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 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").

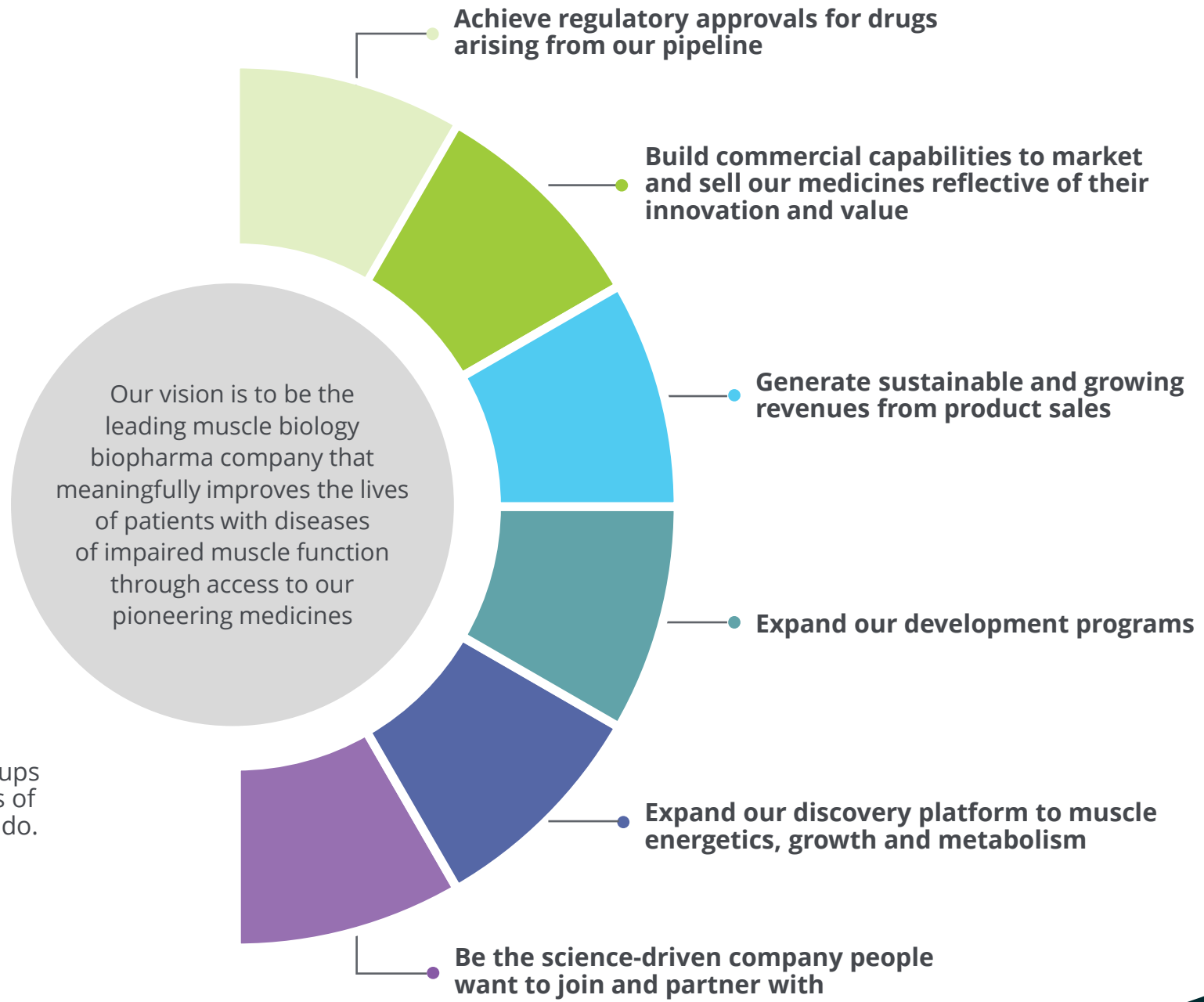
Our Mission

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.



