



Cytokinetics®

EMPOWERING

muscle

EMPOWERING

lives



Vi, diagnosed with HCM
Avonne, diagnosed with HCM
John, diagnosed with heart failure

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 heart failure with preserved ejection fraction (HFpEF); projections regarding the size of the addressable patient population for *aficamten*, *omecamtiv mecarbil*, CK-136, CK-586 or any of our other drug candidates; Cytokinetics’ commercial readiness for *aficamten* or *omecamtiv mecarbil*; our ability to submit a new drug application for *aficamten* with FDA in the third quarter 2024 or a marketing authorization application with EMA in the fourth quarter 2024, the likelihood and/or timing of regulatory approval for our planned new drug application for *aficamten*, *omecamtiv mecarbil* or any future new drug application for any of our other drug candidates or the anticipated timing of any interactions with FDA, EMA or any other regulatory authorities in connection thereto; the timing of completion of MAPLE-HCM, ACACIA-HCM, CEDAR-HCM or any of our other clinical trials, the efficacy or safety of *aficamten*, *omecamtiv mecarbil*, CK-136, CK-586 or any of our other drug candidates, 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 properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, CK-136, CK-586 or any of 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”).

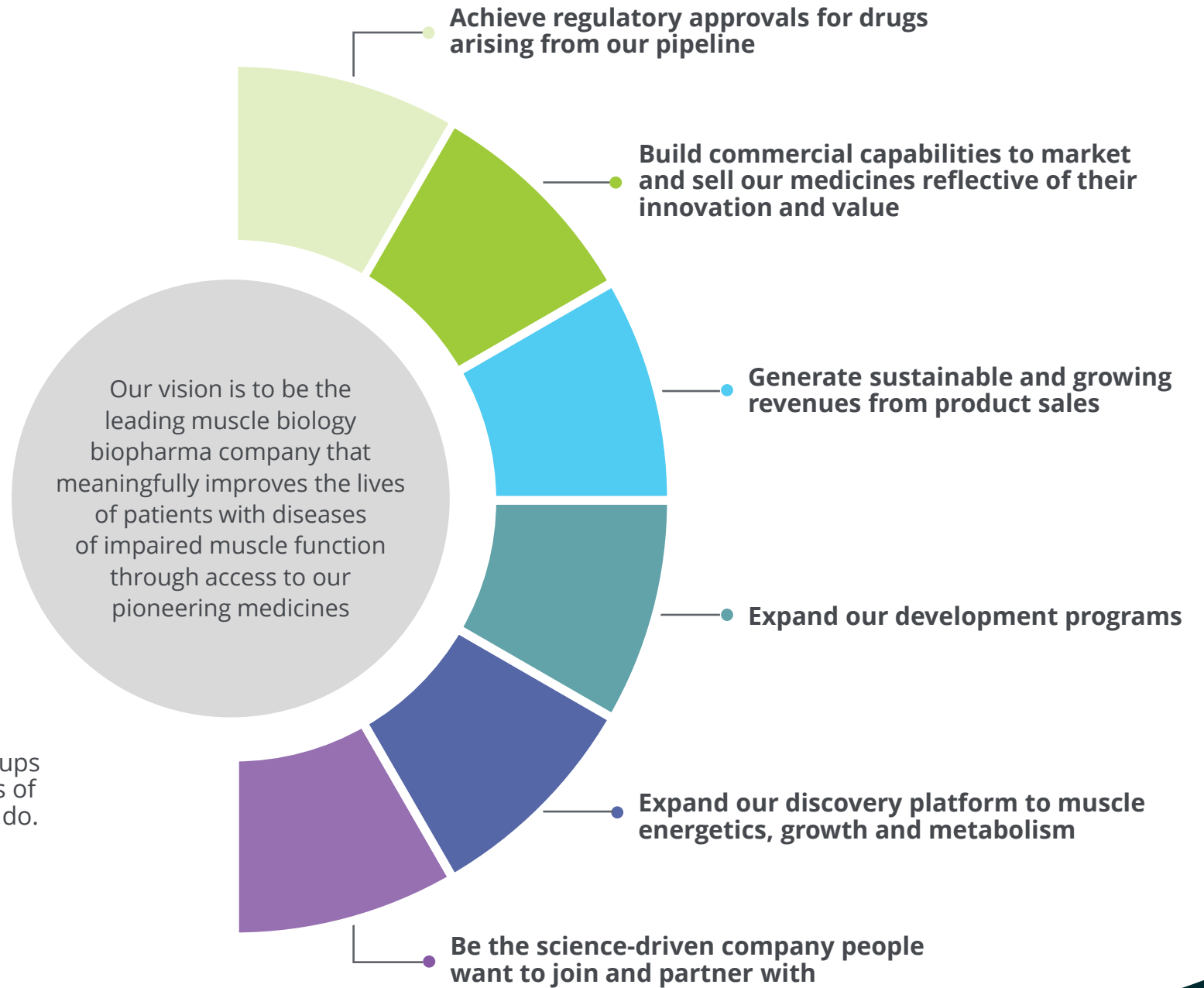
Our Mission

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

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.



A Great Place to Work; Uncommon Continuity of Team

VALUES



patients are
our North Star



science is
in our soul

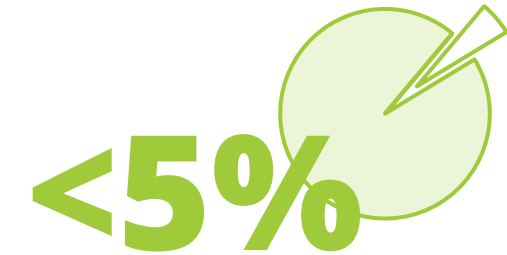


we > me



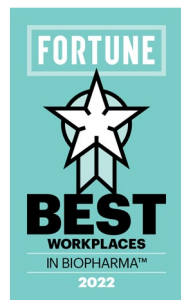
make it
happen

RETENTION



Turnover rate of leadership;
low attrition

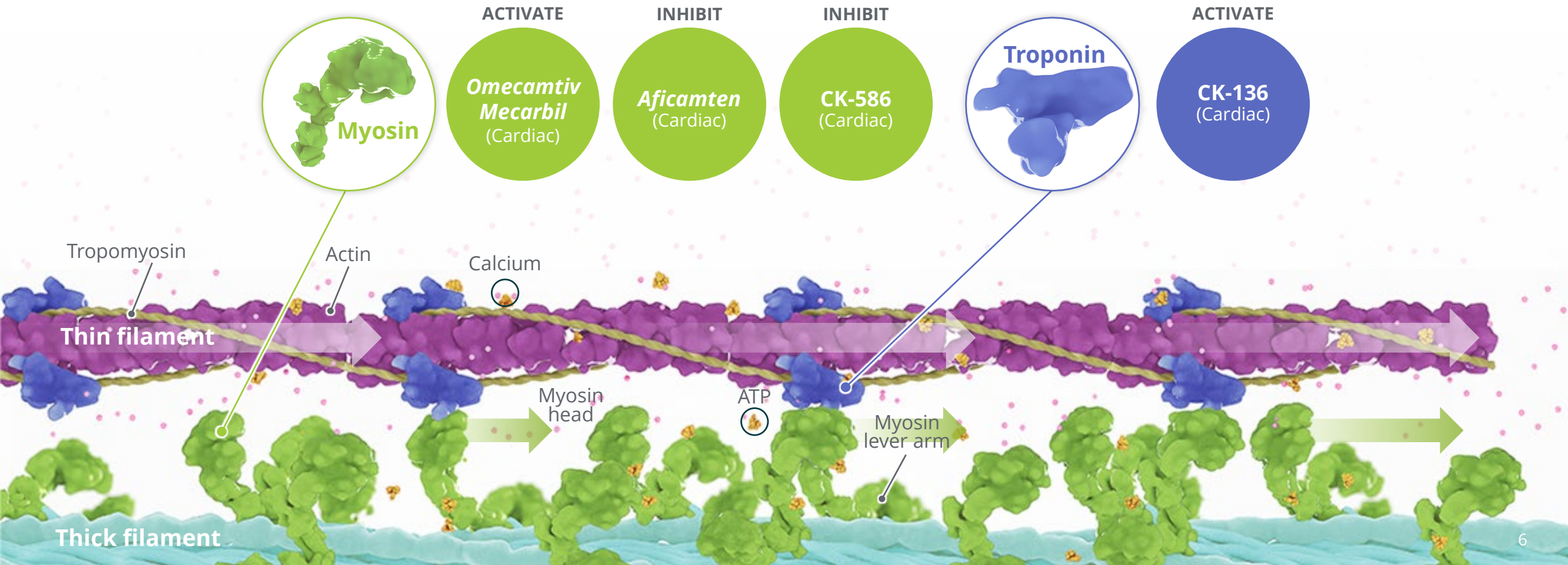
AWARDS



Average tenure of leadership;
high continuity

Sarcomere Directed Drug Development

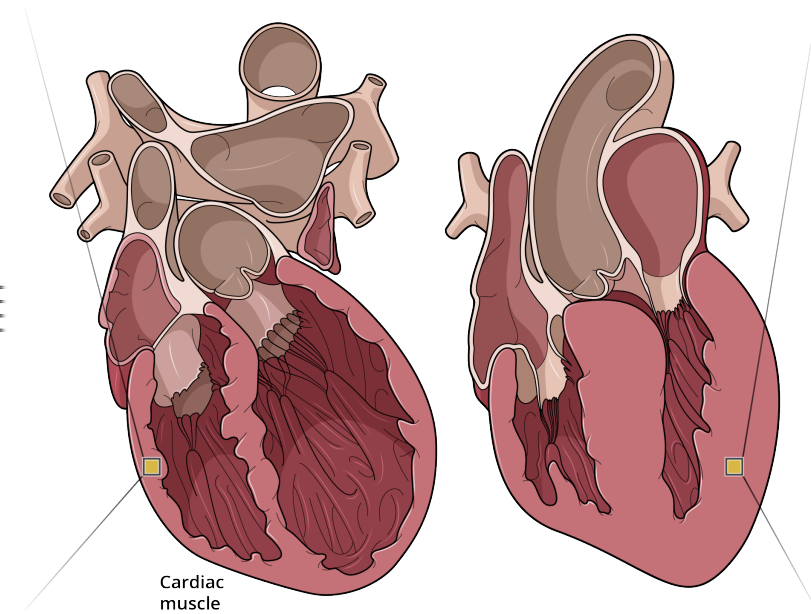
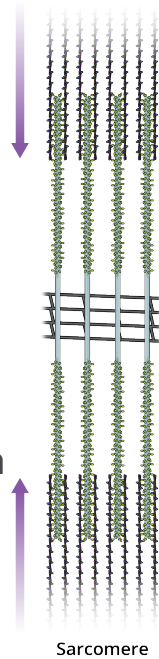
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables myocytes to contract and generate force



Contractile Dysfunction Underlies Cardiac Diseases

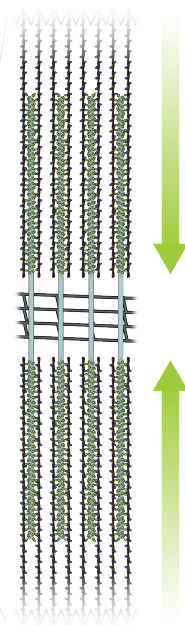
Decreased Cardiac Contractility

- Heart Failure with Reduced Ejection Fraction (HFrEF)
- Genetic Dilated Cardiomyopathy
- Pulmonary Hypertension with Right Ventricular Heart Failure



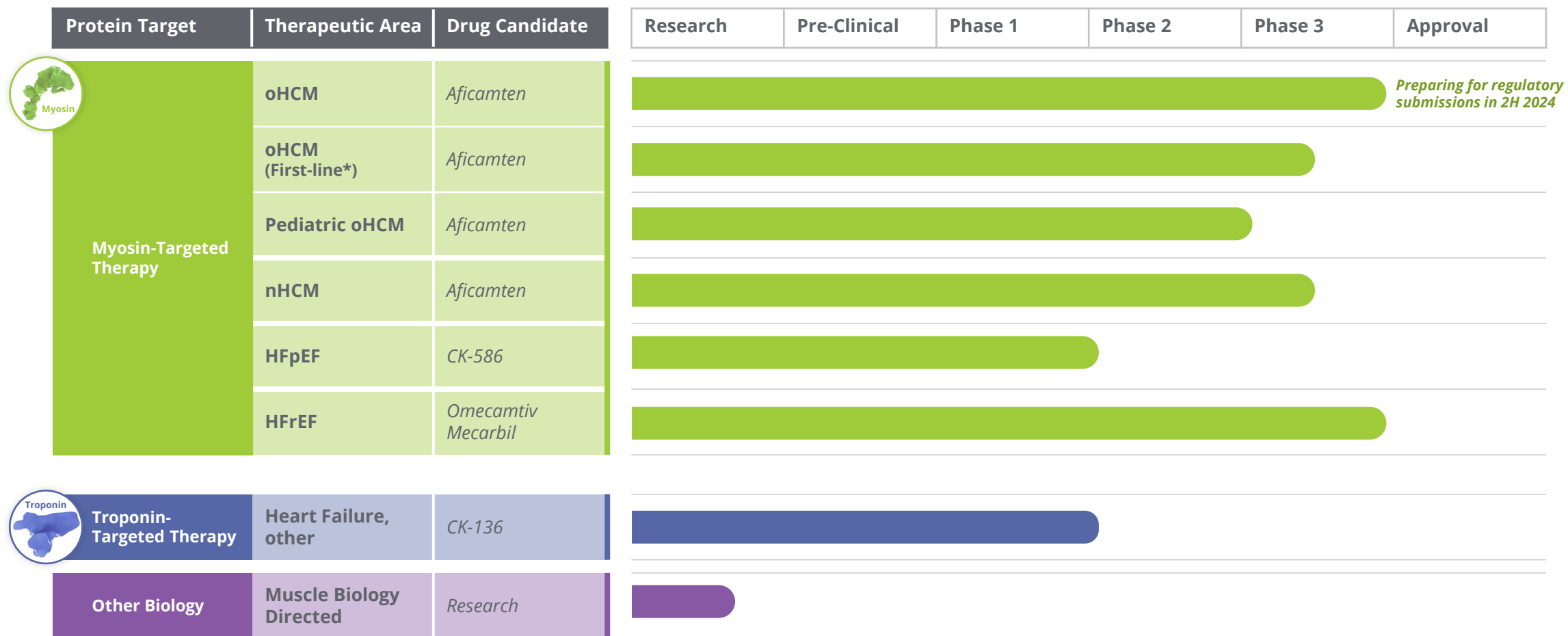
Increased / Preserved Cardiac Contractility

- Non-obstructive Hypertrophic Cardiomyopathy (nHCM)
- Obstructive Hypertrophic Cardiomyopathy (oHCM)
- Heart Failure with Preserved Ejection Fraction (certain HFpEF subsets)



A Commitment to Muscle-Directed Cardiac Medicines

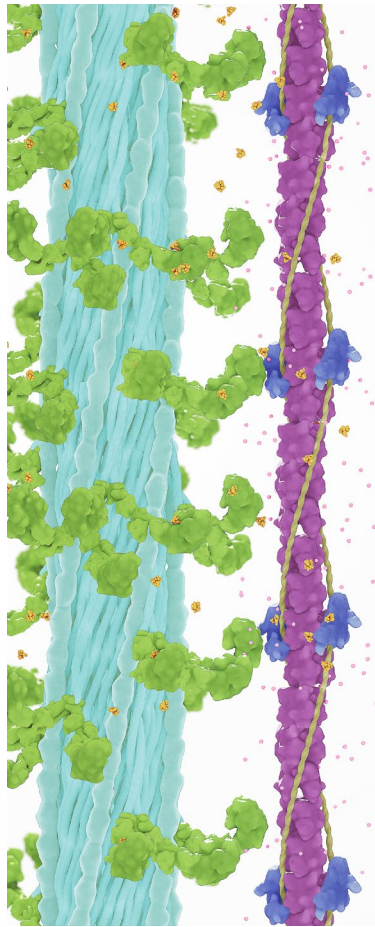
Building a specialty cardiology franchise anchored by *aficamten*



*Pending results from MAPLE-HCM, an ongoing Phase 3 clinical trial evaluating for the potential superiority of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM. All drug candidates above are investigational products and are not approved as safe or effective for any indication.

Building a Specialty Cardiology Franchise Anchored by *Aficamten*

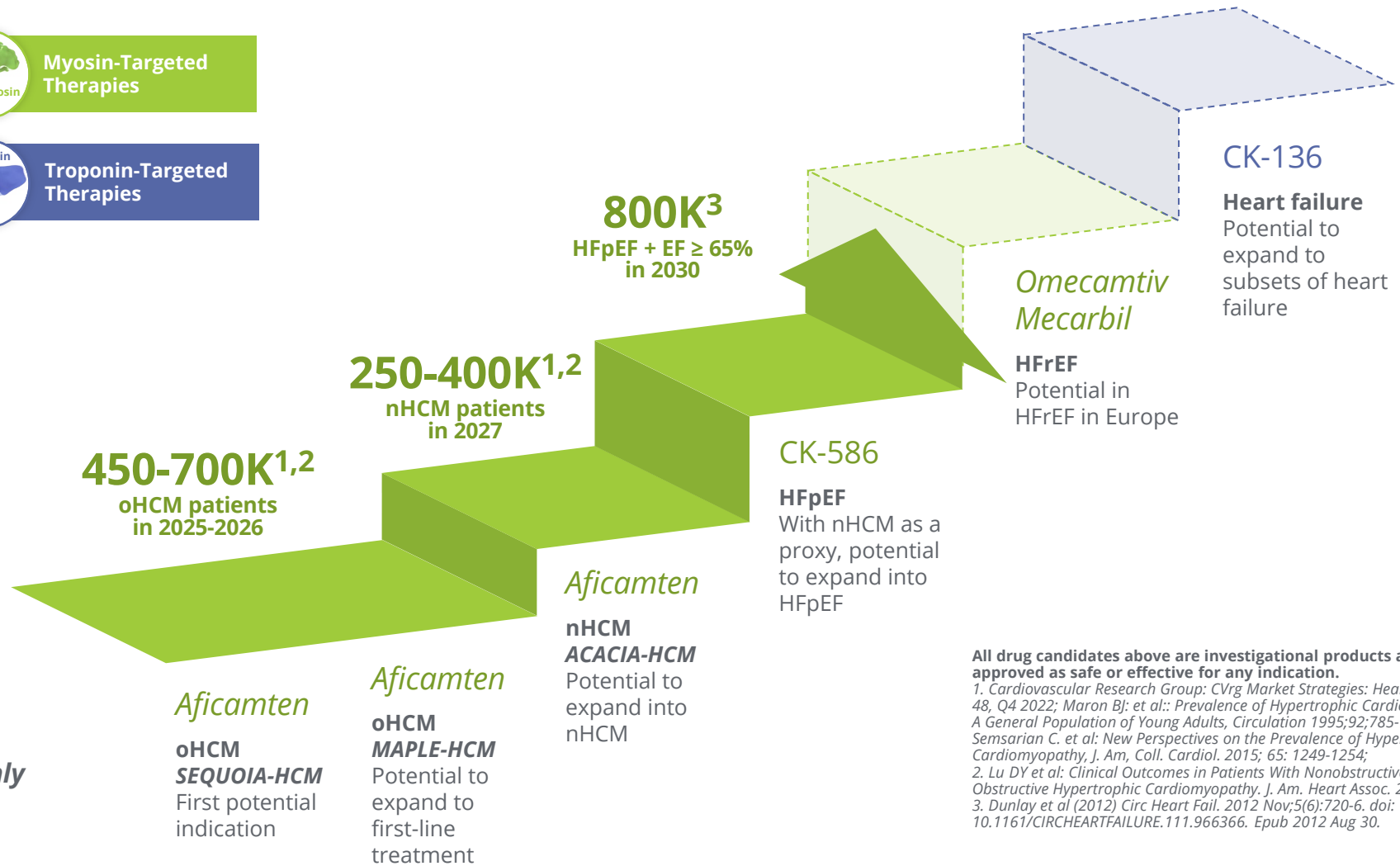
Growing addressable patient market through specialty cardiology franchise strategy



Myosin-Targeted Therapies

Troponin-Targeted Therapies

US only



All drug candidates above are investigational products and are not approved as safe or effective for any indication.

1. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ; et al.: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, *Circulation* 1995;92:785-789; Semsarian C. et al: New Perspectives on the Prevalence of Hypertrophic Cardiomyopathy, *J. Am. Coll. Cardiol.* 2015; 65: 1249-1254;

2. Lu DY et al: Clinical Outcomes in Patients With Nonobstructive, Labile, and Obstructive Hypertrophic Cardiomyopathy. *J. Am. Heart Assoc.* 2018;7:1-11

3. Dunlay et al (2012) *Circ Heart Fail.* 2012 Nov;5(6):720-6. doi: 10.1161/CIRCHEARTFAILURE.111.966366. Epub 2012 Aug 30.

Specialty Cardiovascular Portfolio

Aficamten

Omecamtiv Mecarbil

CK-586

CK-136

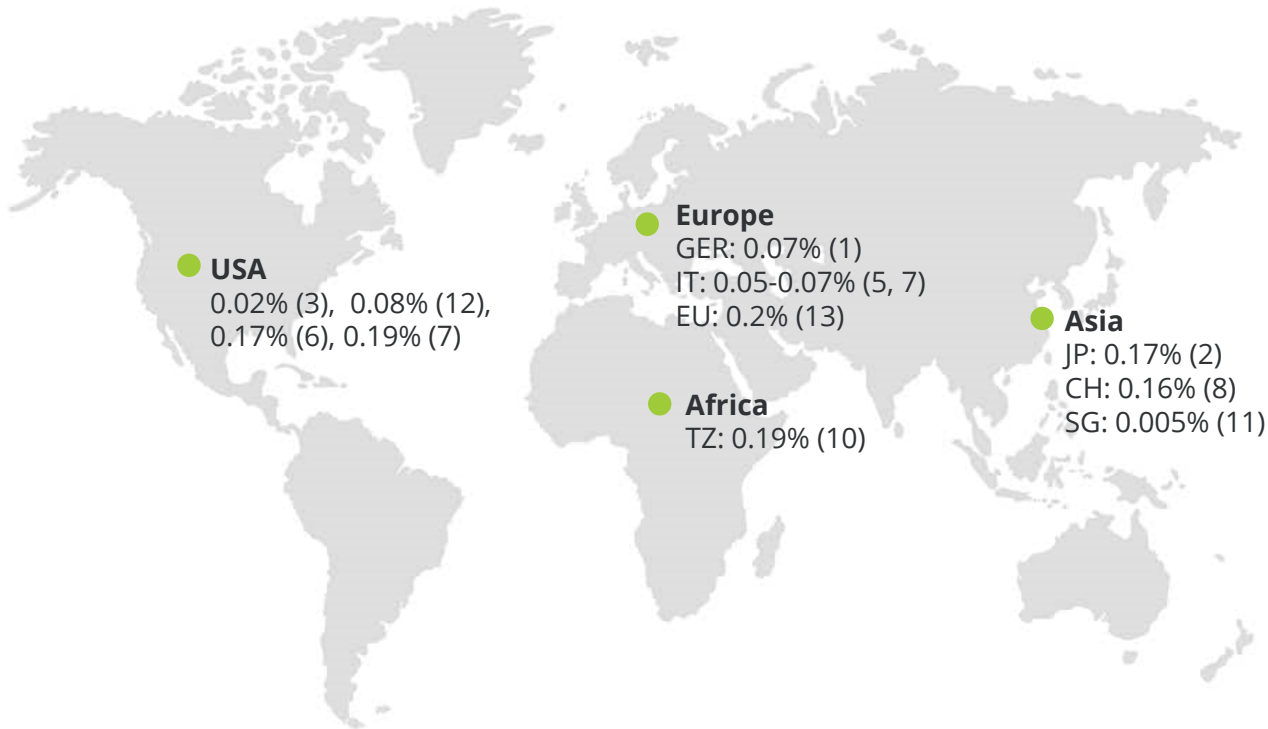
Aficamten, omecamtiv mecarbil, CK-586 and CK-136 are investigational agents and have not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of these product has not been established.

Aficamten

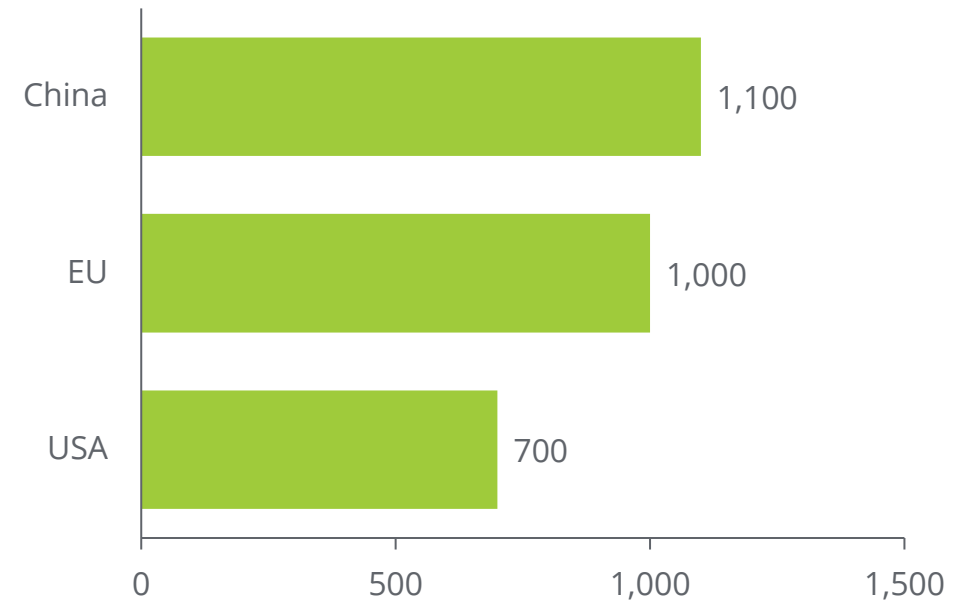
HCM Prevalence: Significant and Growing Globally

HCM prevalence estimates vary across geography and over time

Estimated HCM Prevalence Rates



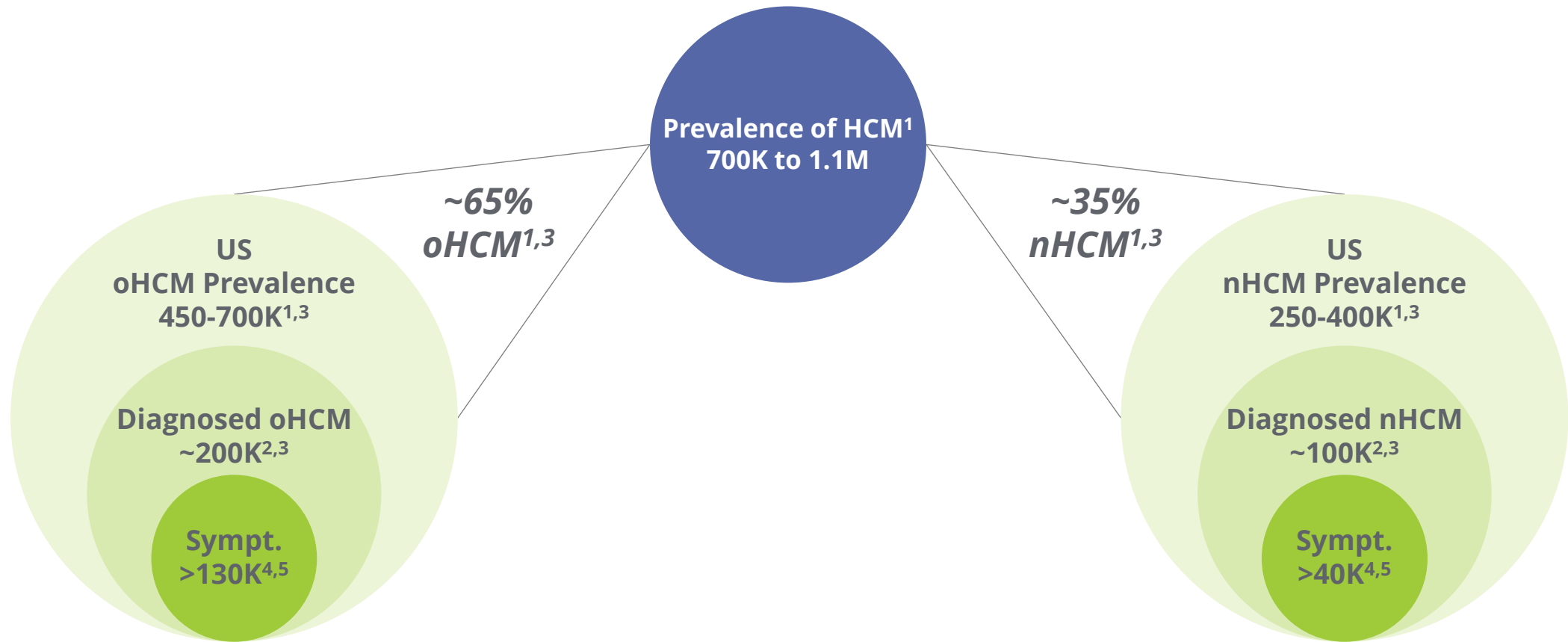
HCM True Patient Prevalence (Est. 2021)



Sources: 1. Husser et al 2018 doi.org/10.1371/journal.pone.0196612; 2. Hada et al [10.1016/s0002-9149\(87\)80107-8](https://doi.org/10.1016/s0002-9149(87)80107-8); 3. Codd 1989 [10.1161/01.cir.80.3.564](https://doi.org/10.1161/01.cir.80.3.564); 4. Maron et al 1995 [10.1161/01.cir.92.4.785](https://doi.org/10.1161/01.cir.92.4.785); 5. Corrado et al 1998 [10.1056/NEJM199808063390602](https://doi.org/10.1056/NEJM199808063390602); 6. Maron et al 1999 [10.1001/jama.281.7.650](https://doi.org/10.1001/jama.281.7.650); 7. Nistri et al 2003 [10.1016/s0002-9149\(03\)00132-2](https://doi.org/10.1016/s0002-9149(03)00132-2); 8. Zou et al 2004 [10.1093/aje/kwh090](https://doi.org/10.1093/aje/kwh090); 9. Maron 2004 <https://doi.org/10.1016/j.amjmed.2003.10.012>; 10. Maro 2006 [10.1258/004947506778604904](https://doi.org/10.1258/004947506778604904); 11. Ng et al 2011 [10.1093/europace/eur051](https://doi.org/10.1093/europace/eur051); 12. Butzner et al 2021 [10.1016/j.amjcard.2021.08.024](https://doi.org/10.1016/j.amjcard.2021.08.024); 13. Cardim et al 2011 [10.1016/j.repc.2011.09.005](https://doi.org/10.1016/j.repc.2011.09.005)

Opportunity for CMI in Diagnosed, Symptomatic HCM Patients

Potential for nearly 200K patients eligible for CMIs in 2025



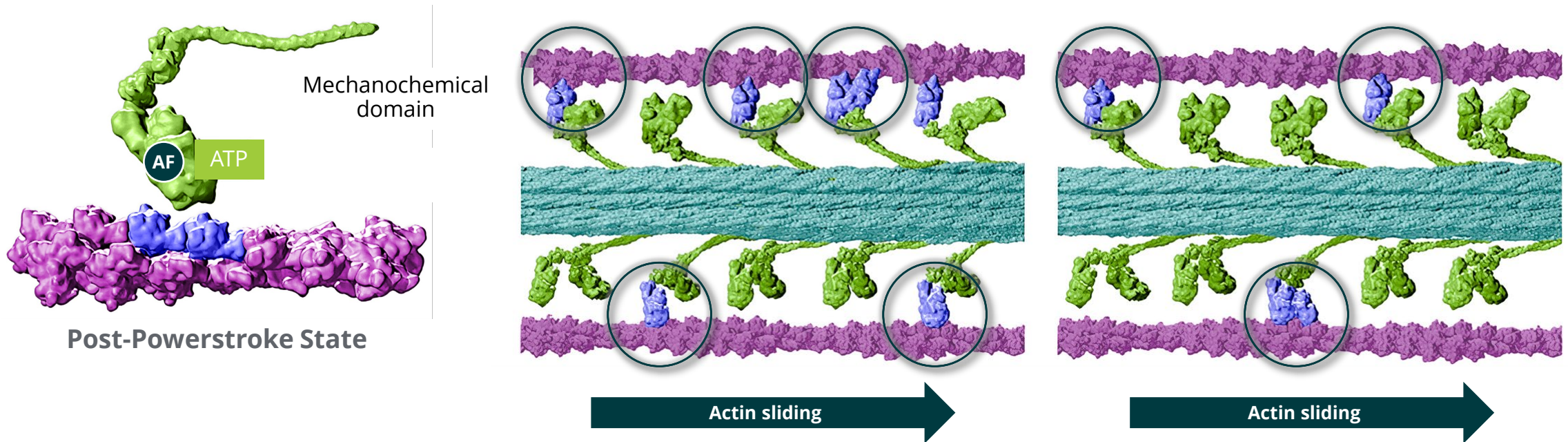
Projections and forecasts for illustration.

1. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ: et al.: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, Circulation 1995;92:785-789; Semsarian C. et al: New Perspectives on the Prevalence of Hypertrophic Cardiomyopathy, J. Am. Coll. Cardiol. 2015; 65: 1249-1254;
2. DoF: SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023);
3. Lu DY et al: Clinical Outcomes in Patients With Nonobstructive, Labile, and Obstructive Hypertrophic Cardiomyopathy. J. Am. Heart Assoc.2018;7:1-11
4. DoF: SHA Symphony PTD (Patient Transaction Data) includes any patients with symptoms in the last 2 years: angina, dyspnea, fatigue, palpitations, syncope, tachycardia; and/or treatments in the past 2 years: bb, ccb, dyso, ralo, Camzyos;
5. DoF Primary market research: 443 HCPs treating HCM - % of nHCM patients not considered under control with current SOC.

Aficamten: Proposed Mechanism of Action

Aficamten stabilizes myosin in the released post-powerstroke state unable to hydrolyze ATP

“Fewer hands pulling on the rope”



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Aficamten: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor



Rapid onset



Rapid reversibility



Speed to optimal dose



Predictable dose response



No teratogenicity



No clinically meaningful P450 liabilities

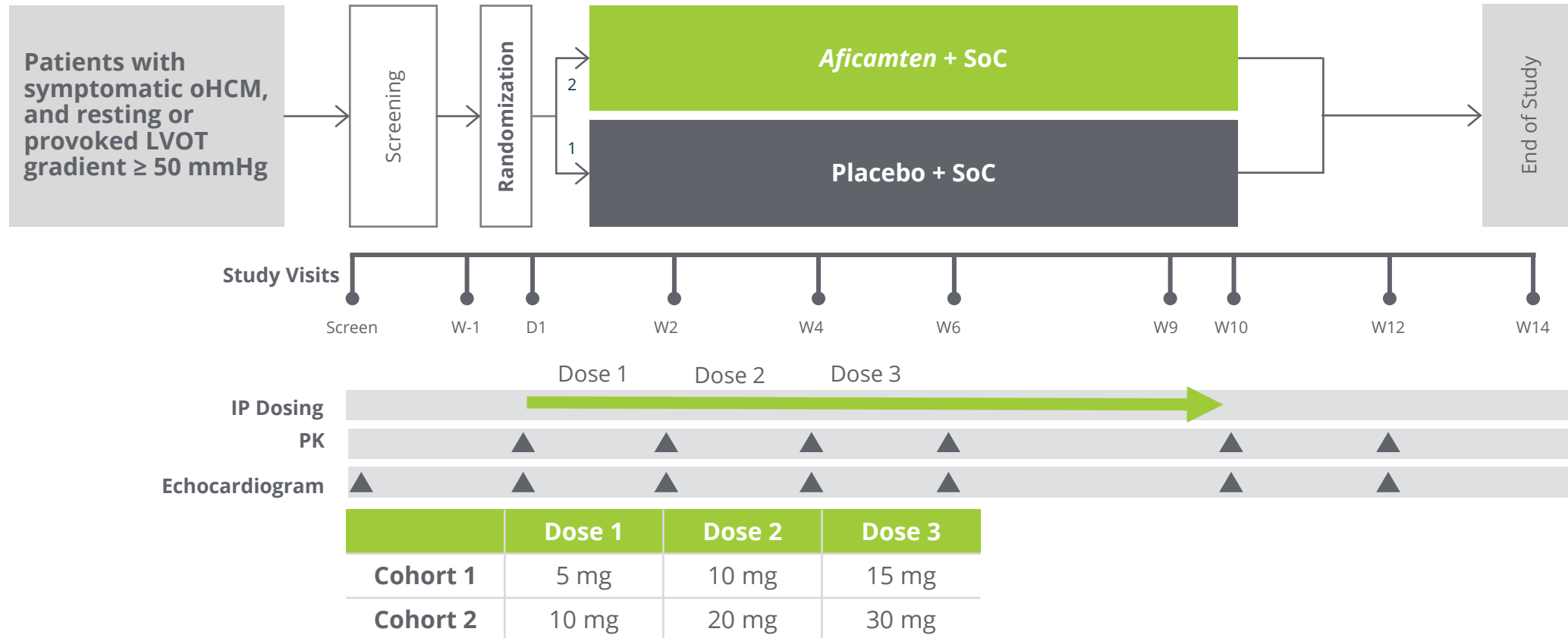
Aspirational information. Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

