symptomatic nHCM on background therapy

Initial results presented at ACC.23; additional data expected in 1H 2023

	Dose 1	Dose 2	Dose 3
Cohort 4	5 mg	10 mg	15 mg

hs-cTnl: high- sensitivity cardiac troponin
*Telephone visits
**Patient can only be down-titrated at Week 6

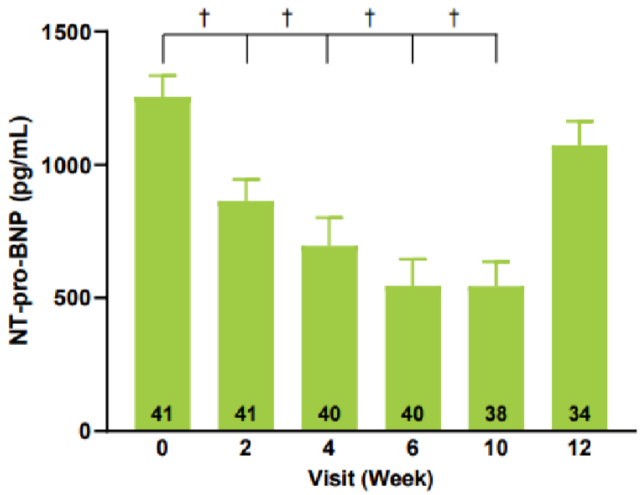
Significant Improvements in Symptoms & Biomarkers

Cohort 4

85% of patients achieved 15 mg dose; no discontinuations due to adverse events

Change from Baseline NT-proBNP

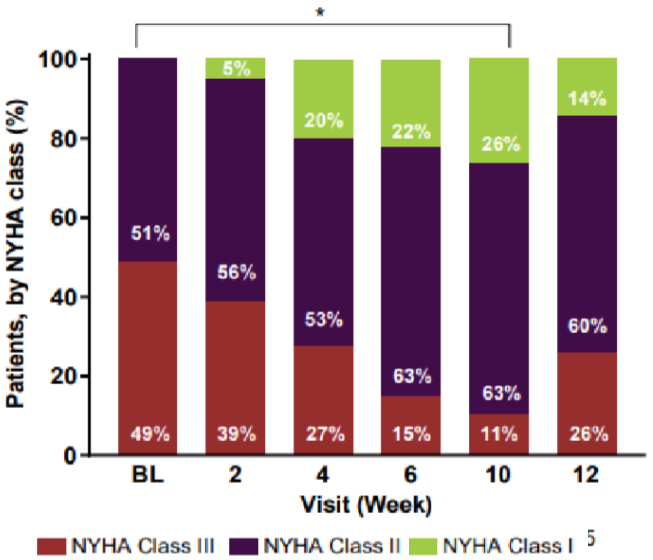
Average decrease of 66% with *P*<0.0001



† *P*<0.0001

Improvement in NYHA Class

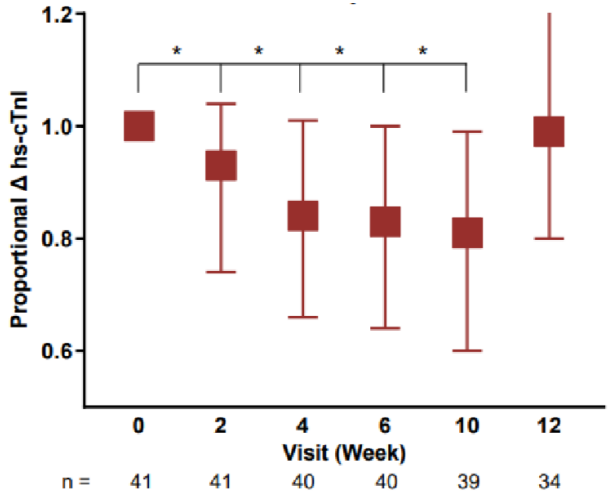
54% of patients experienced a change of ≥1 NYHA class



* *P*<0.05

Change in Baseline hs-cTroponin I

Significant decrease at each study visit compared to baseline *P*<0.05

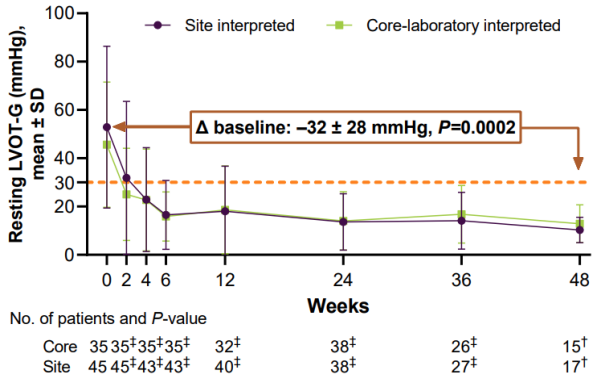


FOREST-HCM: Open Label Extension

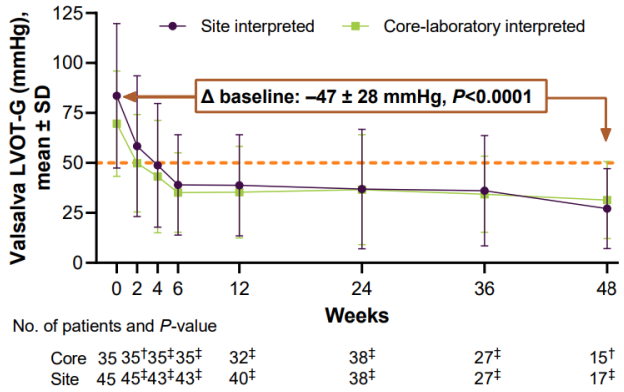
Long-term treatment shows sustained improvement in LVOT-G, NYHA class, KCCQ

Treatment with *aficamten* eliminated SRT eligibility in all patients eligible at baseline