Cytokinetics®

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

AWARDS

FORTUNE BEST WORKPLACES IN BIOPHARMA™ 2022

FORTUNE BEST WORKPLACES IN THE BAY AREA™ 2023

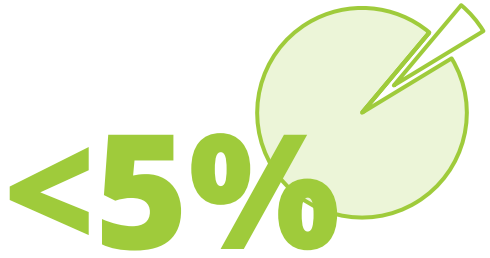
Great Place To Work® Certified FEB 2024-FEB 2025 USA

SAN FRANCISCO BUSINESS TIMES · SILICON VALLEY BUSINESS JOURNAL
BPTW
BEST PLACES TO WORK 2023

FAST COMPANY
BEST WORKPLACES FOR INNOVATORS 2023
SCIENCE & TECHNOLOGY | CYTOKINETICS

Winner in Wellness 3rd
SAN FRANCISCO BUSINESS TIMES
Out of 25 Large Companies

RETENTION

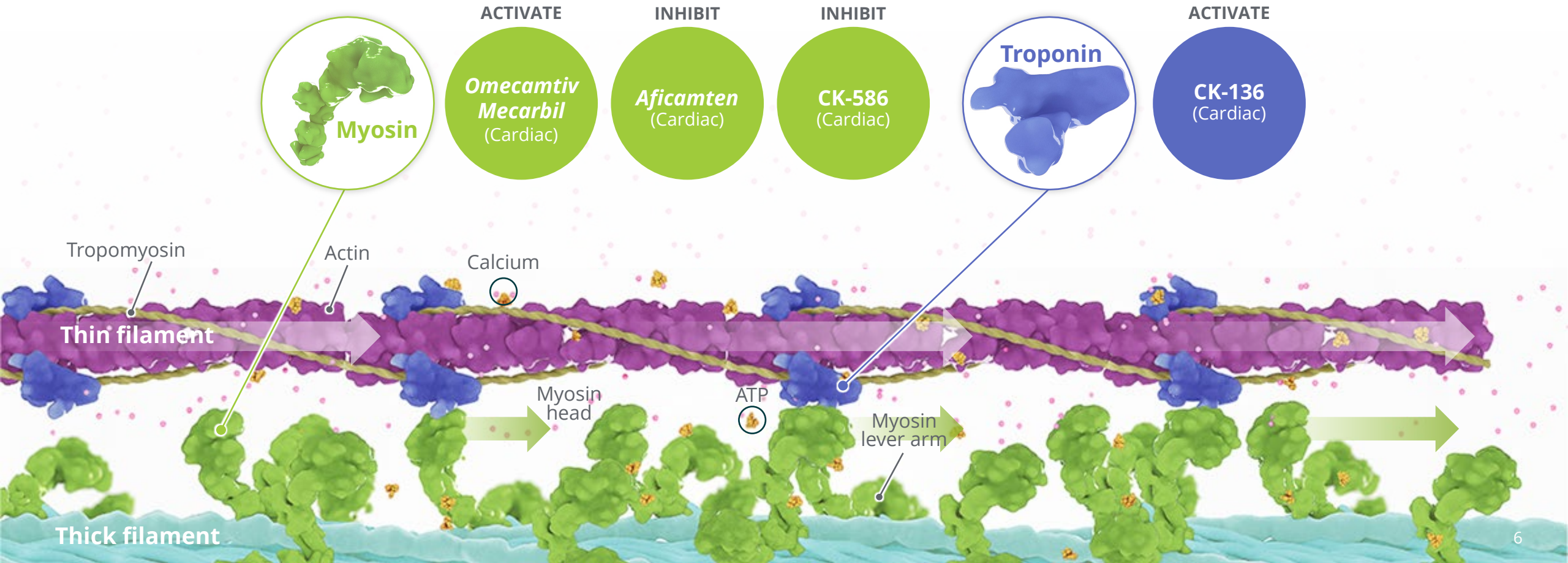


Turnover rate of leadership; low attrition

Average tenure of leadership; high continuity

Sarcomere Directed Drug Development

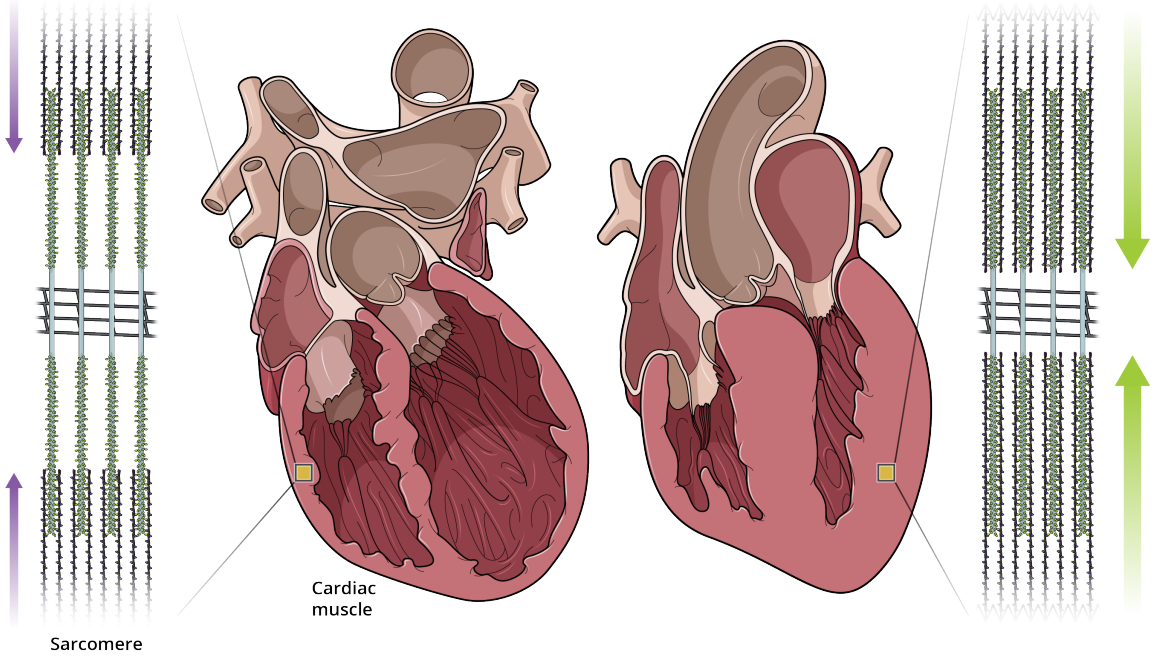
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables myocytes to contract and generate force