REDWOOD-HCM: Cohorts 1 & 2

Patients with symptomatic oHCM on background therapy excluding *disopyramide*



Two sequential dose-finding cohorts



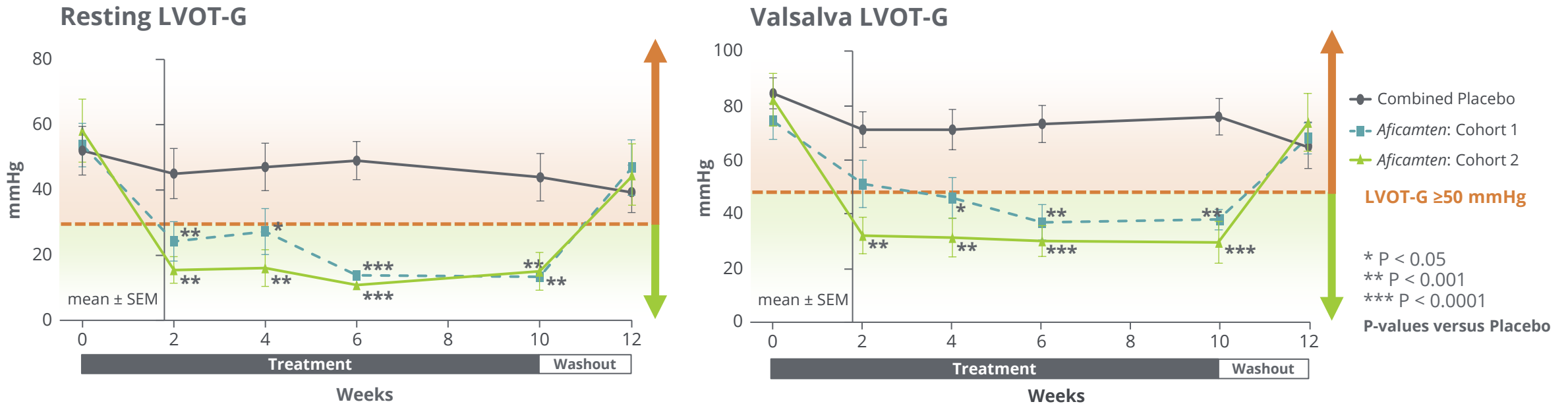
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

REDWOOD-HCM: Robust Reduction of LVOT Gradients

Cohorts 1 & 2



Consistent, **clinically meaningful reductions in LVOT gradients** within two weeks
No treatment interruptions or discontinuations
Reversibility of drug effect demonstrated



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

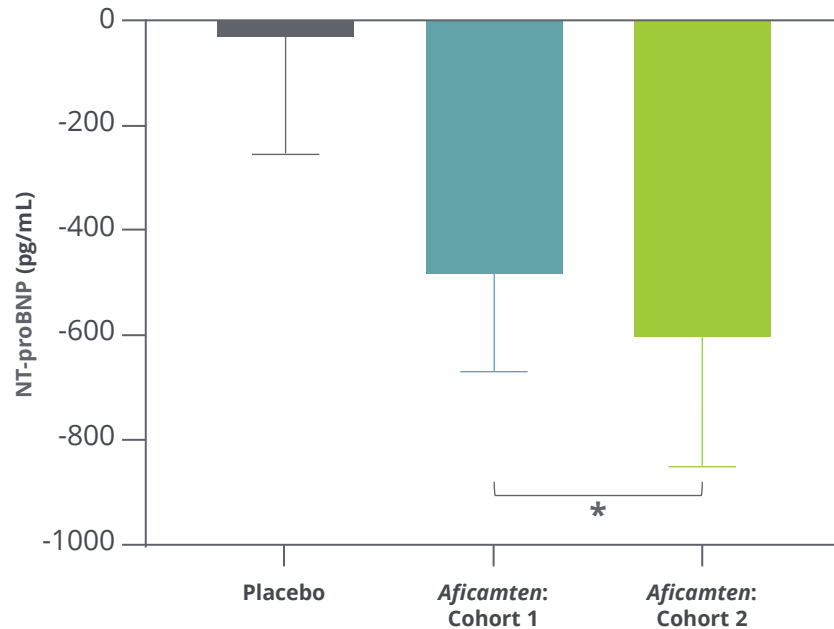
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
 Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, Aficamten, In Obstructive Hypertrophic Cardiomyopathy". HFSA 2021.

Change from Baseline in NT-proBNP & NYHA Class

Cohorts 1 & 2



Change from Baseline NT-proBNP to Week 10

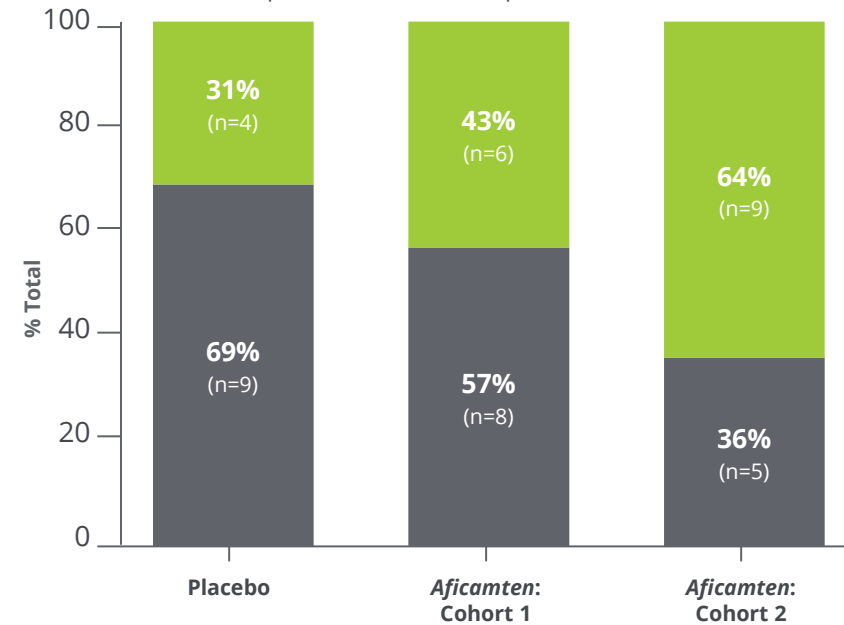


*p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo

- 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

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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". HFSA 2021.

Improved Cardiac Structure and Diastolic Function

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

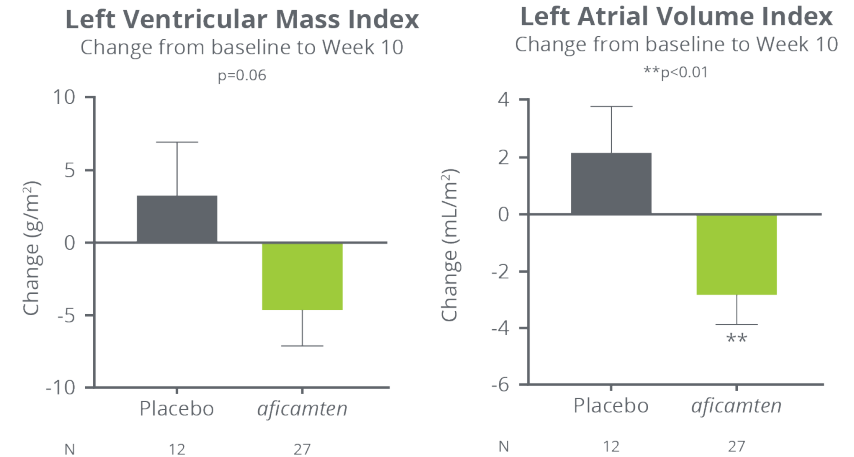


Treatment with *aficamten* for 10 weeks resulted in:

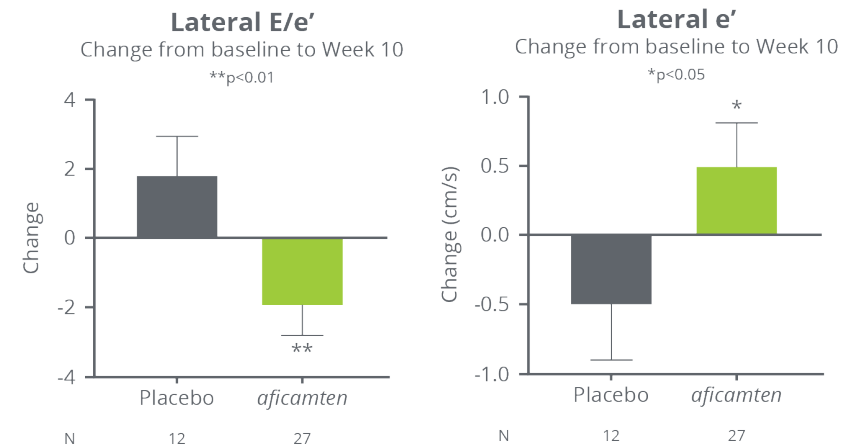
- **Significant reduction in left atrial volume index**
- Trend towards a **reduction in LV mass index**
- **Improved diastolic function**
 - reduction in lateral E/e' (p<0.01)
 - increase in lateral e' (p<0.05)

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
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". ASE 2022.

Cardiac Structure

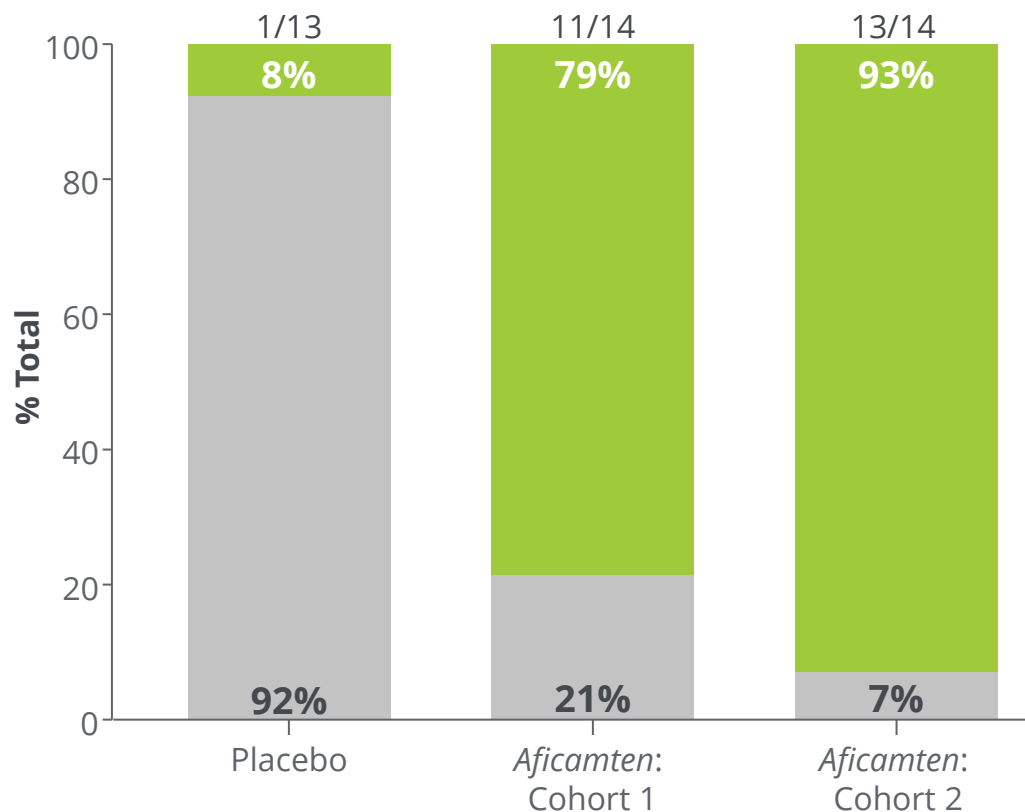


Diastolic Function



Response Rates on Treatment with *Aficamten*

Cohorts 1 & 2



Responder # / Total #

■ Incomplete LVOT-G response

■ Complete LVOT-G response

Responder Definition:

Resting LVOT-G <30 mmHg and post-Valsalva LVOT-G <50 mmHg at Week 10

- 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

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

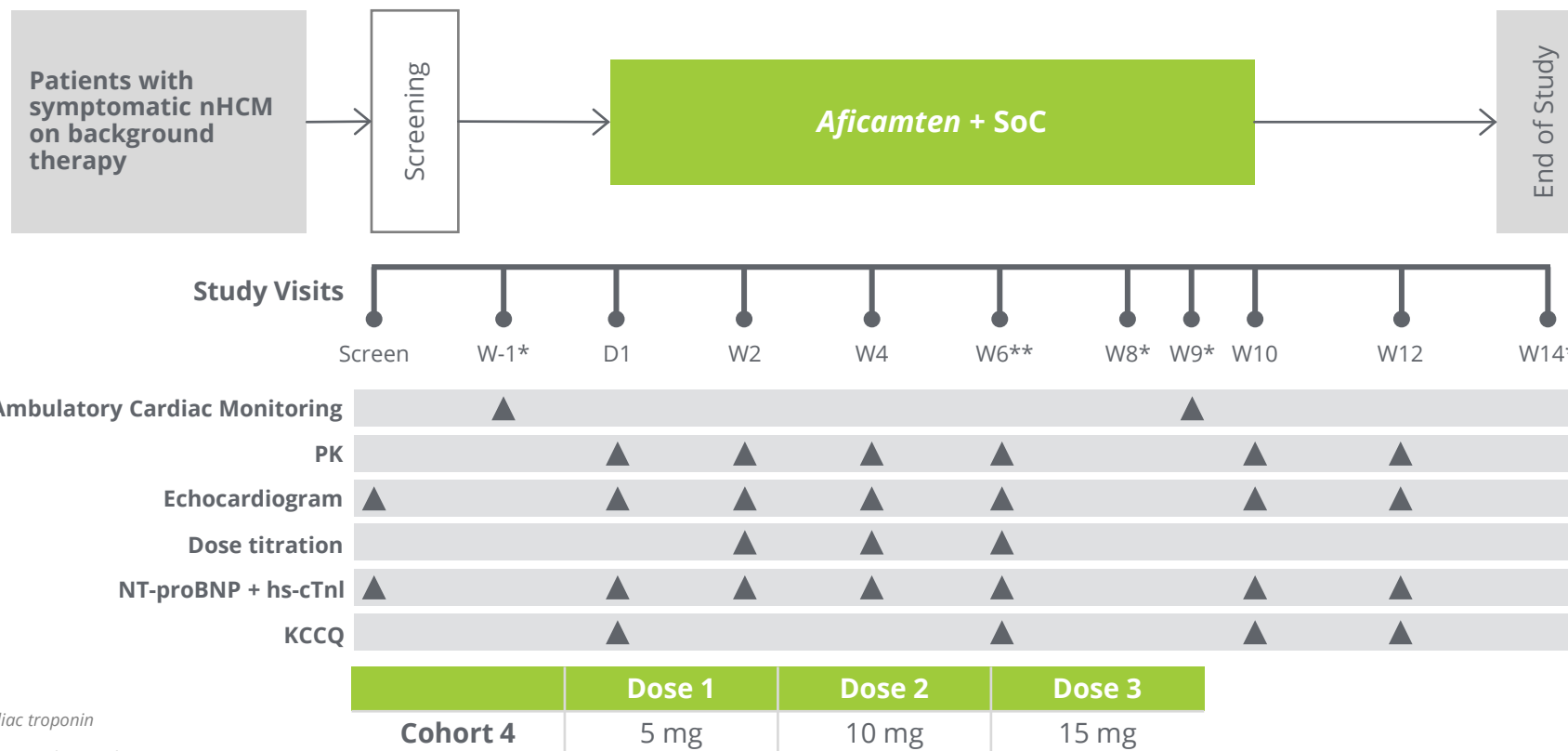
Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, Aficamten, In Obstructive Hypertrophic Cardiomyopathy". HFSA 2021.

REDWOOD-HCM: Cohort 4

Patients with symptomatic nHCM on background therapy



Results presented at Heart Failure 2023



hs-cTnI: high-sensitivity cardiac troponin

*Telephone visits

**Patient can only be down-titrated at Week 6

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Significant Improvements in KCCQ & NYHA Class

Cohort 4



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

Kansas City Cardiomyopathy Questionnaire

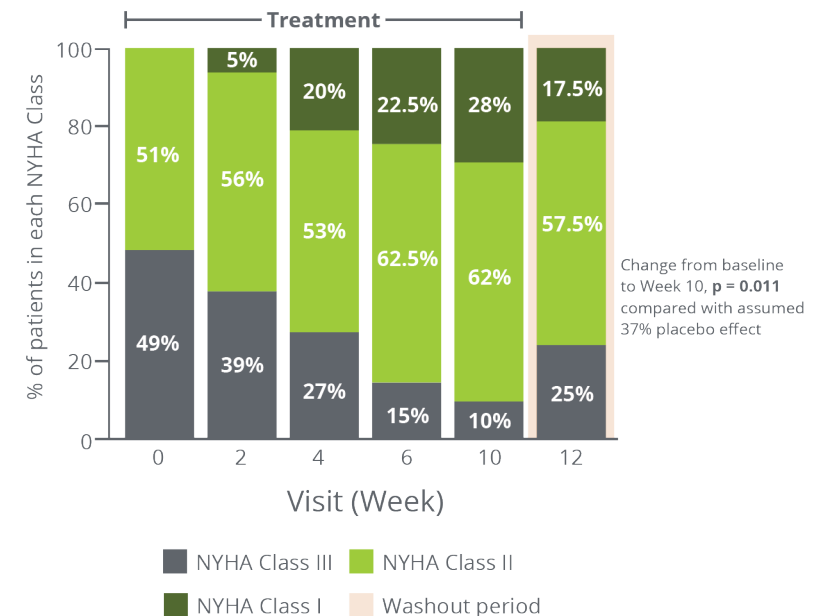
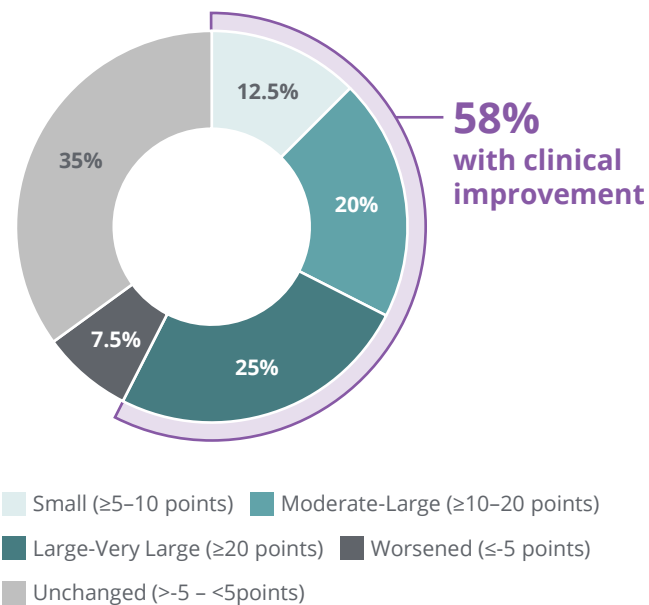
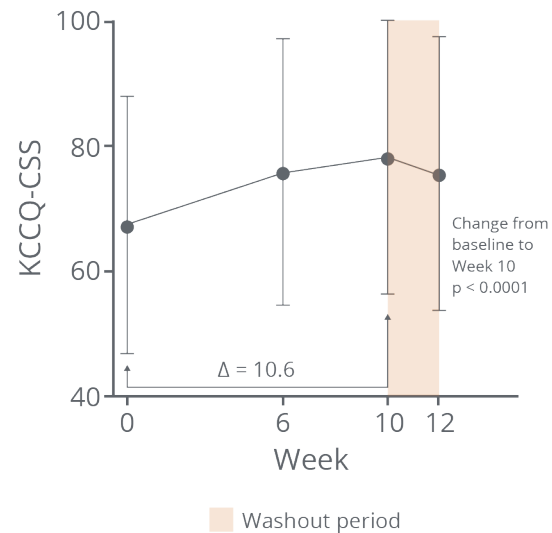
Mean improvement in KCCQ of 10.6 points

Categorical Changes at Week 10 in KCCQ-CSS

NYHA Functional Class

56% of patients improved by ≥1 NYHA class

All nHCM Patients (N = 41)



Data presented as mean and standard deviation

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
 Masri A. et al. "Aficamten in Patients with Symptomatic Non-Obstructive Hypertrophic Cardiomyopathy (REDWOOD-HCM Cohort 4)". ESC HF 2023.