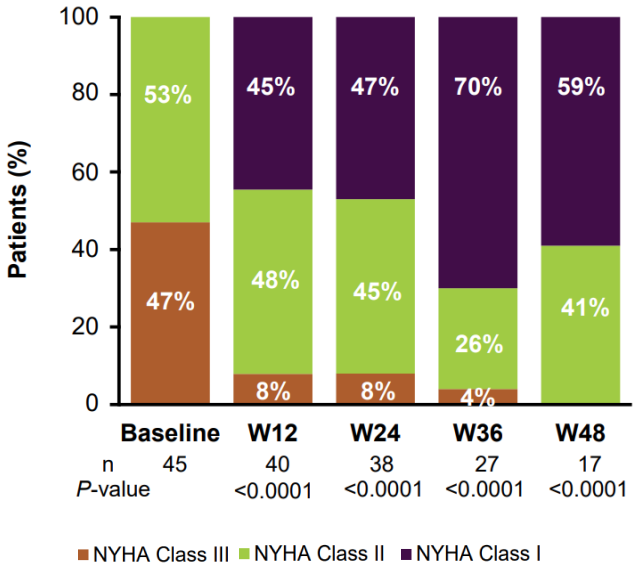
48 Weeks: Resting LVOT Gradient



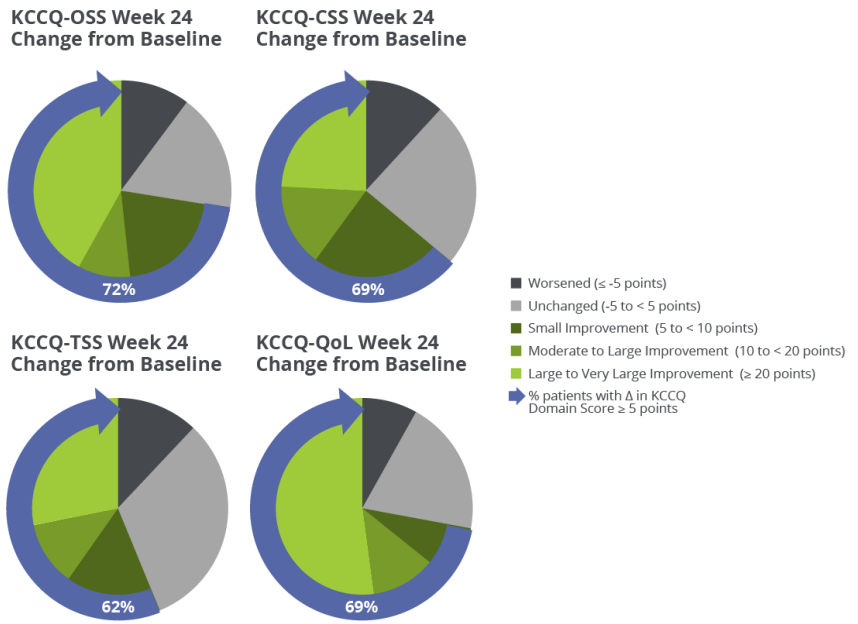
48 Weeks: Valsalva LVOT Gradient



48 Weeks: Improvement in NYHA Class



24 Weeks: Change from Baseline KCCQ Scores



Safety Data: Phase 2 & OLE

- **oHCM → Cohorts 1, 2, & 3: 10-weeks of treatment**
  - 2 SAEs reported in 41 *aficamten*-treated → none were related to *aficamten* treatment
  - No treatment interruptions or discontinuations
  - Transient and asymptomatic decrease in LVEF < 50% occurred in 2 of 41 *aficamten*-treated patients
- **nHCM → Cohort 4: 10-weeks of treatment**
  - Well tolerated - 85% achieved maximal dose (15 mg)
  - Transient and asymptomatic decrease in LVEF < 50% occurred in 3 of 41 *aficamten*-treated patients
  - One death unrelated to *aficamten* treatment - sudden cardiac death (SCD) in patient with history of aborted SCD x 2 prior to participation. Two days before event, LVEF was normal, NT-proBNP was lower and plasma concentration of *aficamten* was within the expected range

- **oHCM → FOREST-HCM: 45 patients and up-to 12-months of treatment**
  - No SAE's related to *aficamten* treatment
- **One treatment interruption in the setting of alcohol-related atrial fibrillation with a transient decrease in LVEF to <50%**

There have been no reported cases of LVEF <40% in **any** patients within the development program

There have been no treatment related dose interruptions or discontinuations

SEQUOIA-HCM: Phase 3 Trial

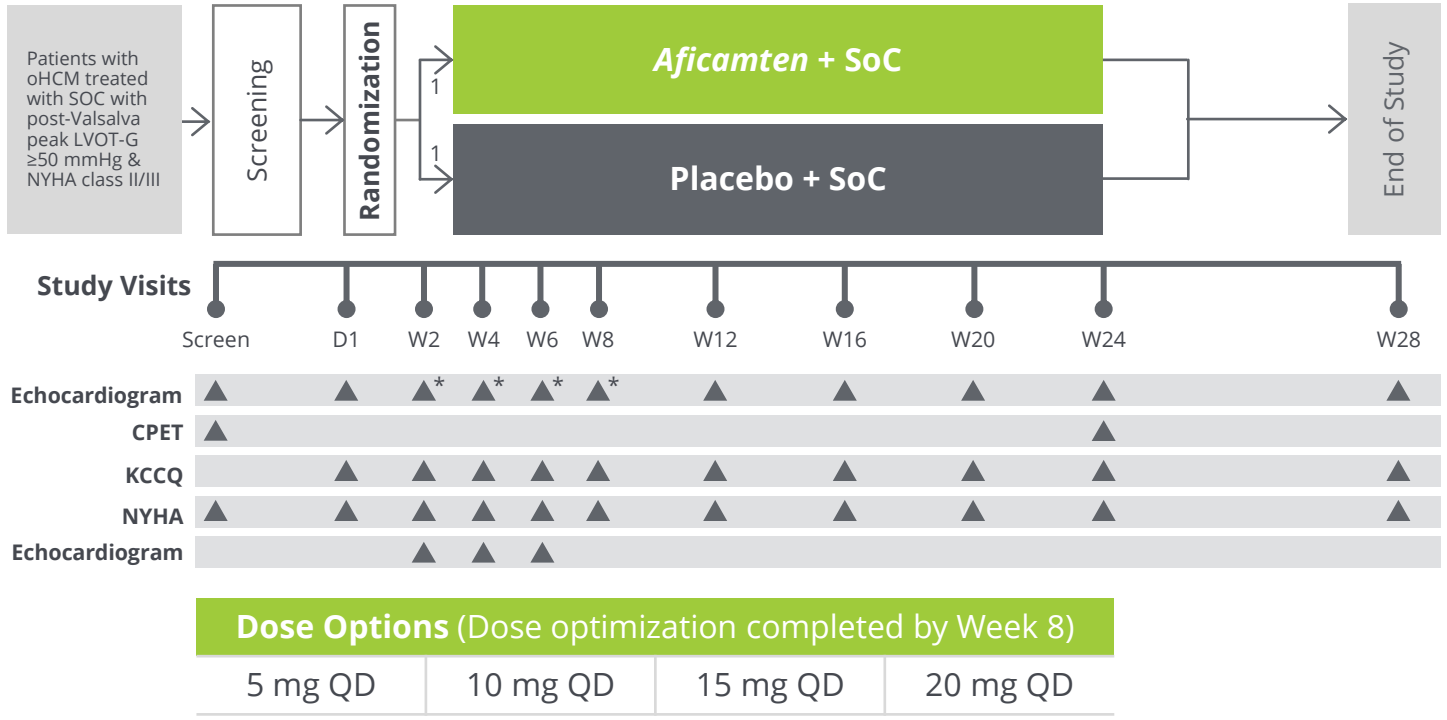
More than two-thirds of patients enrolled; on track to complete enrollment in Q2