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

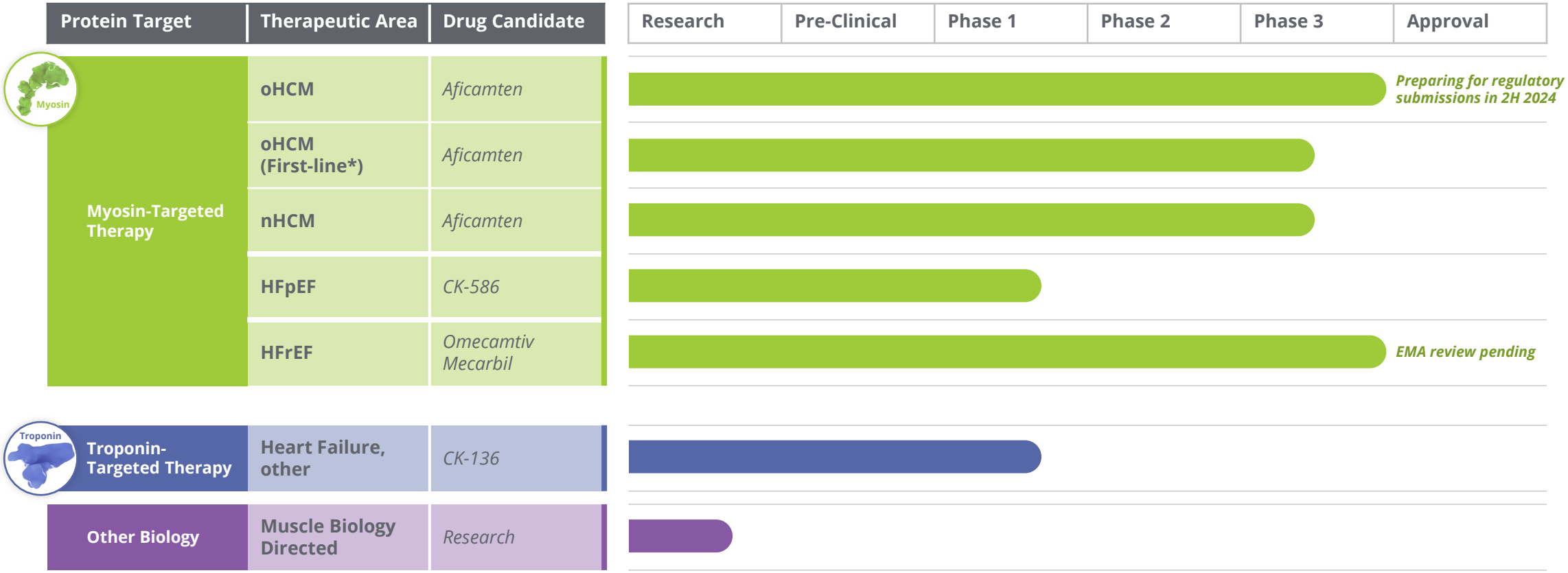


Increased / Preserved Cardiac Contractility

- 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*



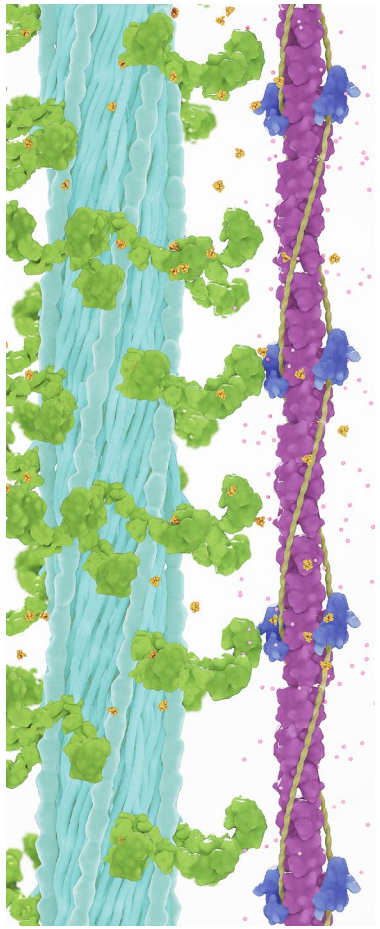
*Pending results from MAPLE-HCM, an ongoing Phase 3 clinical trial evaluating for the potential superiority of aficamten as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM.