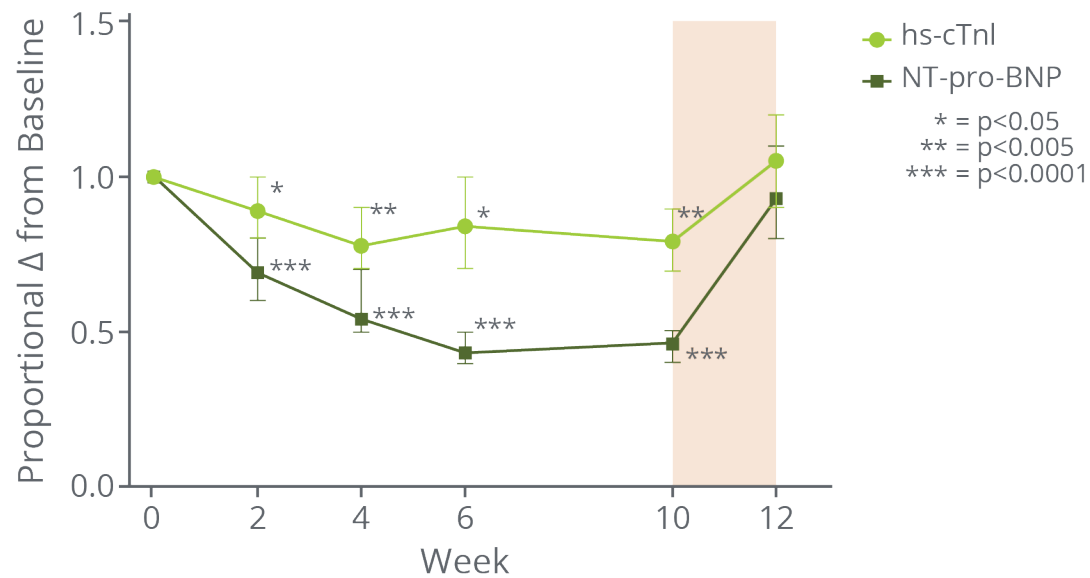
Change in Baseline in Biomarkers & Angina Frequency

Cohort 4



Proportional Change from Baseline in Cardiac Biomarkers

Mean reduction in high-sensitivity cardiac troponin of 21%
 Mean reduction in NT-proBNP of 55%



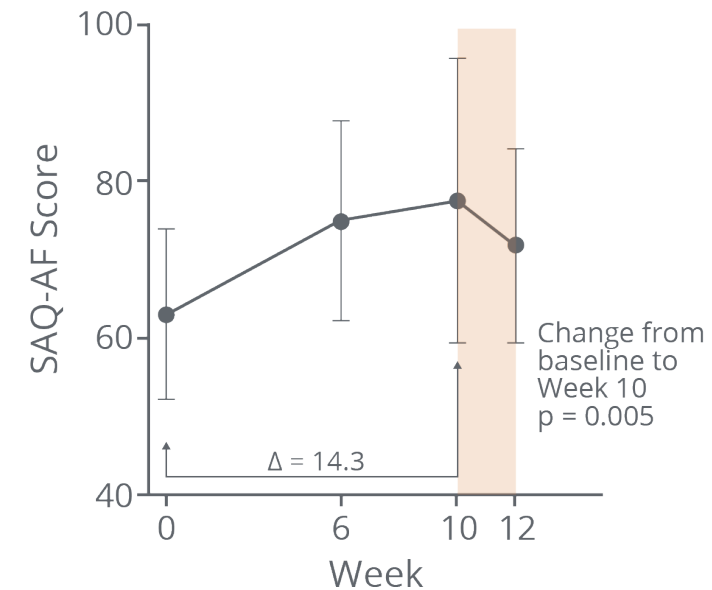
Washout period

Data presented as the mean proportional change and 95% CI

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
 Masri A. et al. "Aficamten in Patients with Symptomatic Non-Obstructive Hypertrophic Cardiomyopathy (REDWOOD-HCM Cohort 4)". ESC HF 2023.

Seattle Angina Questionnaire Angina Frequency (SAQ-AF)

Reduction in frequency of angina from daily or weekly, to weekly or monthly



Washout period

Data presented as mean and standard deviation

FOREST-HCM: Baseline Characteristics

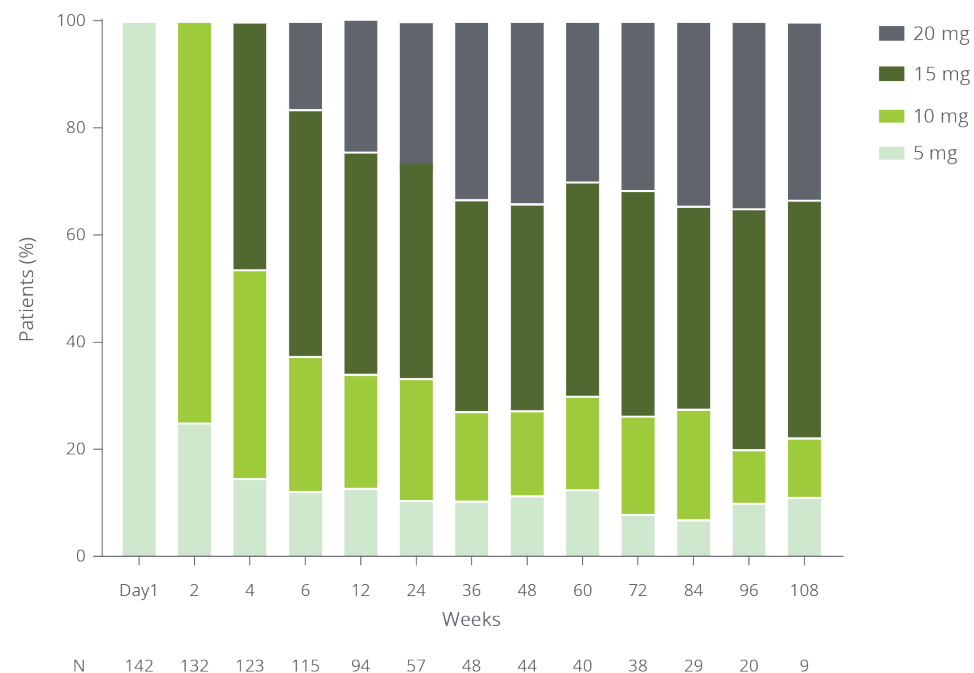
FOREST-HCM data cut as of September 15, 2023



Baseline characteristics indicate substantial disease burden; ~2/3 patients achieving 15 or 20 mg

	FOREST-HCM oHCM N=143
Age (Years), Mean (SD)	60.4 (13.2)
Female, n (%)	65 (45.5)
BMI (kg/m ²), Mean (SD) [Range]	29.2 (4.5)
NYHA Class, n (%)	
Class II	82 (58)
Class III	60 (42)
Familial HCM, n (%)	40 (28.0)
Beta Blocker Use, n (%)	90 (62.9)
Calcium Channel Blocker Use, n (%)	14 (9.8)
Disopyramide Use, n (%)	27 (18.9)
LVEF* at Screening (%), Mean (SD)	69 (5)
LVOT-G*, Rest at Screening (mmHg), Mean (SD)	56.8 (33.2)
LVOT-G*, Valsalva at Screening (mmHg), Mean (SD)	93.1 (37.9)

Dose of Aficamten



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Few Dose Reductions During Maintenance

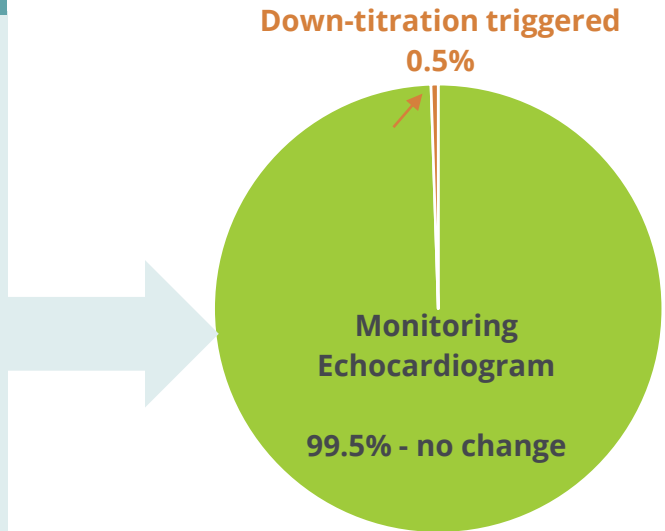


Dose Titration Phase

- No treatment-related LVEF <50% during the titration period
- Of the 94 patients having completed the titration period, ~2/3 are receiving 15 and 20 mg qd
- Approximately 30% of patients have reduced doses or discontinued background therapy at the discretion of the treating physician and/or request from the patient

Maintenance Phase

- 579 monitoring echocardiograms completed* in oHCM patients
- None with LVEF <40% requiring treatment interruption
- 3 patients (0.5%) with LVEF <50%
 - Two asymptomatic patients (LVEF of 47% and 49%) resulting in per-protocol dose reduction
 - One patient with atrial fibrillation (unrelated) and LVEF of 47%
- All 3 patients are currently receiving *aficamten* with apparent relief from obstruction, symptoms & improved biomarkers



Target dose defined as achieved if Valsalva LVOT-G ≤ 30 mmHg or no dose change for 2 consecutive visits

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
* As of Sept 15, 2023.

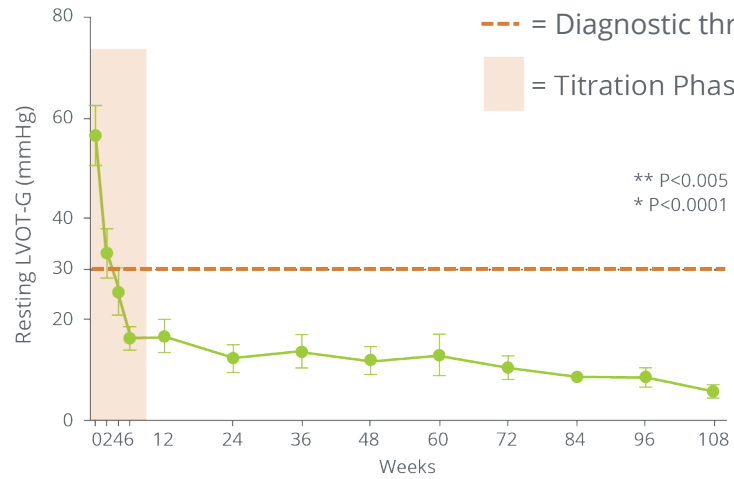
Observed Durable Effects of *Aficamten* on LVOT-G & LVEF

FOREST-HCM data cut as of September 15, 2023



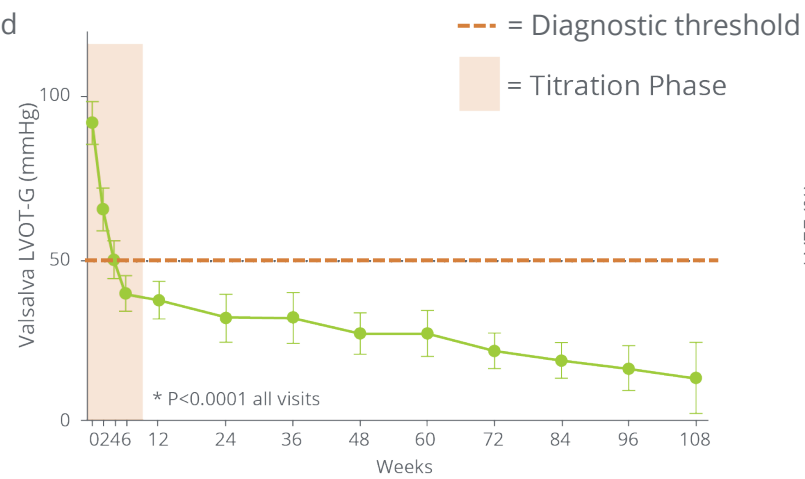
Resting & provoked gradients remain below diagnostic threshold for >2 years, LVEF remains flat after titration

Resting LVOT Gradient



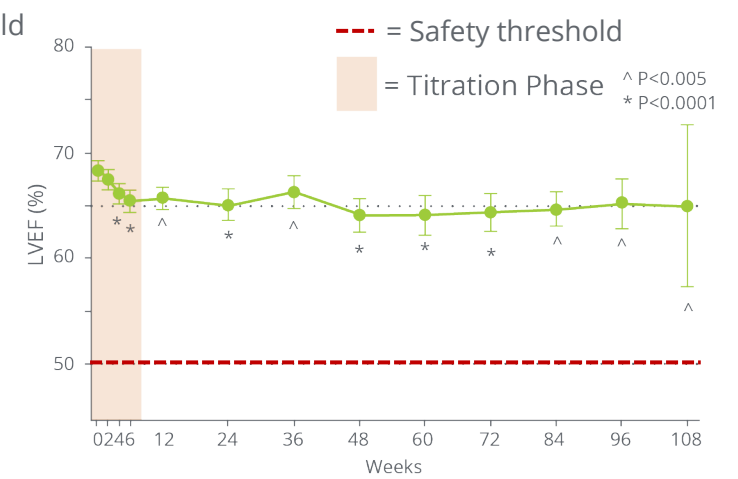
N 134 94 55 44 44 41 39 30 20 8

Valsalva LVOT Gradient



N 134 95 55 45 44 41 39 30 20 8

LVEF



N 134 95 55 46 44 40 39 30 20 8

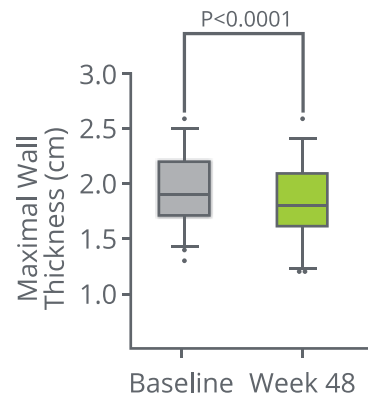
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Observed Durable Effects of *Aficamten* on Cardiac Structure, Function & NT-proBNP



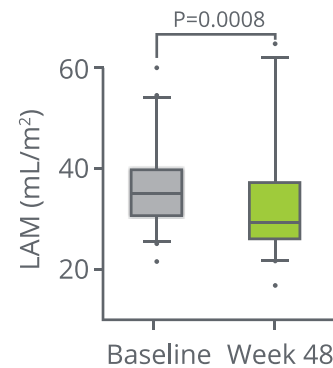
Maximal Wall Thickness

Data cut as of October 31, 2023



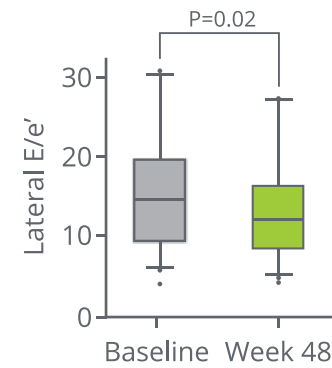
LA Volume Index

Data cut as of October 31, 2023



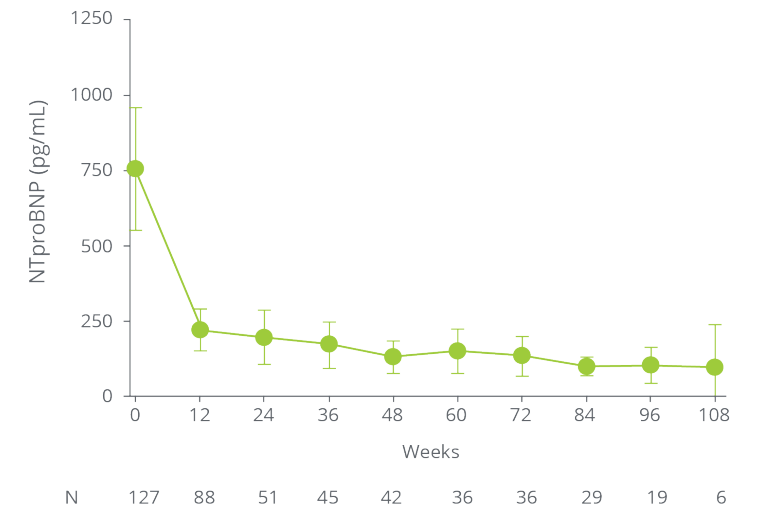
Lateral E/e'

Data cut as of October 31, 2023



NT-proBNP

Data cut as of September 15, 2023



Mean and 95% CI in all figures

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

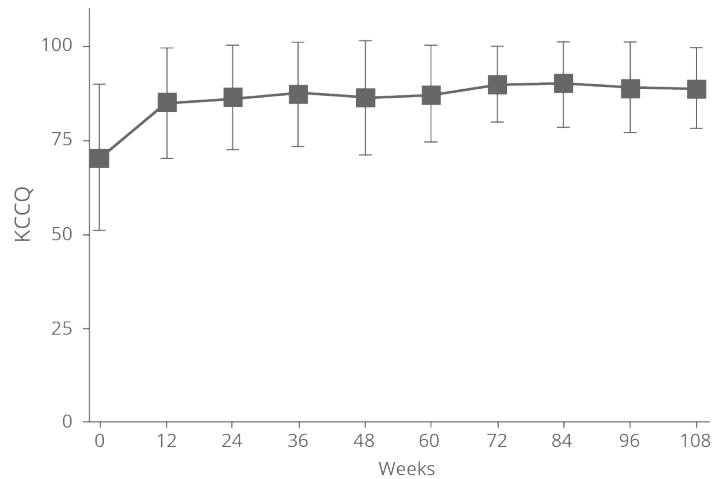
Observed Durable Effects of *Aficamten* on Clinical Endpoints