Primary endpoint: **Change in pVO_2 by CPET from baseline to Week 24**

Secondary objectives include measuring **change in KCCQ & improvement in NYHA class at week 12 and 24**

Enrolling 270 patients treated with standard of care with:
- **resting LVOT-G ≥30 mmHg,**
- **post-Valsalva LVOT-G ≥50 mmHg,**
- **NYHA Class II or III,**
- **exercise performance <80% predicted**

Individualized dose up-titration based on echocardiography: LVEF ≥55%, post-Valsalva LVOT-G ≥30 mmHg



Dose Options (Dose optimization completed by Week 8)			
5 mg QD	10 mg QD	15 mg QD	20 mg QD

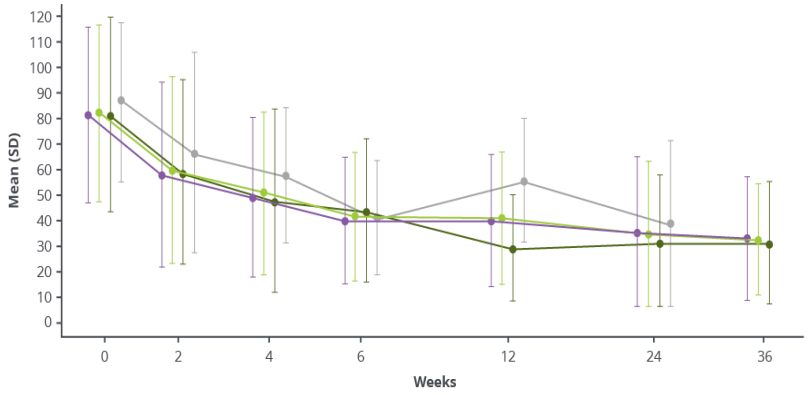
SOC: standard of care
* Focused echocardiogram
** Plan to enroll in US, Italy, France, Germany, Czech Republic, Denmark, Hungary, Netherlands, Poland, Portugal, Spain, UK, Israel & China

Monotherapy Trial, Supported by FOREST-HCM

Initial FOREST-HCM data on reduction/withdrawal of background medications supports monotherapy trial

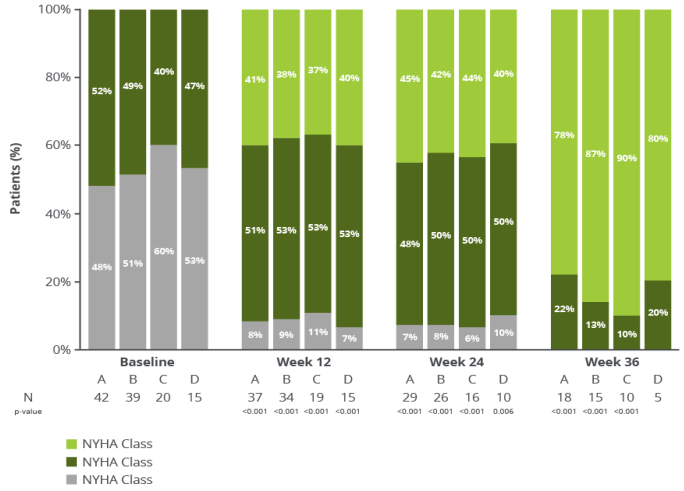
Reduction or Withdrawal of Standard of Care Therapies

Valsalva LVOT-G

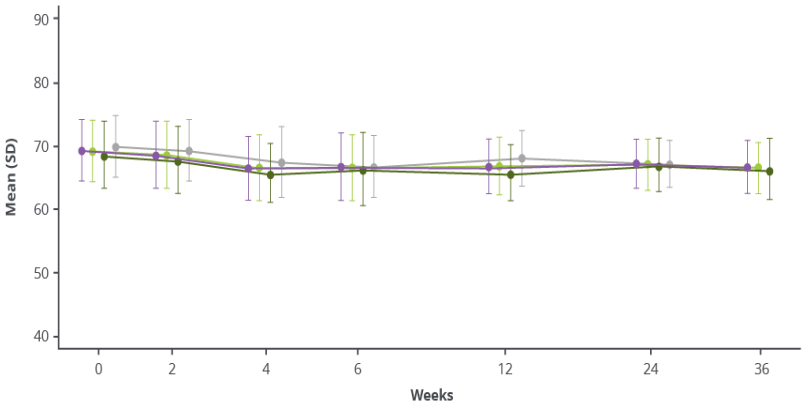


# of subjects and P-values							
A	42	42***	41****	41****	37****	29****	18****
B	39	39***	38****	36****	34****	26****	15****
C	20	20*	20****	20**	19****	16***	10***
D	15	15 (p=0.0926)	15**	15***	15**	10***	

NYHA Class



LVEF



# of subjects and P-values							
A	42	42 (p=0.3749)	41***	41**	37**	29**	18*
B	39	39 (p=0.4649)	38**	38**	34*	26**	15*
C	20	20 (p=0.4262)	20*	20*	19 (p=0.0578)	16 (p=0.0748)	10 (p=0.2320)
D	15	15 (p=0.6614)	15*	15*	15 (p=0.2291)	10*	

A: All patients
B: On background therapy (BT)
C: Patients with background therapy reduction/withdrawal (BTR/W) attempt
D: Patients on BT without BTR/W attempt