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

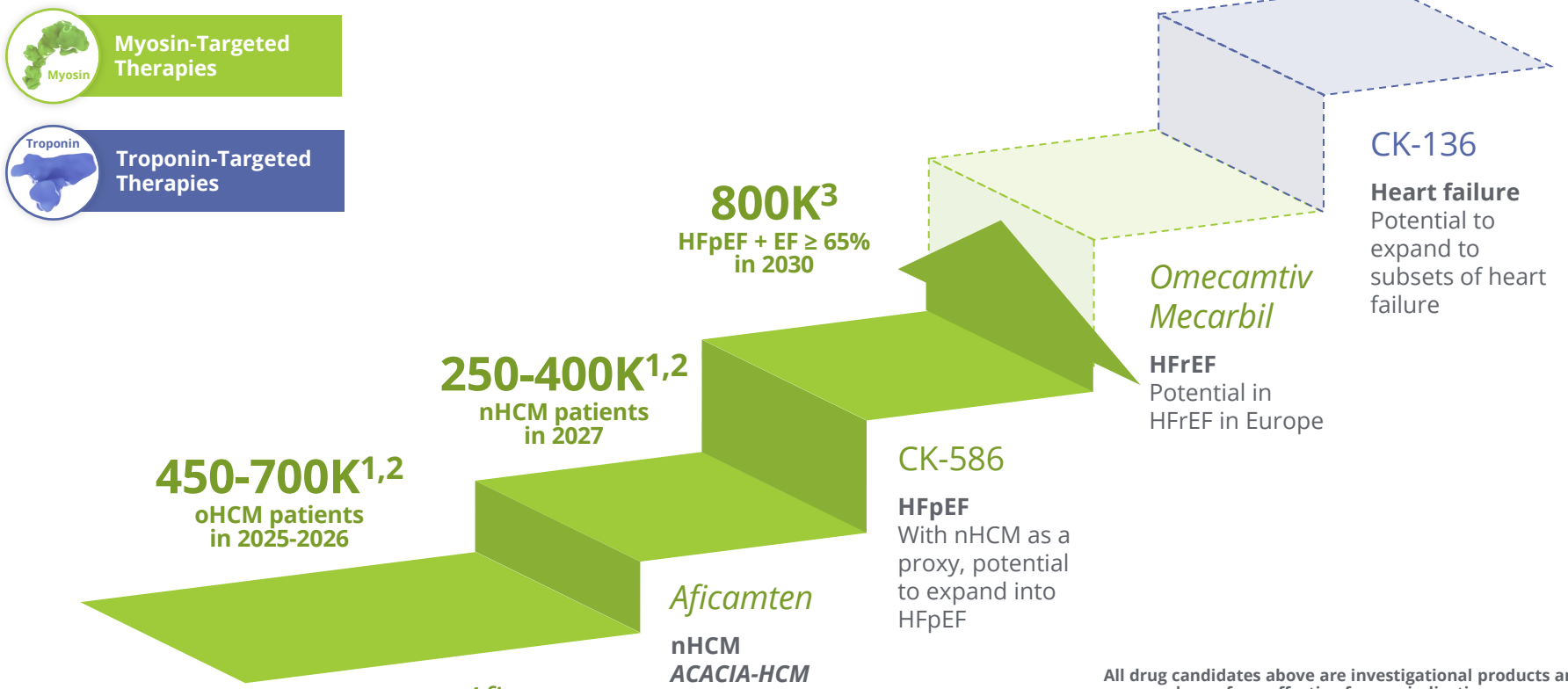
Cytokinetics®

Building a Specialty Cardiology Franchise Anchored by *Aficamten*

Growing addressable patient market through specialty cardiology franchise strategy



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.

Cytokinetics®

Specialty Cardiovascular Portfolio

Aficamten
Omecamtiv Mecarbil
Emerging Pipeline – CK-586 & CK-136

Cytokinetics®

Omecamtiv mecarbil , aficamten, 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