KCCQ-CSS

Data cut as of September 15, 2023

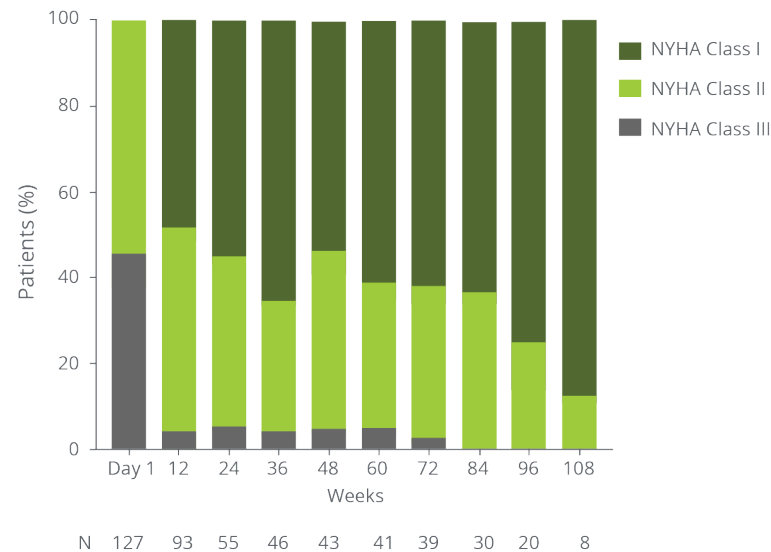
71% of patients had ≥ 5 -point KCCQ-CSS increase
 30% of patients had ≥ 10 -point KCCQ-CSS increase



NYHA Class

Data cut as of September 15, 2023

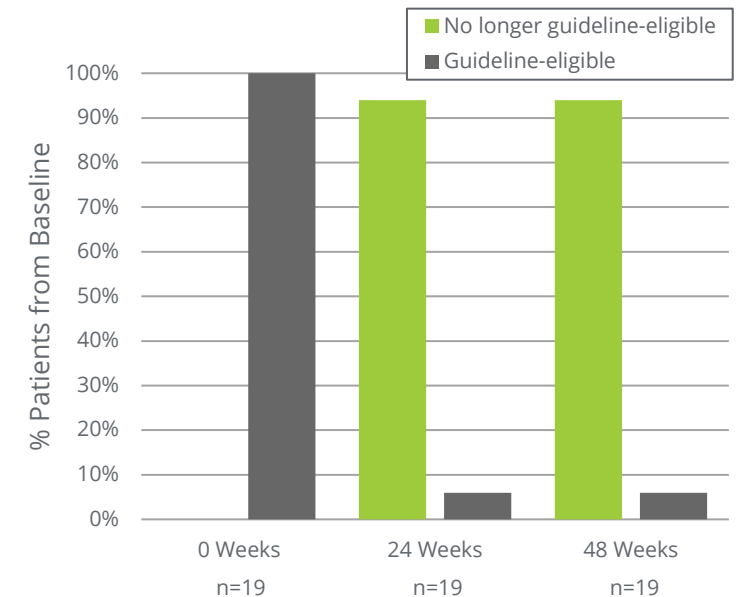
\sim 50% of patients were asymptomatic at 1 year
 $>$ 80% of patients improved ≥ 1 NYHA Class at every visit after initiation of *aficamten*



Guideline-Eligible for SRT

Data cut as of October 31, 2023

94% of SRT-eligible patients at baseline are no longer SRT-eligible



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Safety Data: Phase 2 & OLE



oHCM → **Cohorts 1, 2, & 3: After 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: After 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

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.



- **Almost all eligible patients choose to participate** in the OLE
- Echocardiography-guided dose titration of *aficamten* is **managed entirely by the treating physicians**
- 2/3 of patients achieve **higher doses**; no low LVEF events requiring treatment interruption
- 94 patients have **completed the titration period** - none have experienced LVEF <50%
- **99.5% of monitoring echocardiograms have not led to a dose reduction**
- Clinical, hemodynamic & biochemical markers of efficacy continue to indicate **sustained efficacy** following exposures for > 2-years
- Of the patients that are guideline-eligible for septal reduction therapies at baseline, **~90% are no longer eligible** after dose titration
- *Aficamten* has been **generally well-tolerated**, with 60% of patients experiencing at least one treatment emergent adverse event (TEAE) but there were no treatment-related serious adverse events (SAEs) as assessed by investigators, and no patient deaths

SEQUOIA-HCM: Phase 3 Trial



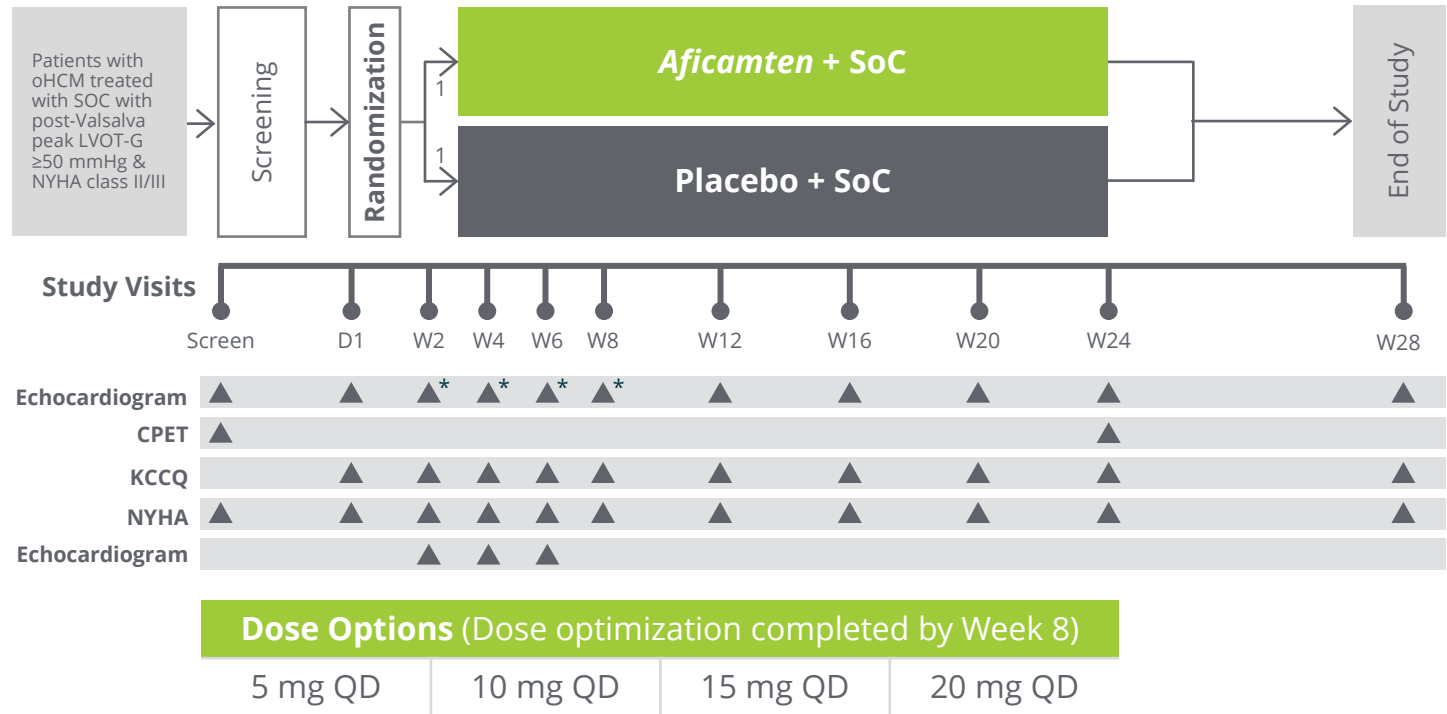
Announced positive topline results in December 2023; presented primary results at Heart Failure 2024

Primary endpoint: **Change in pVO₂ by CPET from baseline to Week 24**

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

- Enrolled 282 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



SOC: standard of care
 *Focused echocardiogram
 Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: Efficacy & Safety Summary



Efficacy

- **Primary endpoint and all 10 pre-specified secondary endpoints** were clinically meaningful and statistically significant (all p-values < 0.0001)
- Treatment with *aficamten* **increased pVO₂ by a least square mean difference of 1.74 mL/kg/min (p=0.000002)**
 - No evidence of subgroup heterogeneity
 - No attenuation of effect in patients treated with beta-blockers
- *Aficamten* **improved heart failure symptoms** based on improvement in both KCCQ-CSS and NYHA functional class

Safety

- *Aficamten* was **safe and well-tolerated** with an overall incidence of adverse events similar to that of placebo
 - Serious AEs were more frequent with placebo
- There was a **low incidence** of core laboratory reported LVEF <50% with *aficamten* (n=5); **none of these patients experienced coincident heart failure AEs**
- There were **no treatment interruptions for low LVEF**

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: Probability Values (p-value)



Endpoints	p-value
<i>Primary Endpoint</i>	
pVO₂ change from baseline to Week 24	<0.0001
<i>Secondary Endpoints</i>	
KCCQ-CSS change from baseline to Week 24	<0.0001
NYHA Class Improvement by at least 1 class at Week 24	<0.0001
Valsalva LVOT-G change from baseline to Week 24	<0.0001
% Valsalva LVOT-G < 30 mmHg at Week 24	<0.0001
Duration of SRT Eligible during 24 Weeks of Treatment	<0.0001
KCCQ-CSS change from baseline to Week 12	<0.0001
NYHA Class Improvement by at least 1 class at Week 12	<0.0001
Valsalva LVOT-G change from baseline to Week 12	<0.0001
% Valsalva LVOT-G < 30 mmHg at Week 12	<0.0001
Total workload change from baseline to Week 24	<0.0001

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: Baseline Characteristics



Baseline characteristics reflect highly symptomatic patient population with reduced exercise capacity

- Significant **symptom burden** despite background therapy
- 61% of patients on **beta-blockers**
- Baseline pVO₂ reflects patient population with **reduced exercise capacity**

Baseline Characteristics (N=282)	n (%) or Mean (SD) ^a
<i>Demographics</i>	
Age, years	59.1 (12.9)
Female	114 (40.4)
<i>Race/ethnicity^b</i>	
White	222 (78.7)
Black	3 (1.1)
Asian	53 (18.8)
Hispanic	9 (3.2)
Other	4 (1.4)
<i>Region</i>	
United States	94 (33.3)
China	46 (16.3)
Europe and Israel	142 (50.4)
<i>Vital Signs</i>	
Weight, kg	81.6 (15.7)
Body mass index, kg/m ²	28.1 (3.7)
Systolic blood pressure, mmHg	125.3 (16.1)
Diastolic blood pressure, mmHg	74.4 (10.6)
Heart rate, bpm	65.6 (11.2)
<i>HCM History</i>	
History of known HCM-causing gene mutation	48 (17.0)
Positive family history of HCM	71 (25.2)
Time since initial HCM diagnosis, median (IQR), years	4.3 (1.7 – 8.5)

Baseline Characteristics (N=282)	n (%) or Mean (SD) ^a
<i>HCM Medical Therapies</i>	
Beta-blocker	172 (61.0)
Non-dihydropyridine calcium channel blocker	75 (26.6)
Disopyramide	36 (12.8)
<i>HCM Symptoms</i>	
KCCQ-CSS	74.7 (18.0)
NYHA class II/III/IV	214 (75.9)
	67 (23.8)
	1 (0.4)
SRT guideline eligible	68 (24.1)
<i>Comorbidities</i>	
Hypertension ^d	136 (48.2)
Diabetes ^e	24 (8.5)
Permanent atrial fibrillation	1 (0.4)
Paroxysmal atrial fibrillation	40 (14.2)
<i>CPET Metrics</i>	
Treadmill	155 (55.0)
Peak VO ₂ , mL/kg/min	18.5 (4.5)
Peak VO ₂ , % of predicted maximum ^f	56.9 (11.8)
Total workload, watts	122.4 (41.2)
<i>Biomarker</i>	
hs-cTnI median (IQR), ng/L	12.1 (7.7 – 27.3)

^a Unless otherwise indicated.

^b >100% total due to overlap in ethnicity and race.

^c NYHA FC III and any LVOTO ≥50 mmHg

^d Combines hypertension and essential hypertension.

^e Combines T2DM, T1DM, and DM

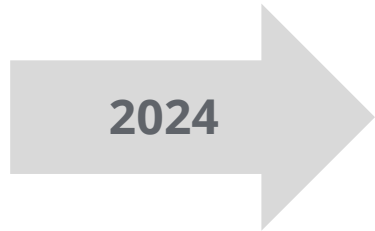
^f CCB, calcium channel blocker; DM, diabetes mellitus, including types 1 and 2; IQR, interquartile range

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Preparing for Regulatory Submissions to FDA, EMA



Positive Results from
SEQUOIA-HCM



- Participated in **two meetings with FDA** in Q1 2024
- **Type B meeting with FDA** to occur in Q2 2024
- **Meetings with EMA** in Q2 2024
- **Expect to submit NDA to FDA** in Q3 2024 and **MAA to EMA** in Q4 2024: development of all modules underway and manufacturing activities on track

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

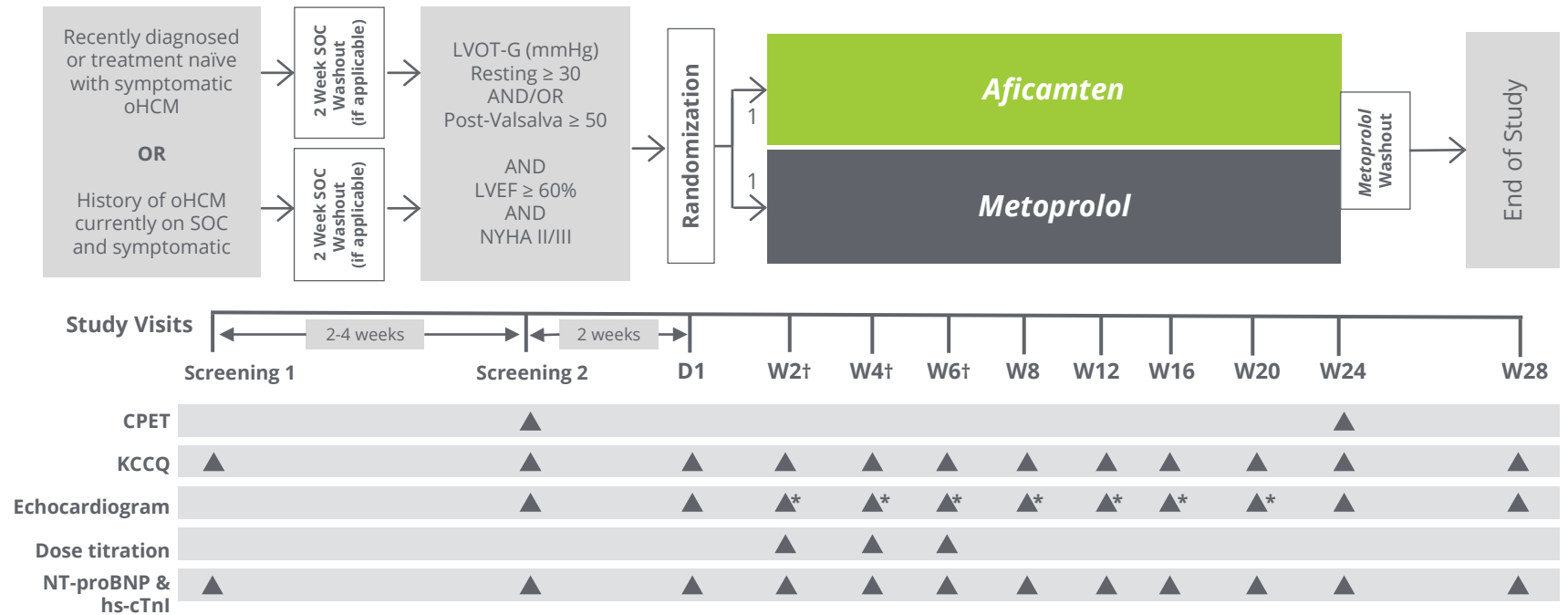
MAPLE-HCM: Phase 3 Monotherapy Trial

Currently enrolling



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**



SOC: standard of care
*Focused echocardiogram

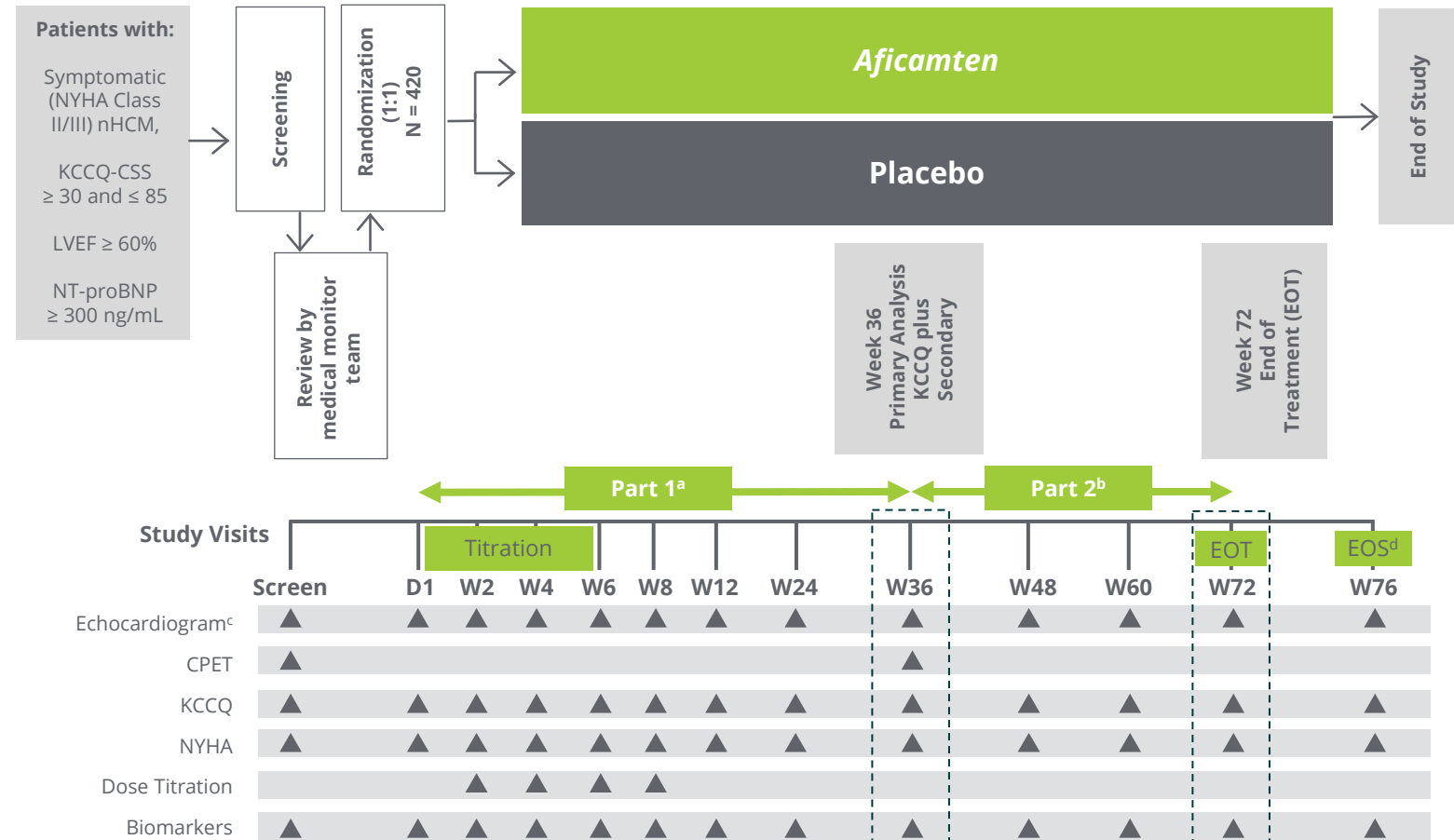
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

ACACIA-HCM: Pivotal Phase 3 Trial in nHCM

Currently enrolling



- Trial to enroll approximately **420 symptomatic nHCM patients**
- Primary endpoint: **change in KCCQ Clinical Summary Score** from baseline to Week 36
- **5-20 mg doses**; 6-week titration period
- Secondary endpoints:
 - Change in pVO₂, Ve/VCO₂,
 - Left atrial volume index (LAVI)
 - NT-proBNP
 - Proportion of patients with ≥1 class improvement in NYHA from baseline to Week 36
 - Time to first cardiovascular event



^aPart 1: All participants followed until week 36

^bPart 2: Participants completing Week 36 continue until either Week 72 (followed by EOS at Week 76) OR the last randomized participant in Part 1 completes Week 36.