**** = p < 0.0001
*** = p < 0.001
** p = < 0.005
* = p < 0.05

Masri M, et al. "Withdrawal of Background Standard of Care Medical Therapy in Patients with Obstructive Hypertrophic Cardiomyopathy Treated with *Aficamten* in REDWOOD-HCM OLE

MAPLE-HCM: Phase 3 Monotherapy Trial

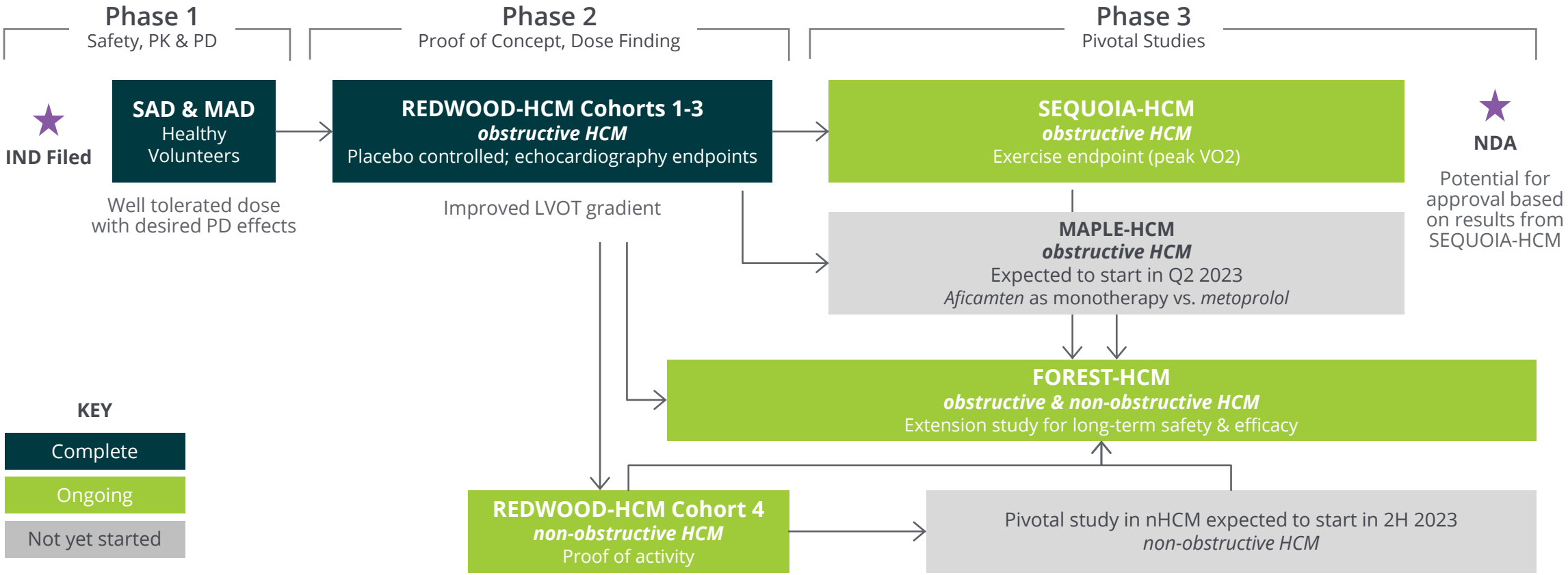
Opening to enrollment in Q2

Active-comparator trial of *aficamten* as monotherapy vs. *metoprolol* in patients with oHCM

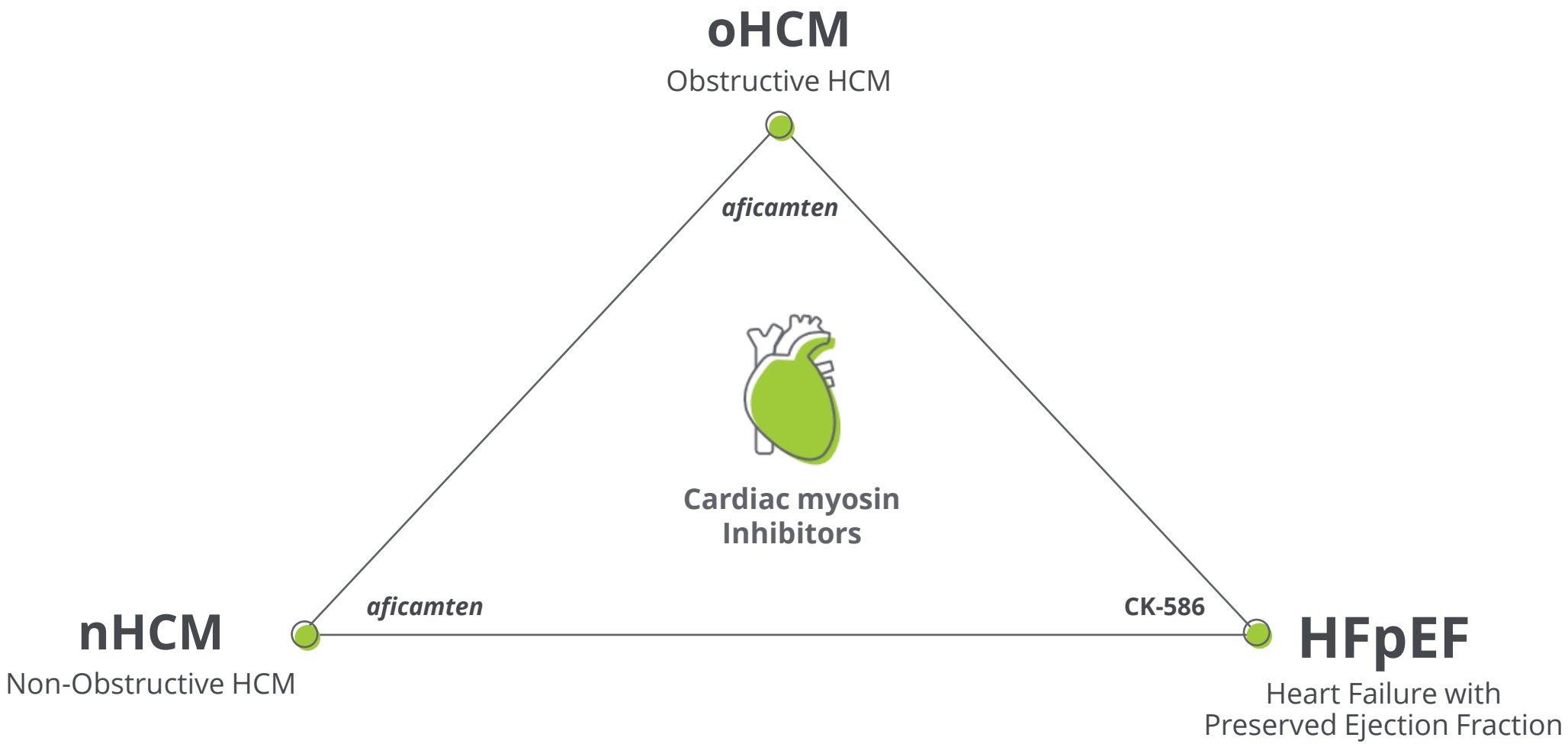
- Trial to enroll approximately **170 patients**
- Primary endpoint: **change in peak VO2, assessed by CPET from baseline to Week 24**
- Secondary endpoints: **change in NYHA class, KCCQ, NT-proBNP, and measures of structural remodeling**