^cSite-read focused echocardiogram for titration visit (sole criterion). *Aficamten* dose range 5-20 mg.

^d4-week follow up after last dose

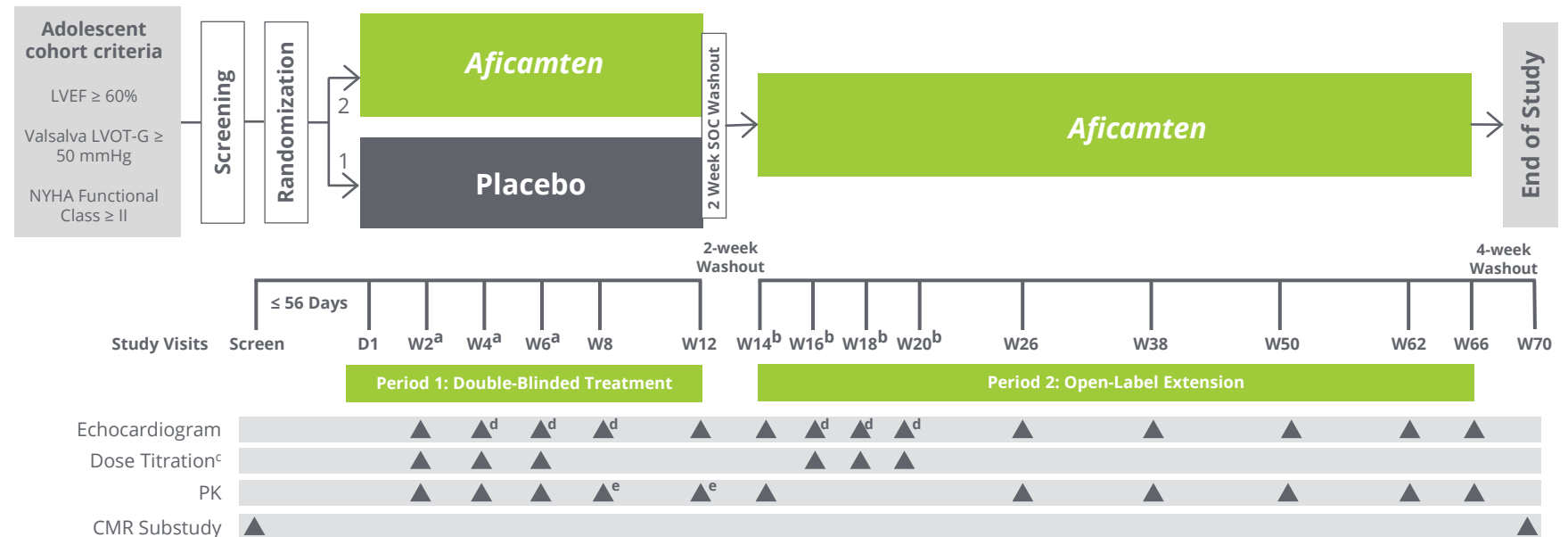
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

CEDAR-HCM: Clinical Trial in Pediatric Population

Currently enrolling



- Expected to enroll initial cohort of **~40 adolescent patients aged 12 to 17**
- Data from adolescent patients will support decision to enroll **cohort of ~8 to 10 patients aged 6 to 11**
- **5-20 mg doses; 6-week titration period**
- Primary endpoint: **change in LVOT-G** from baseline to Week 12
- Secondary endpoints: **change in resting LVOT-G, NYHA Functional Class, pharmacokinetics & cardiac biomarkers**



^a Up-titration to the next dose in Period 1 will be managed by the IRT system and will only occur if Valsalva LVOT-G is ≥ 30 mmHg and biplane LVEF is $\geq 55\%$

^b In Period 2, participants will start dosing with aficamten at the lowest dose (5 mg) and up-titration to the next dose (10, 15, or 20 mg) will be managed by the Principal Investigator or designee if Valsalva LVOT-G is ≥ 30 mmHg and biplane LVEF is $\geq 55\%$. Up-titrations may occur no more frequently than every 2 weeks

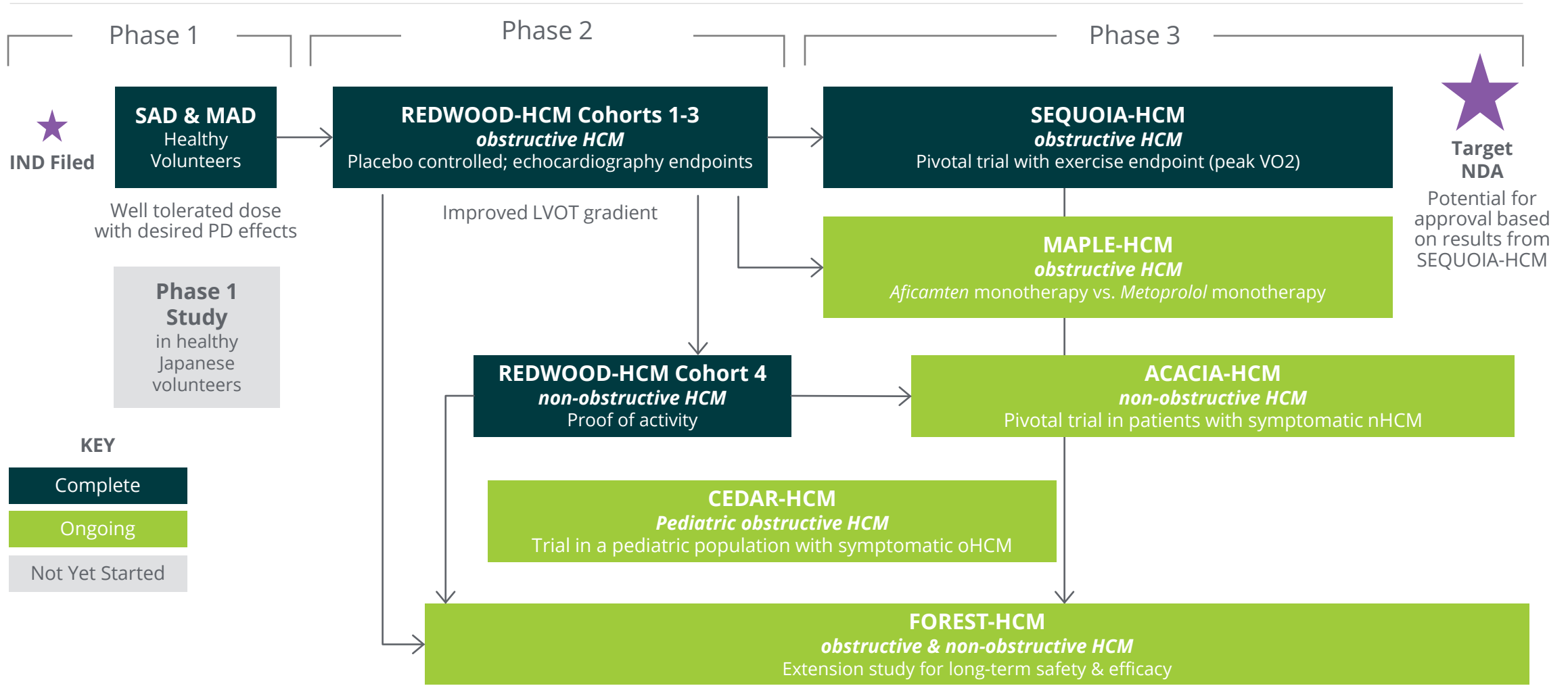
^c Additional ad hoc titrations after Week 20 may occur at ad hoc titration visits (at least 2 weeks apart) or during a planned visit (ie, Weeks 26, 38, 50, or 62). A titration follow-up visit is required 2 weeks after any titration occurring after Week 20

^d Focused echocardiogram (LVOT-G and LVEF only)

^e Intensive PK substudy may occur at Week 8 or Week 12

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Aficamten: Clinical Development Plan for HCM



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Aficamten: Planned Commercial Approach

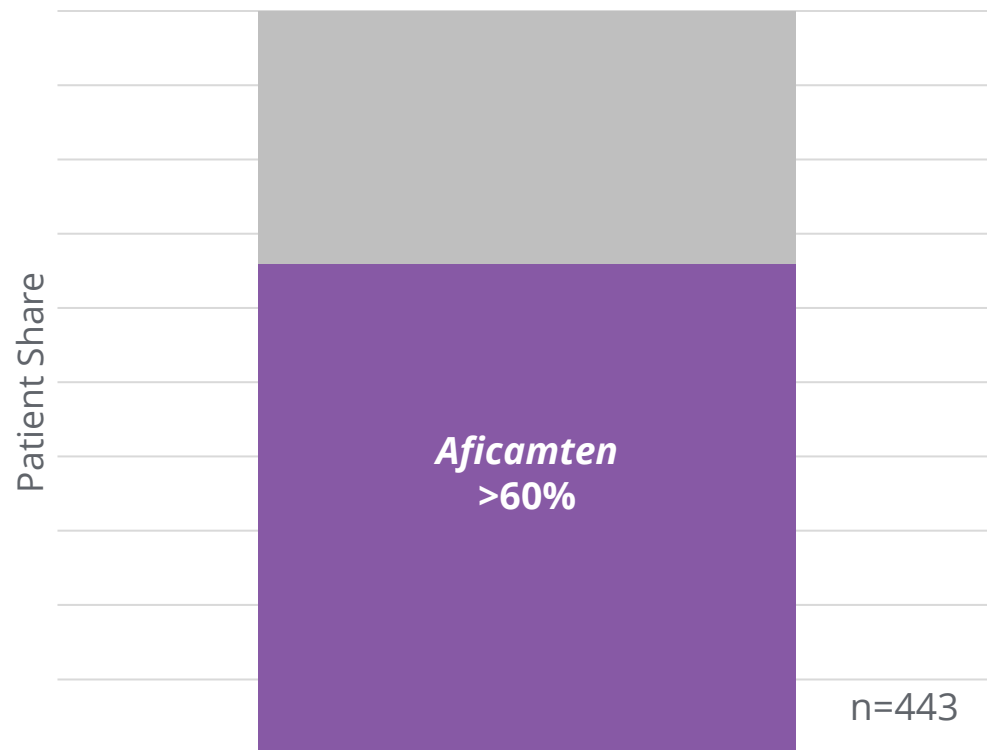
Driven by a relentless focus on our North Star: the HCM patient



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Market Research Shows *Aficamten* May Achieve High Share & Grow Category

oHCM CMI Preference Shares in Eligible Patient Population*



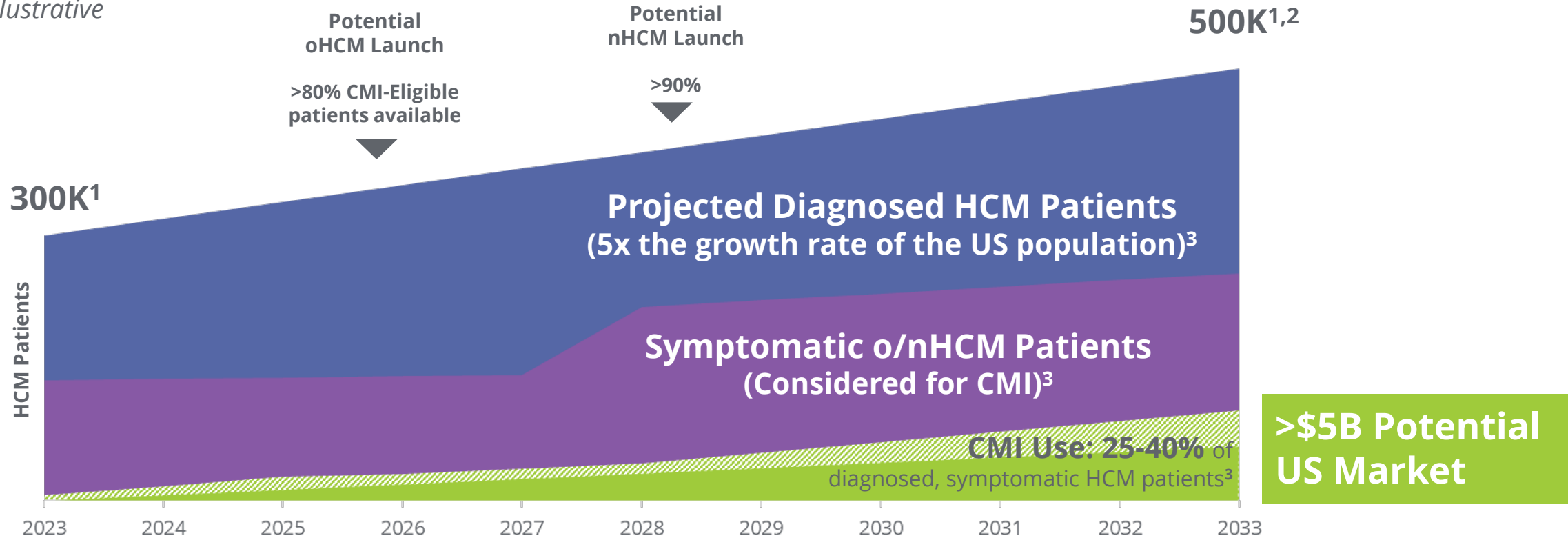
- Potential target product profile for *aficamten* interest creates **share opportunity** in newly treated CMI patients
- *Aficamten* is **also expected to expand the total CMI market**
- Key attributes that may drive preference include the potential for:
 - LVOT gradient reduction
 - Change in NYHA Functional Class
 - Pharmacodynamics/LVEF maintenance
 - Change in KCCQ
 - Absence of DDI

*Source: *Aficamten* Impact of Product Attributes on Product Preference Share n=443 cardiologists, Quantitative research including conjoint - Cogent
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

If *Aficamten* is Approved, Expect Majority of CMI-Eligible Patients Available at Launch
Diagnosis of HCM anticipated to grow 5x the rate of the general population

US HCM Patients (in '000)

Illustrative



1. DoF: SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023);

2. Butzner et al 2021 estimated a 8% growth rate in diagnosed HCM patients between 2013-2019 [https://www.ajconline.org/article/S0002-9149\(21\)00783-9/fulltext](https://www.ajconline.org/article/S0002-9149(21)00783-9/fulltext); CYTK is forecasting an average growth rate of 5% over the coming decade;

3. Internal forecasts

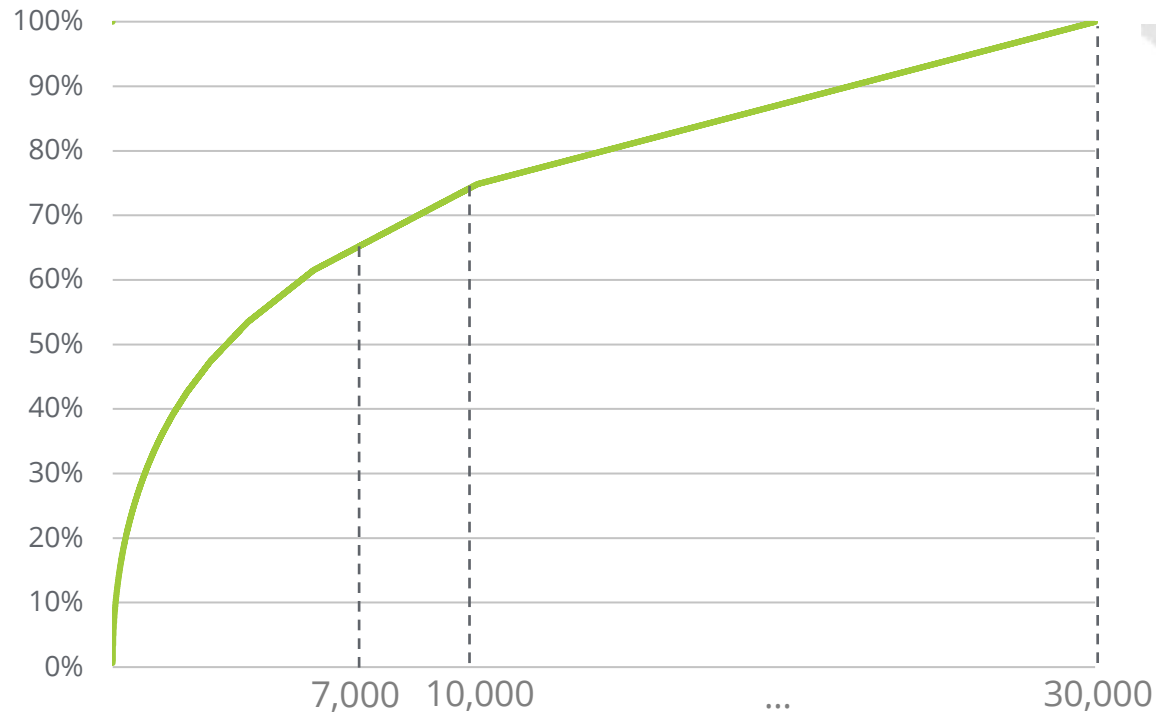
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Projections and forecasts for illustration