Aficamten: Clinical Development Plan for HCM

MAPLE-HCM to begin in Q2 2023; pivotal Phase 3 trial in nHCM beginning 2H 2023



Novel Approach May Address Multiple Unmet Patient Needs



Aficamten: Targeting Patients with Unmet Need

Positive HCP Anticipation for *Aficamten*

Majority of KOLs see *aficamten* as an improvement to standard-of-care given the unique MOA; particularly interested in:

- Rapid and sustained LVOT-G reduction
- Rapid improvement in symptoms
- Reduction in septal wall thickness

Characteristics of the Ideal US HCM Patient for *Aficamten*

- Symptomatic, uncontrolled (non-responsive, refractory) to standard-of-care

  or

- Contra-indication for standard-of-care or other cardiac myosin inhibitors

  or

- Newly diagnosed patients

Cogent Primary Mkt Research, USA 2022 (n = 150)
Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Aficamten: Brand Strategy

Aspirational Brand Goal: Establish *aficamten* as foundational therapy for HCM patients

COMPETE:
In HCM Market

- Differentiate on product attributes of value to patients and physicians

EXPAND:
Customer Base

- Leverage differentiated safety profile and limited drug-drug interactions
- Leverage CV franchise infrastructure, market understanding, and relationships

MAINTAIN:
Patient on Therapy

- Ensure access through patient support services
- Provide patient support tools to manage dosing regimens and persistence

GROW:
Undiagnosed

- Invest in disease education and genetic testing programs

Aficamten: Market Access Strategy

Get rapid and parity access

- Learn from first to market access experience
- Leverage existing access relationships
- Secure profitable access to support efficient, desired prescribing position
- Devise distribution network to complement product strategy

Clear pricing based on benefit

- Relative pricing position to be supported by market research
- Pricing strategy consistent with product strategy

Develop value proposition and value story

- Driven by clinical benefit and utility relative to alternatives
- Generate, disseminate and communicate health economics & outcomes research supporting value of differentiated treatment

Gated Build of Commercial Infrastructure

Re-deployment of cardiovascular franchise commercial team to *aficamten*

Activities initiated upon key de-risking events

Underway Pre-NDA filing
Market access
Pricing strategy
Distribution approach
Payer engagement
Brand strategy
Sales force planning

To be initiated upon NDA acceptance
Launch campaign
Commercial training
PIE deployment (payers)
Technology build
Omnichannel execution

To be initiated upon FDA approval
Media purchases
Patient support programs

Headquarters team in place

- Commercial leadership
- Marketing
- HEOR
- Patient services
- Access & distribution
- Sales team leads
- First line field managers
- Sales operations
- Commercial learning & development

Omecamtiv Mecarbil

Cytokinetics

Omecamtiv mecarbil is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Omecamtiv Mecarbil: Current Status

No plans to conduct additional clinical trial of *omecamtiv mecarbil*

Received CRL from FDA
Feb 28, 2023

GALACTIC-HF not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic HFrEF

2023

- **Engage with FDA** to understand what may be required to support potential approval of *omecamtiv mecarbil*
- Continue to pursue **international approvals** of *omecamtiv mecarbil*
  - MAA on file with EMA
- Continue to seek partnerships in Europe and Japan

Sarcomere Directed Drug Development

Skeletal Muscle

Reldesemtiv

Cytokinetics

Reldesemtiv

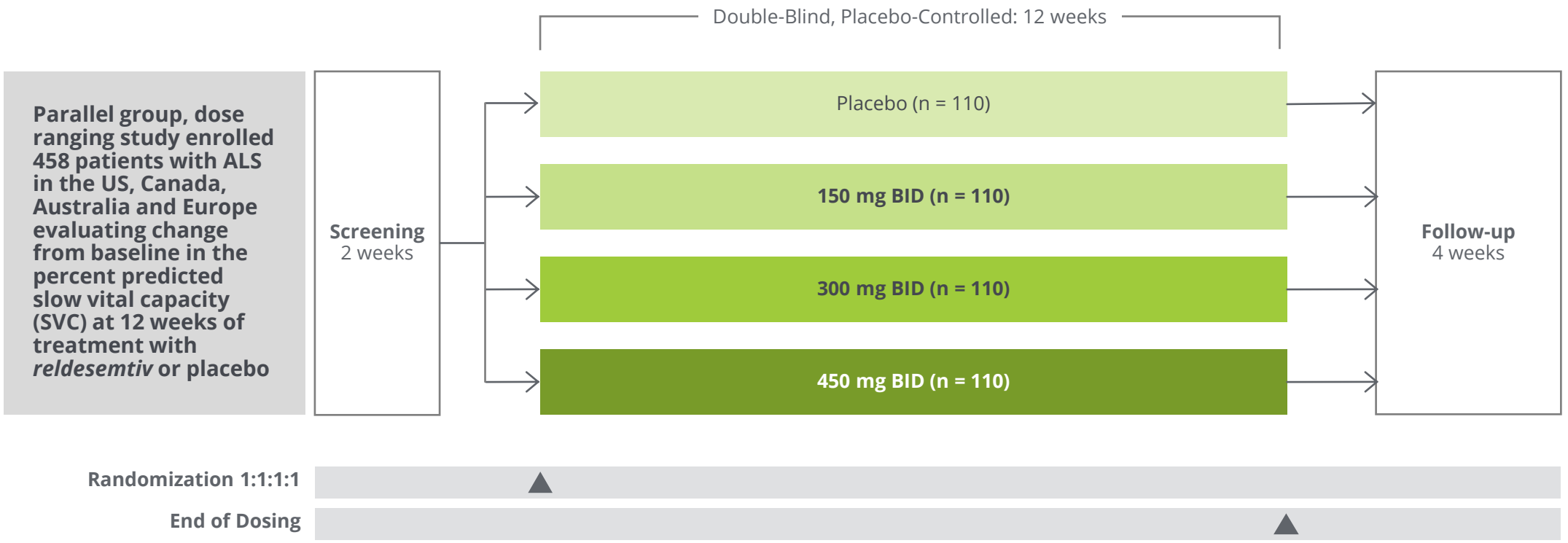
Cytokinetics

Reldesemtiv is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.

Phase 2 Clinical Trial in ALS

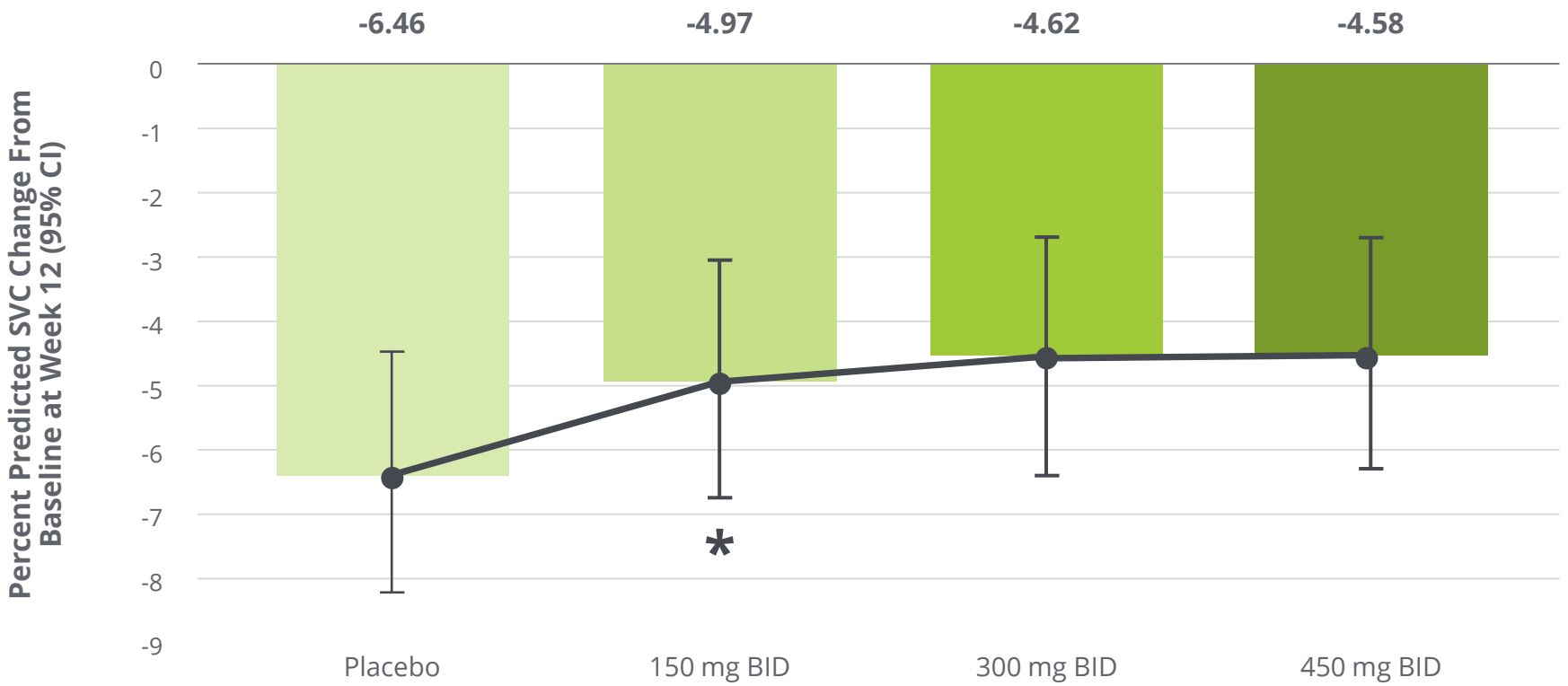
FORTITUDE ALS

Results presented at American Academy of Neurology 2019 Annual Meeting



Primary Endpoint: SVC

Change from baseline in percent predicted SVC at week 12



Primary Analysis*

P = 0.11 for weighted dose-response relationship

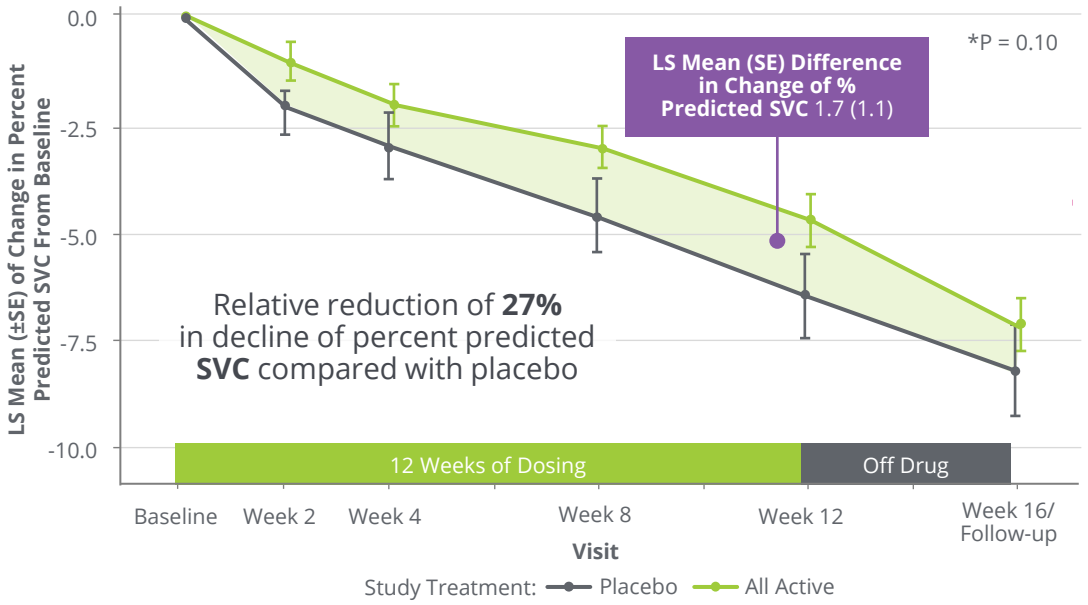
*Based on Mixed Model for Repeated Measures (MMRM) with the contrasts of (-5, -1, 3, 3) for placebo, *reldesemtiv* 150 mg, 300 mg and 450 mg BID, respectively