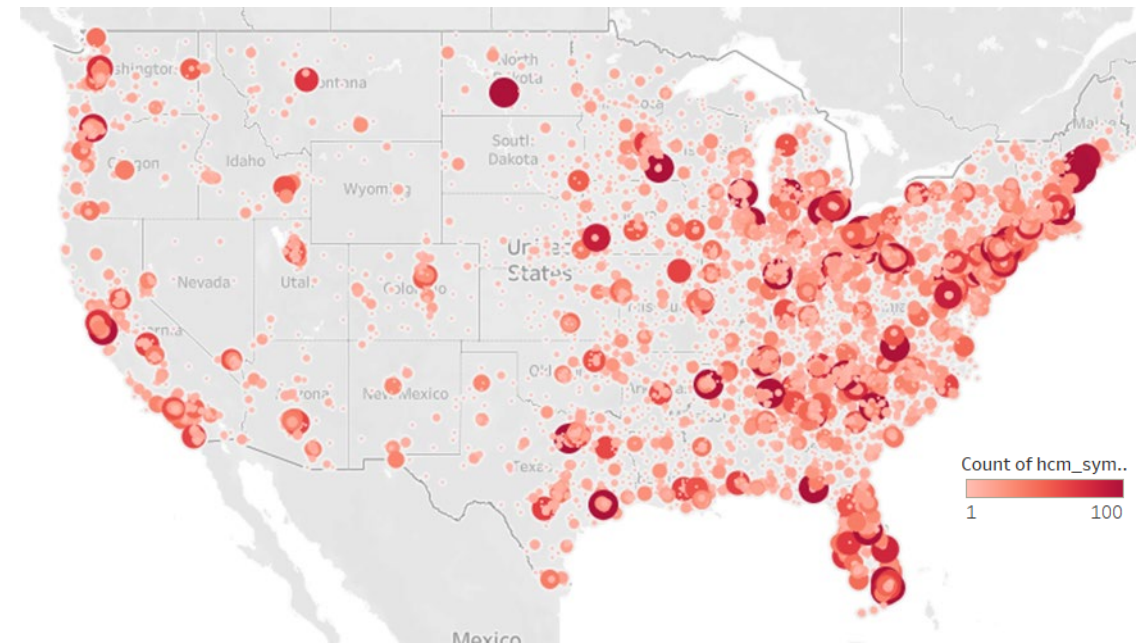
Cardiologists Located in Concentrated Geographic Clusters Across the US

75% of the HCM patient volume is treated by 10,000 cardiologists

HCM Patient Concentration by Cardiologist



Geographic Distribution of HCM Patients

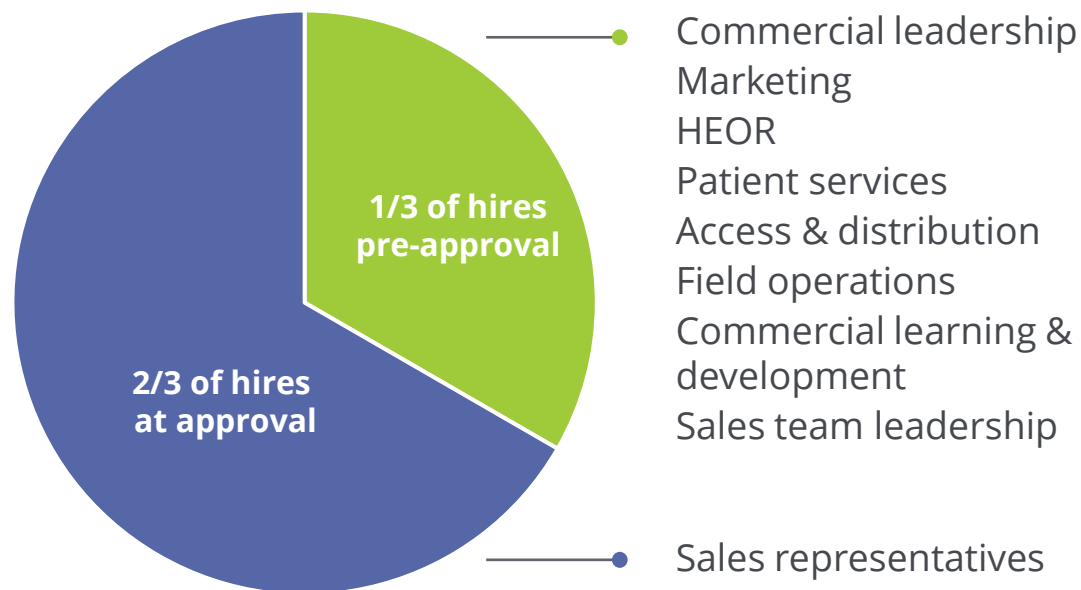


Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients
Source: Symphony PTD (Patient Transaction Data); mapping of HCPs to HCOs using Definitive Healthcare Data 2023 and 7/2023 mapping; Patient volume by dominant Cardiologist Location 7/2023
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Gated Build of Commercial Infrastructure

Majority of spending to occur closer to approval in 2025

2/3 of hiring to occur at-approval



Key activities after SEQUOIA-HCM readout



- Continued insight generation
- Market access strategy validation
- Pricing strategy finalization
- Distribution approach
- Payer engagement
- Brand strategy evolution
- Customer account identification
- Launch campaign development
- Customer Experience
- Payer Pre-approval Information Exchange
- Sales force planning
- Data & Technology Infrastructure build
- Omnichannel execution
- Market development rollout



Initiated upon FDA approval

- Media purchases
- Patient support programs
- Peer to peer engagement
- HCP Omnichannel launched



Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

US Commercial Readiness Milestones for *Aficamten*

2024-2025

	2024	2025
Launch Planning	<p>Final GTM Strategy</p> <p>Launch Tactical Plan</p>	<p>Launch Ready</p>
Marketing	<p>Final Positioning</p> <p>Market Development</p> <p>Full Campaign Development</p>	<p>Digital / Omnichannel</p> <p>HCP Branded Messages & Campaign Finalized</p> <p>Patient Campaign Finalized</p>
Value & Access	<p>Pricing Research</p> <p>Distribution Model Finalized</p> <p>Value Proposition & Payer Deck</p> <p>Patient Support Strategy</p>	<p>Value Dossier</p> <p>Final Market Price</p>
Sales	<p>Field Roles & Responsibilities</p> <p>Target Accounts & Territory Alignments</p>	<p>Sales Representative Recruiting</p>
Medical Affairs	<p>Investigator Spon. Studies Launch</p> <p>CME Launch</p> <p>Clinical Value Payer Deck</p> <p>Publish Primary & Key Secondary SEQUOIA-HCM Results</p>	<p>Medical Contact Center</p> <p>AMCP Dossier</p>

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Omecamtiv Mecarbil

Omecamtiv Mecarbil: Current Status

Received CRL from FDA

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

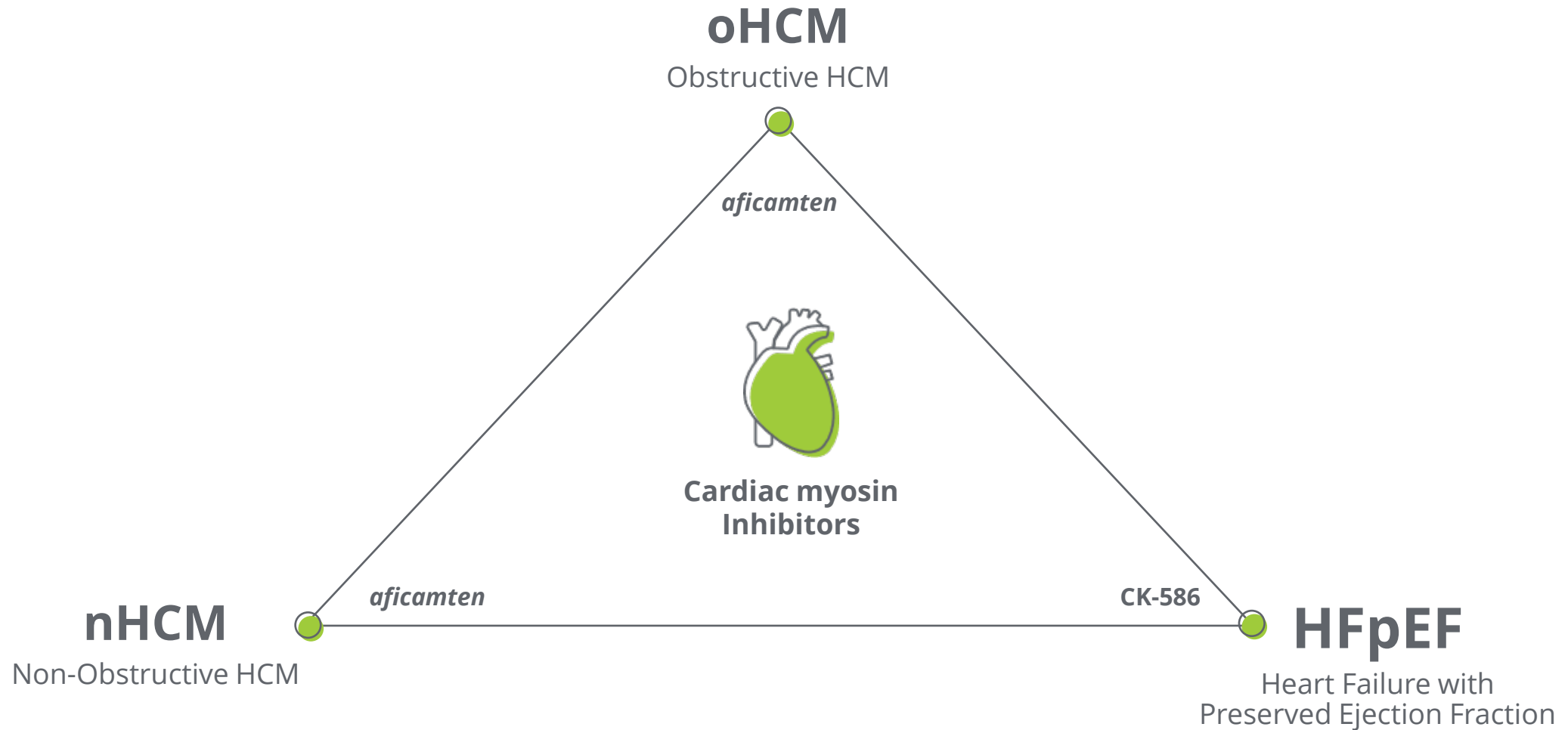
Withdrew MAA from EMA

Withdrew the MAA from the EMA based on feedback from the CHMP indicating that the Committee will not be able to conclude that the benefits outweigh the risks on the basis of the results from GALACTIC-HF alone

Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

CK-586

Novel Approach May Address Multiple Unmet Patient Needs



Heart Failure with Preserved Ejection Fraction (HFpEF)

Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor¹



8.5 million

Americans will have heart failure by 2030²



~50%

HF patients have HFpEF³ & prevalence of HFpEF is increasing^{2,4}



~75%

HFpEF patients will die within five years of initial hospitalization²



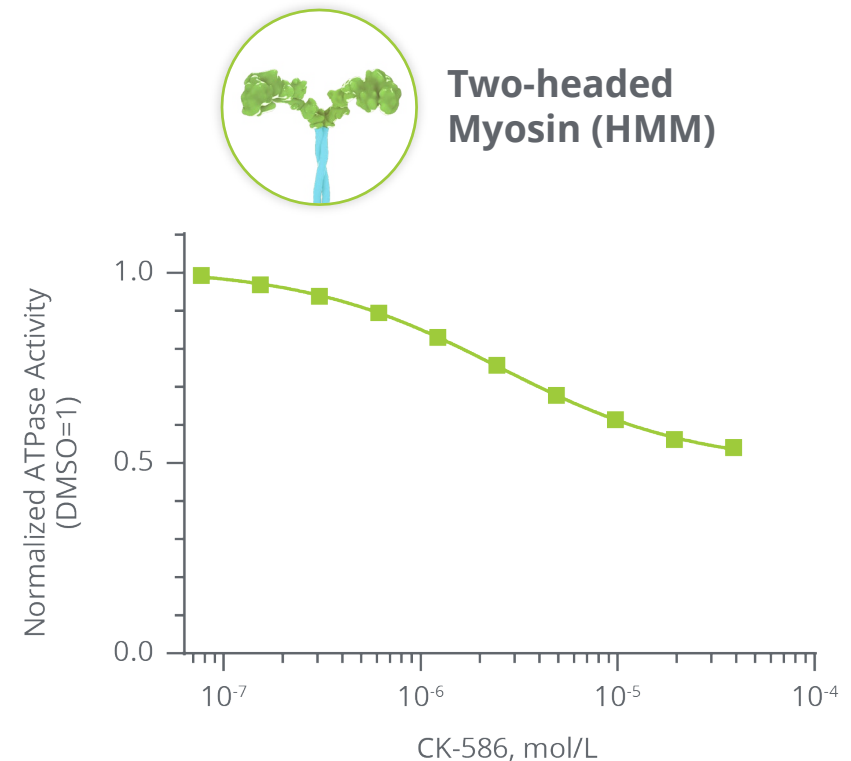
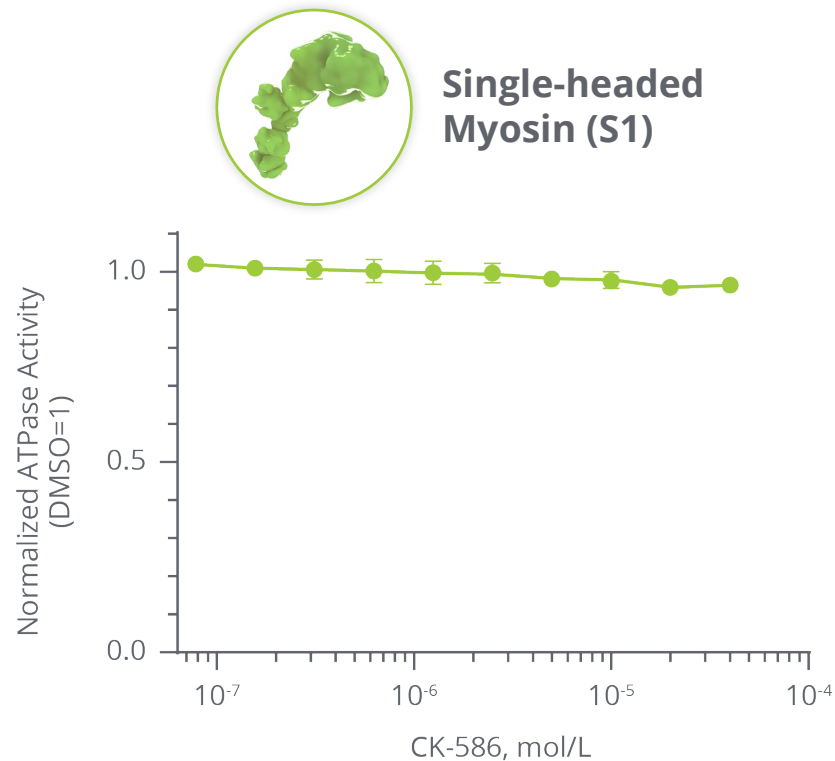
~84%

HFpEF patients will be rehospitalized²

1. Jhund PS, MacIntyre K, Simpson CR, et al. Long-Term Trends in First Hospitalization for Heart Failure and Subsequent Survival Between 1986 and 2003. *Circulation*. 2009;119:515-523.
2. Bozkurt B, Ahmad T, Alexander KM, Baker WL, Bosak K, Breathett K, Fonarow GC, Heidenreich P, Ho JE, Hsieh E, Ibrahim NE, Jones LM, Khan SS, Khazanie P, Koelling T, Krumholz HM, Khush KK, Lee C, Morris AA, Page RL 2nd, Pandey A, Piano MR, Stehlik J, Stevenson LW, Teerlink JR, Vaduganathan M, Ziaeian B; Writing Committee Members. Heart Failure Epidemiology and Outcomes Statistics: A Report of the Heart Failure Society of America. *J Card Fail*. 2023 Oct;29(10):1412-1451. doi: 10.1016/j.cardfail.2023.07.006. Epub 2023 Sep 26. PMID: 37797885; PMCID: PMC10864030.
3. Dunlay SM, Roger VL, Weston SA, Jiang R, Redfield MM. Longitudinal changes in ejection fraction in heart failure patients with preserved and reduced ejection fraction. *Circ Heart Fail*. 2012 Nov;5(6):720-6. doi: 10.1161/CIRCHEARTFAILURE.111.966366. Epub 2012 Aug 30. PMID: 22936826; PMCID: PMC3661289.
4. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240-e327.

CK-586: Distinct Mechanism of Action from *Aficamten*

CK-586 inhibits actin-activated ATPase of HMM only; *aficamten* inhibits both S1 and HMM

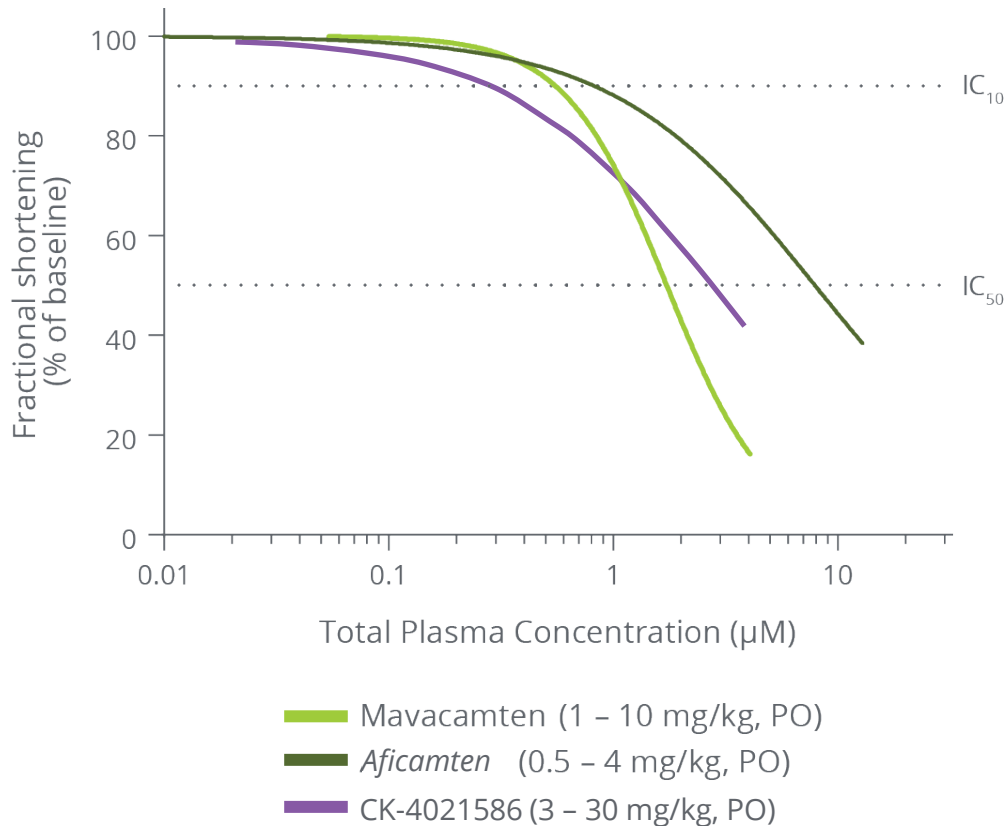


Based on preclinical testing

CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

CK-586: Shallow *In Vivo* Concentration-Response

CK-586 is predicted to have a shorter half-life in humans than *aficamten*



Pharmacodynamic window Fractional shortening IC ₅₀ /IC ₁₀ ratio	
mavacamten	2.8x
<i>aficamten</i>	9.9x
CK-586	9.3x