Phase 2 Clinical Trial

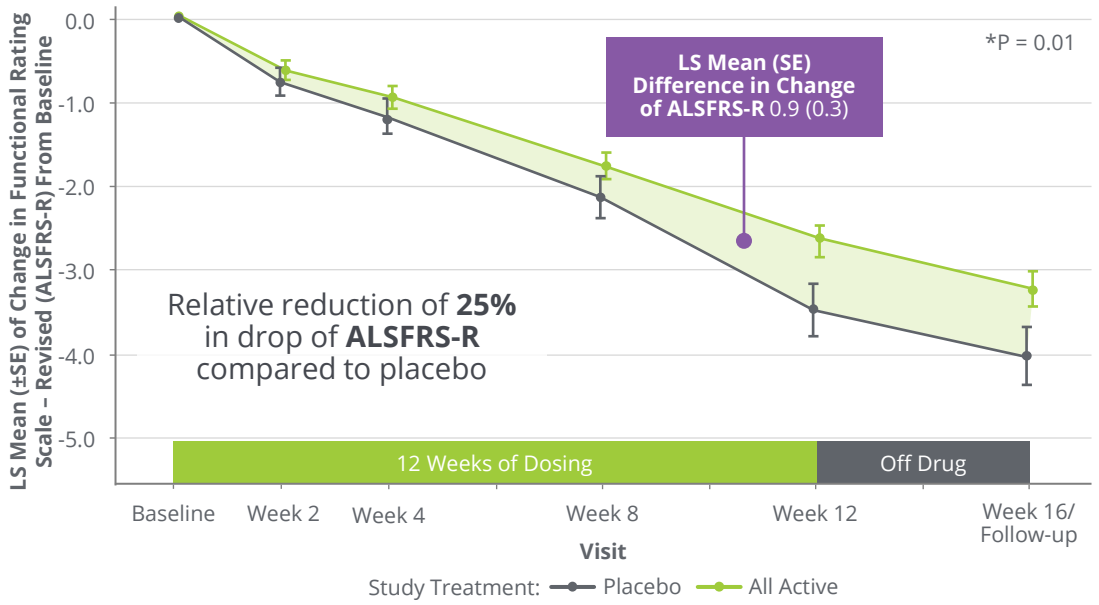
FORTITUDE ALS

Primary analysis not statistically significant; patients on all doses of *reldesemtiv* declined less than patients on placebo*

SVC Change From Baseline
(All Active vs Placebo)



ALSFRS-R Change From Baseline
(All Active vs Placebo)



*post hoc analysis
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

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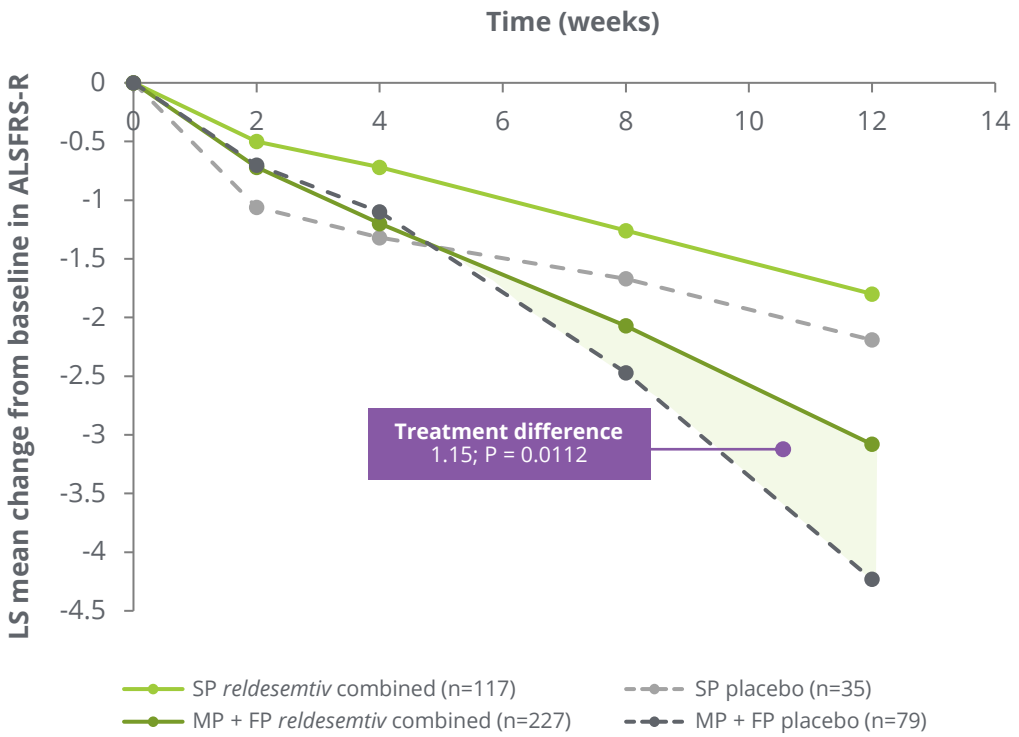
Post-Hoc Analyses Inform Phase 3 Design

FORTITUDE ALS

Change From Baseline in ALSFRS-R by Progressor Tertiles



Majority of Patients Who Meet 24/44 Criteria Have Short or Intermediate Predicted Survival

24/44 criteria: symptoms for ≤24 months; baseline ALSFRS-R total score ≤44

All patients in COURAGE-ALS must meet the 24/44 criteria

Risk Group (Predicted Survival) n (%)	Met 24/44 Criteria (n=272)	Did not meet 24/44 criteria (n=184)	P value
G1 (very short)	38 (14.0)	0 (0)	<0.0001
G2 (short)	81 (29.8)	8 (4.3)	<0.0001
G3 (intermediate)	80 (29.4)	26 (14.1)	0.0002
G4 (long)	61 (22.4)	68 (37.0)	0.0007
G5 (very long)	12 (4.4)	82 (44.6)	<0.0001