IC₁₀: plasma concentration at 10% relative reduction in fractional shortening
 IC₅₀: plasma concentration at 50% relative reduction in fractional shortening

Compound half-life in humans	Actual	Predicted
<i>aficamten</i>	~3 days	2.8 days
CK-586	TBD	15 hours

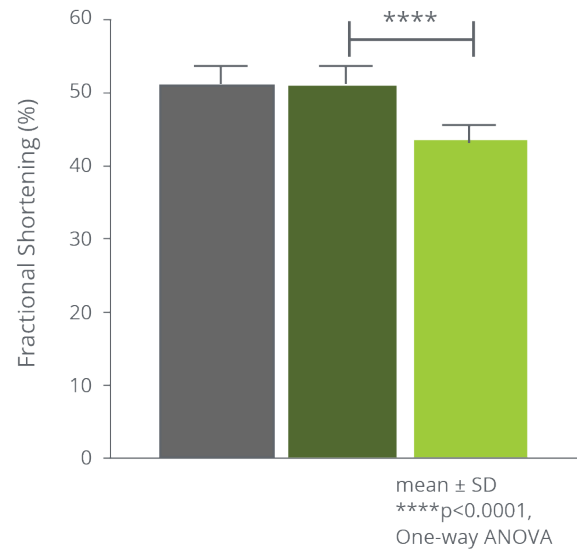
CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

CK-586 is Efficacious in ZSF1 Obese Rat Model of HFpEF

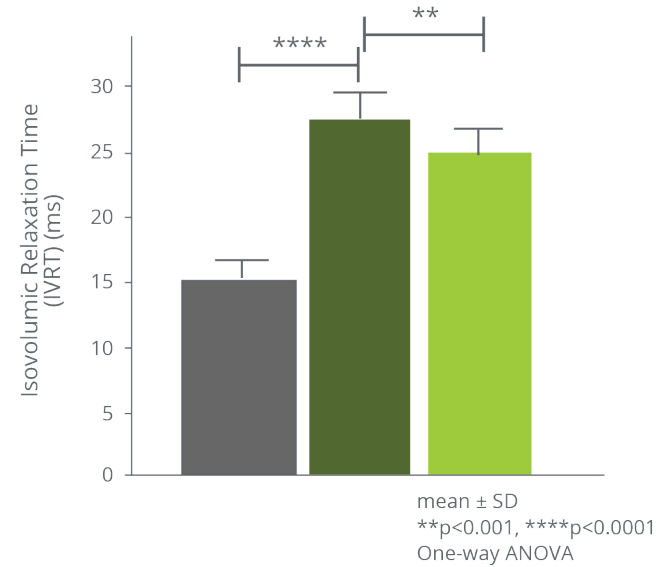
Model is representative of hypertensive, diabetic, metabolic aspects of HFpEF

10 weeks of treatment improved diastolic function and reduced cardiac fibrosis

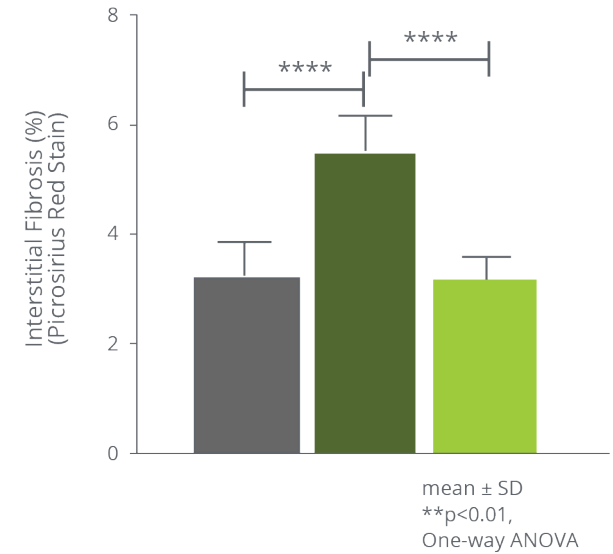
Reduced Fractional Shortening



Improved Diastolic Function



Reduced Fibrosis



■ ZSF1 Lean + Vehicle ■ ZSF1 Obese + Vehicle ■ ZSF1 Obese + CK-586 (10 mg/kg, PO QD)

CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Phase 1 Data Support Advancement to Phase 2 Clinical Trial

Full data to be presented at a medical congress in 2H 2024

Phase 1 Design

- **7 SAD cohorts** (10 mg to 600 mg) comprised of 10 participants each
- **2 MAD cohorts** (100 and 200 mg once daily) comprised of 10 participants each

Key Findings

- Pharmacodynamics were evaluated using echocardiography and **consistent with expectations**
- CK-586 was **safe and well-tolerated** with **linear PK**
- **No series adverse events** were observed
- **Stopping criteria were not met** in the study

CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

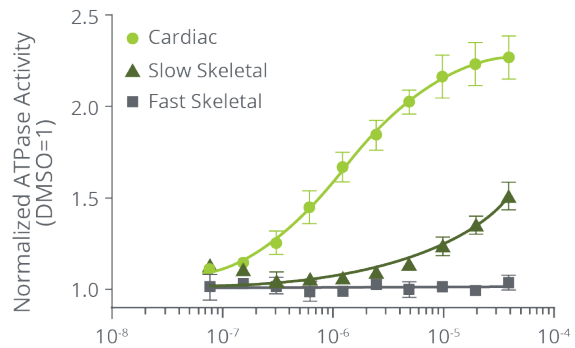
CK-136

CK-136: Mechanism of Action

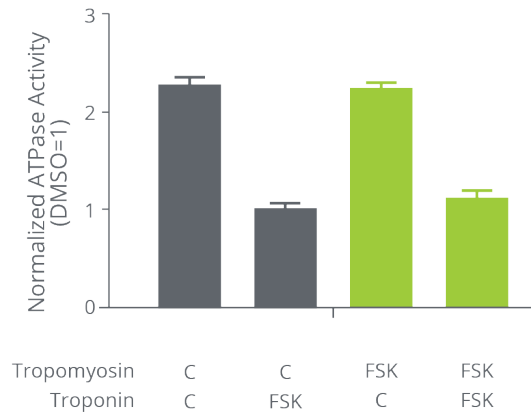
Key biochemical and cellular features

The first selective cardiac troponin activator

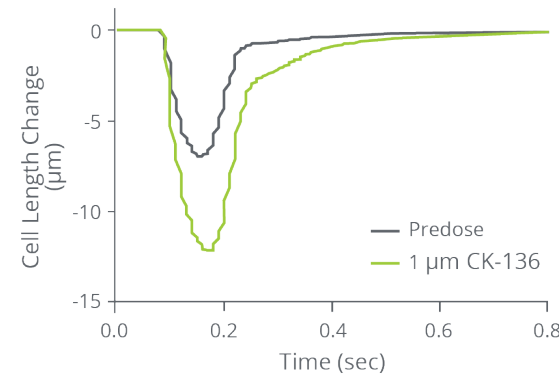
Greater ATPase Activity



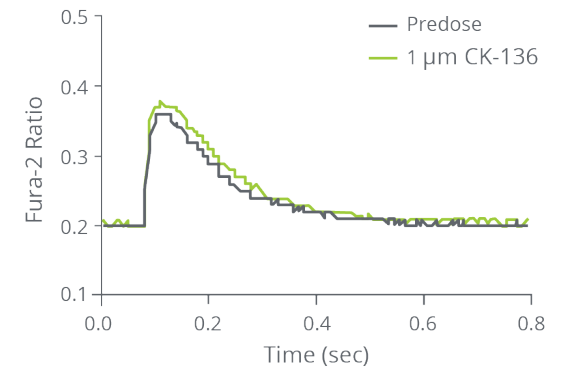
Greater ATPase Activity



Contractability Strongly Activated After Treatment



Calcium Transients Unchanged After Treatment



¹PD Window = Maximum Tolerated Concentration (MTC) / 10% increase in Fractional Shortening (FS)

CK-136 is an investigational agent and has not been approved for use by any regulatory agency. Its safety and efficacy have not been established.

CK-136: Exposure Response Relationship

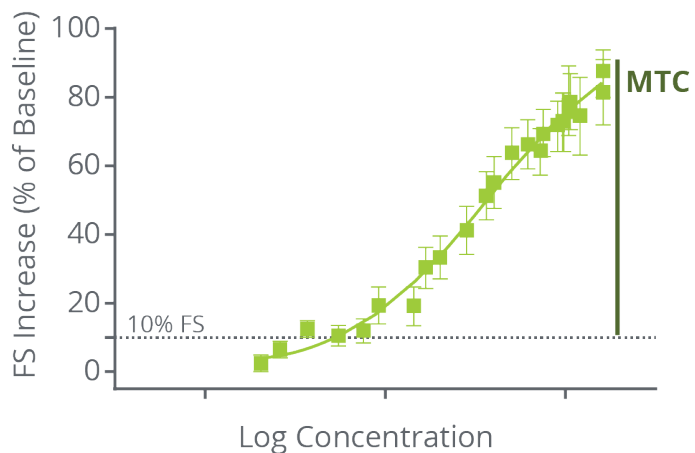
Exposure-response of troponin activator is shallower than myosin activator

Completed Phase 1 study and have begun analyzing data

Animal Models of Cardiac Function

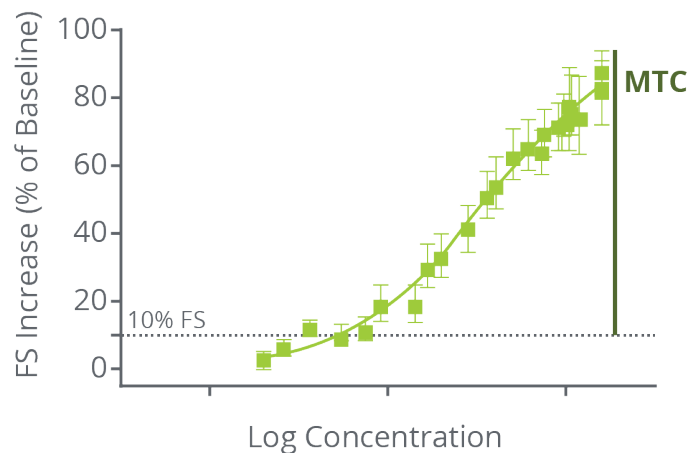
Healthy Rats PD Window¹

≥15X



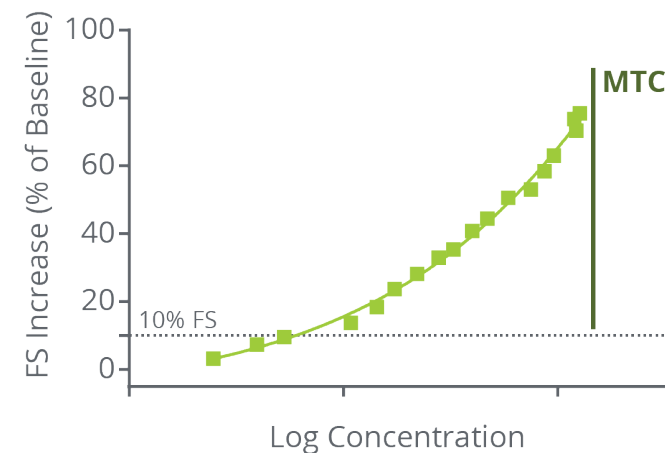
MI Rats PD Window¹

≥15X



Healthy Dogs PD Window¹

≥15X





¹PD Window = Maximum Tolerated Concentration (MTC) / 10% increase in Fractional Shortening (FS)

CK-136 is an investigational agent and has not been approved for use by any regulatory agency. Its safety and efficacy have not been established.

Corporate Profile

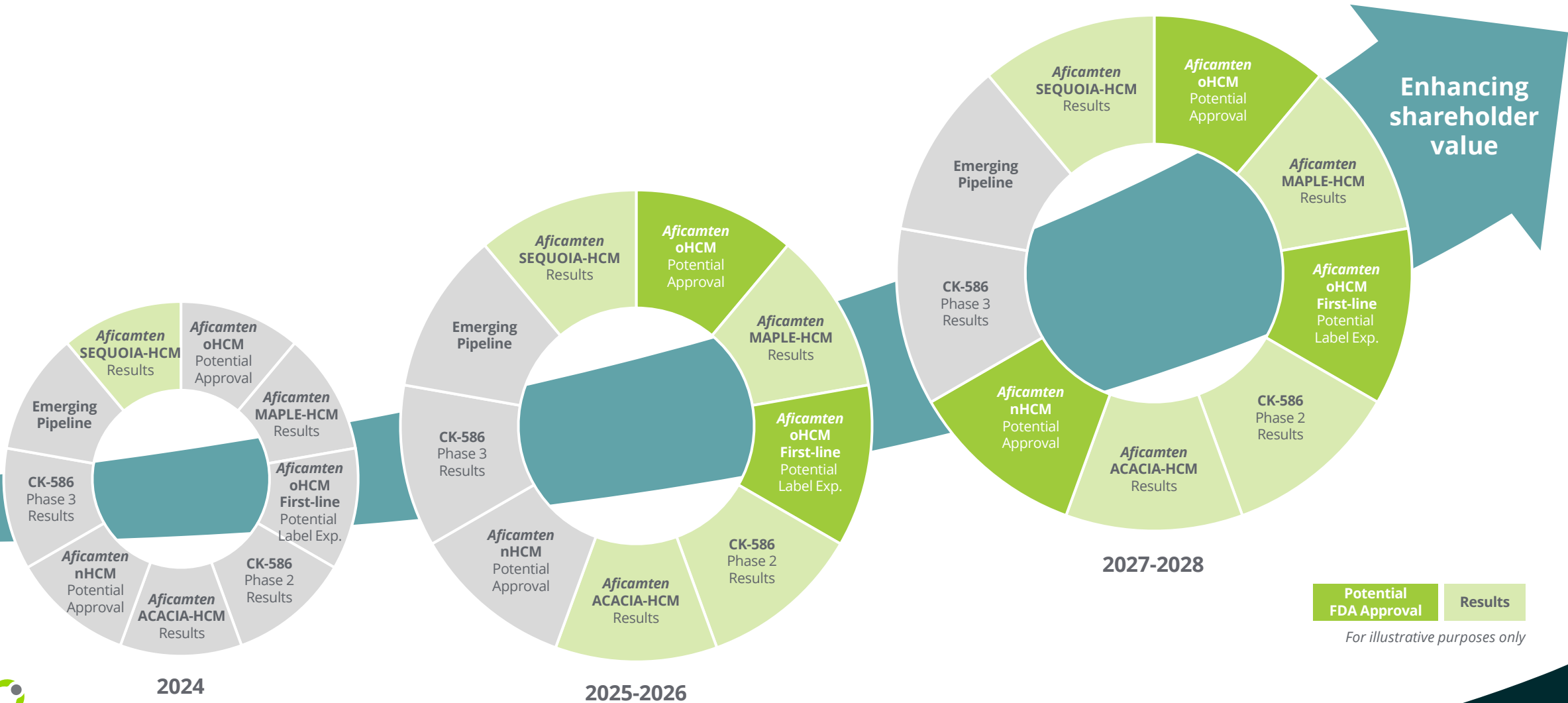
Robust Pipeline, Solid Financial Position

Pipeline	1 Potential commercial launch in 2025	3 Clinical stage programs	Ongoing muscle biology directed research
Programs	HCM Aficamten <ul style="list-style-type: none"> SEQUOIA-HCM: Positive Phase 3 results MAPLE-HCM: Phase 3 monotherapy trial in oHCM ongoing ACACIA-HCM: Phase 3 trial in nHCM ongoing CEDAR-HCM: Trial in pediatric population FOREST-HCM: OLE ongoing 	Heart Failure Omecamtiv mecarbil <ul style="list-style-type: none"> Considering potential next steps CK-136 <ul style="list-style-type: none"> Analyzing data from Phase 1 study CK-586 <ul style="list-style-type: none"> Phase 1 results support advancement to Phase 2 	Ongoing R&D  <p>Additional research in muscle biology, energetics & metabolism</p>
Foundations	 ~415 Full time employees As of April 2024	~\$634M At Q1 2024	Approximately 2 years of cash runway based on 2024 Financial Guidance*

*Including capital we expect to be available to us under our deal with Royalty Pharma, upon satisfaction of conditions

Expected Value Unlocked with Future Catalysts

Myosin platform drives value and growth with multiple data milestones and expected approvals



Cytokinetics: Uniquely Positioned for Success



Leadership in muscle biology

Pioneer in CMI space
Multiple drug candidates
arising from our research
Core research engine



Depth in cardiology

Late-stage HCM program
HFrEF opportunity in Europe
Bridge to HFpEF
Expand to advanced HF



Relationships with stakeholders

Seasoned commercial team
Strong existing payer
relationships
Strong relationships with
cardiologists and institutions



Access to capital

Strong cash runway based on
2024 financial guidance
Access to capital through
Royalty Pharma transaction,
subject to satisfaction of
certain conditions

CMI: cardiac myosin inhibitor

Balance Sheet & Financial Guidance

Approximately 2 years of cash runway based on 2024 guidance*

2024 Condensed Balance Sheet

As of 3/31/2024

	<i>in millions</i>
	Total
Cash and investments	\$634.3
Accounts receivable	\$0.8
PPE	\$68.0
Leased assets	\$78.2
Other assets	\$26.8
Total Assets	\$808.1
Convertible Debt, net	\$549.8
Liability related to sale of future royalties	\$390.2
Lease liability	\$136.8
Other liabilities	\$127.4
Total Liabilities	\$1,204.2
Working capital	\$549.8
Accumulated deficit	(\$2,247.9)
Stockholders' deficit	(\$396.2)
Wtd Avg Basic Shares Outstanding (million)	101.9

2024 Financial Guidance

in millions

	Total
Cash Revenue	\$3-5
Operating Expenses	\$420-450
Net	~ \$390-420

*Including capital we expect to be available to us under our deal with Royalty Pharma, upon satisfaction of conditions

Expected 2024 Milestones

Aficamten

Present primary results from SEQUOIA-HCM at HFA in Q2 2024

Continue enrollment of ACACIA-HCM in 2024

Submit NDA to FDA in Q3 2024 and MAA to EMA in Q4 2024

Continue enrollment of CEDAR-HCM in 2024

Complete enrollment in MAPLE-HCM in Q3 2024

Begin Phase 1 study of *aficamten* in healthy Japanese volunteers in Q2 2024

CK-586

Share full data from Phase 1 study of CK-586 in 2H 2024

Initiate Phase 2 study of CK-586 in Q4 2024

Pre-Clinical Development & Ongoing Research

Initiate clinical development with another muscle-directed compound in 2024

Aficamten and CK-586 are investigational drugs and have not been approved. *Their* safety and efficacy have not been established.



Cytokinetics®

thank
you



Vi, diagnosed with HCM
Avonne, diagnosed with HCM
John, diagnosed with heart failure