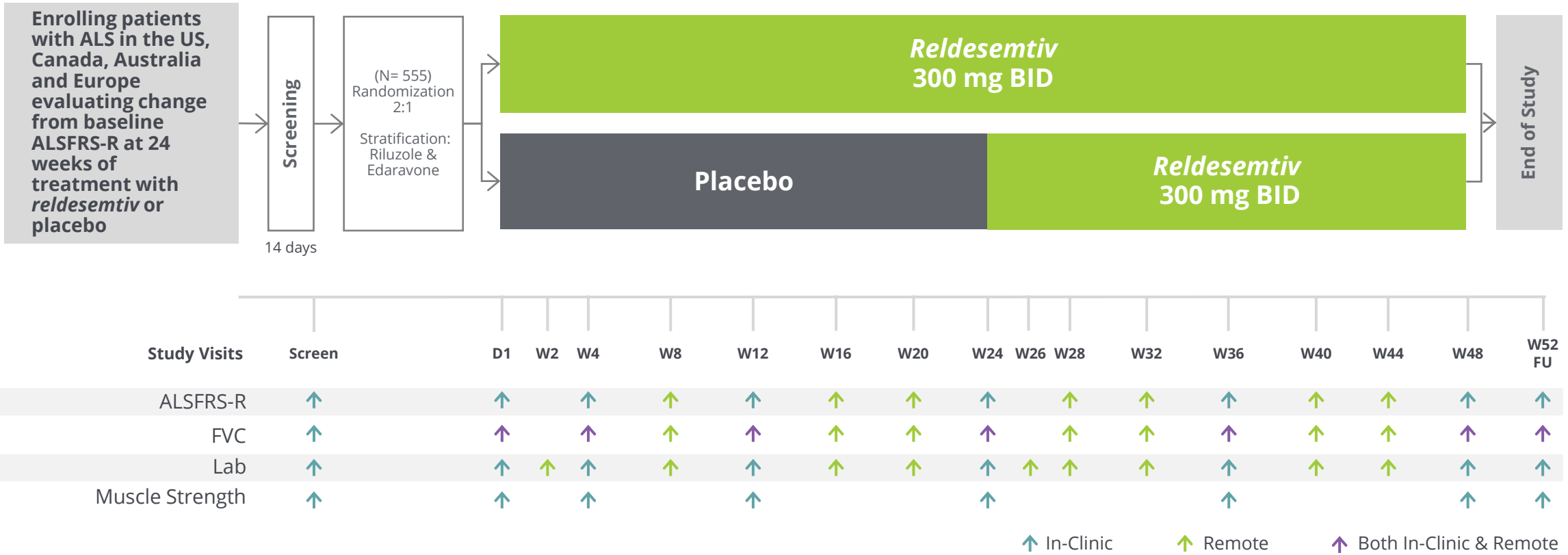
FP, fast progressing; MP, medium progressing; SP, slow progressing
*post hoc analysis
FORTITUDE-ALS did not achieve statistical significance, but patients on all dose groups of *reldesemtiv* declined less than patients on placebo

Phase 3 Clinical Trial Design

>75% of patients enrolled; on track to complete enrollment in Q2

COURAGE ALS

Second interim analysis expected in 1H 2023 (futility & potential fixed increase in enrollment)



Sarcomere Directed Therapies

Corporate Profile

Cytokinetics

Robust Pipeline, Solid Financial Position

Pipeline

1 Potential commercial launch in 2024

2 Programs in Phase 3 trials

2 Potential FDA approvals by 2025

5 Clinical stage programs

10 Development programs by 2025

Programs

HCM

Aficamten

- 1 ongoing Phase 3 trial in oHCM
- Add'l Phase 3 trial in oHCM starting Q2
- Phase 3 trial in nHCM starting 2H
- Ongoing OLE

Heart Failure

Omecamtiv mecarbil

- Engaging with FDA
- Pursuing international approvals

CK-136

- Results from Phase 1 2H

CK-586

- Starting Phase 1 study 1H

ALS

Reldesemtiv

- Complete enrollment in Phase 3 trial in Q2

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

~415
Full time employees
As of March 2023

~$830M
At Q4 2022

>2 years
Cash runway
based on 2023 Financial Guidance

Timelines and milestones reflect Cytokinetics' current expectations and beliefs

Balance Sheet & Financial Guidance

>2 years cash runway based on 2023 guidance

2022 Condensed Balance Sheet

As of 12/31/2022

in millions

	Total
Cash and investments	$829.3
Accounts receivable	$0.1
PPE	$80.5
Leased assets	$82.7
Other assets	$22.2
Total Assets	**$1,014.8**
Convertible Debt	$545.0
Liability related to sale of future royalties	$300.5
Deferred Revenue	$0
Lease liability	$139.7
Other liabilities	$137.5
Total Liabilities	**$1,122.7**
Working capital	$710.6
Accumulated deficit	($1,586.0)
Stockholders' deficit	($107.9)
Wtd Avg Basic Shares Outstanding	**89.8**

1. Cytokinetics internal planning data. Outside services spend for clinical trials, CMC and toxicology studies

2023 Financial Guidance

in millions

	Total
Cash Revenue	$5*
Cash Operating Expenses	$420-450
Net	**~ $350-375**

* Expect to receive $50M from Royalty Pharma upon the start of the Phase 3 clinical trial of *aficamten* in nHCM

Expected 2023 Milestones

Aficamten		*Omecamtiv Mecarbil*	*Reldesemtiv*	Early Pipeline
Begin **MAPLE-HCM, second Phase 3 trial of *aficamten*** in oHCM in Q2	Present results from **Cohort 4 of REDWOOD-HCM** at ACC.23 in Q1	**Engage with FDA** regarding CRL for *omecamtiv mecarbil*	Expect **second interim analysis** from COURAGE-ALS in Q2	Expect results from **Phase 1 study of CK-136** in 2H
Complete **enrollment in SEQUOIA-HCM** in Q2 2023; results expected in Q4	Begin **Phase 3 trial of *aficamten* in nHCM** in 2H	Pursue **international approvals** for *omecamtiv mecarbil*	Complete **enrollment in COURAGE-ALS** in Q2, subject to second interim analysis	Advance **CK-586** into clinical development in 1H

Cytokinetics

Thank You

Sarcomere directed therapies


Jillian, *diagnosed with HCM*


Chuck, *diagnosed with ALS*


Nefertari, *diagnosed with heart failure*