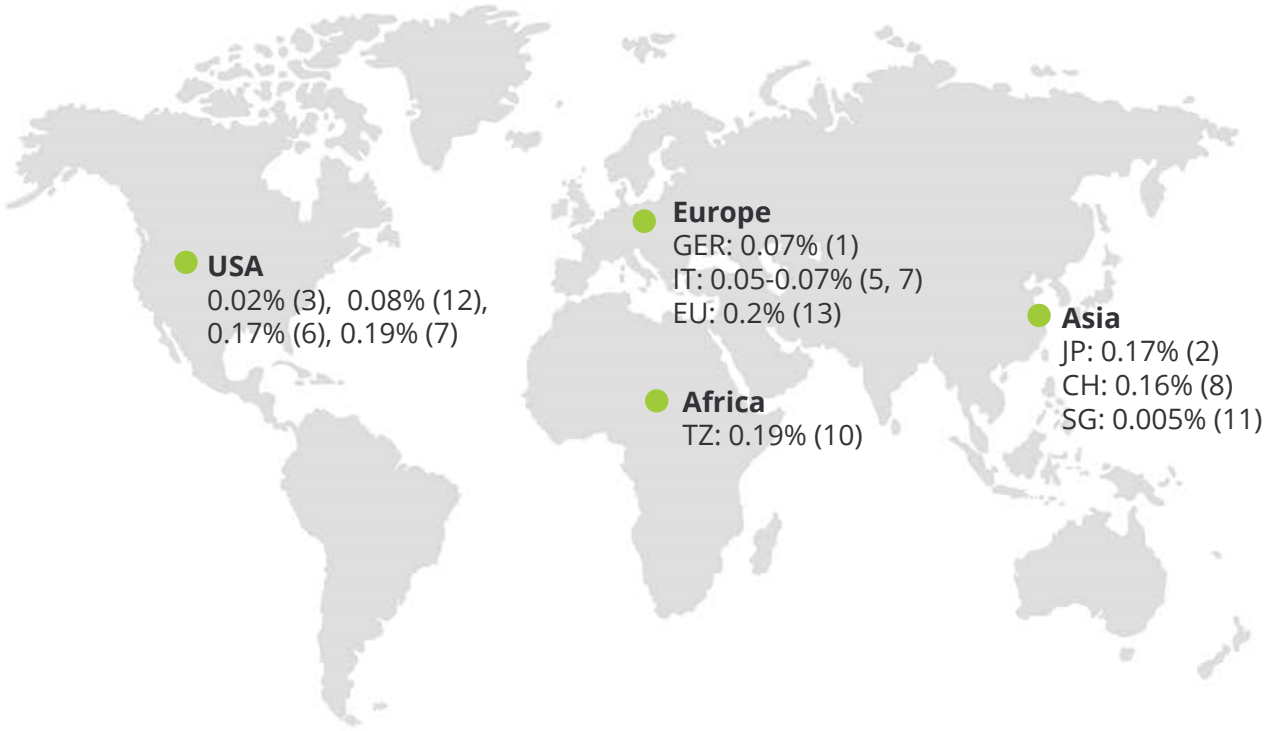
Cytokinetics®

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.

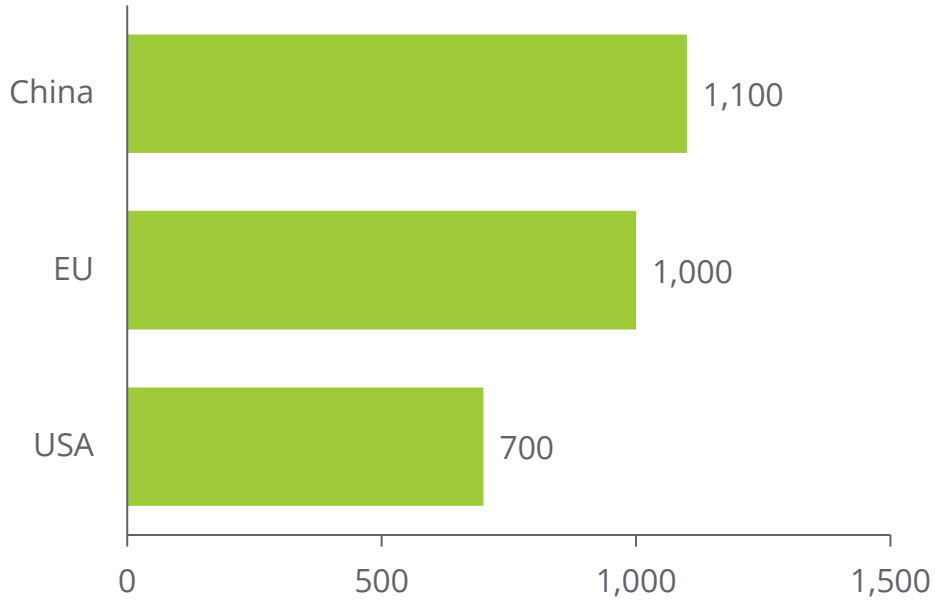
HCM Prevalence: Significant and Growing Globally

HCM prevalence estimates vary across geography and over time

Estimated HCM Prevalence Rates



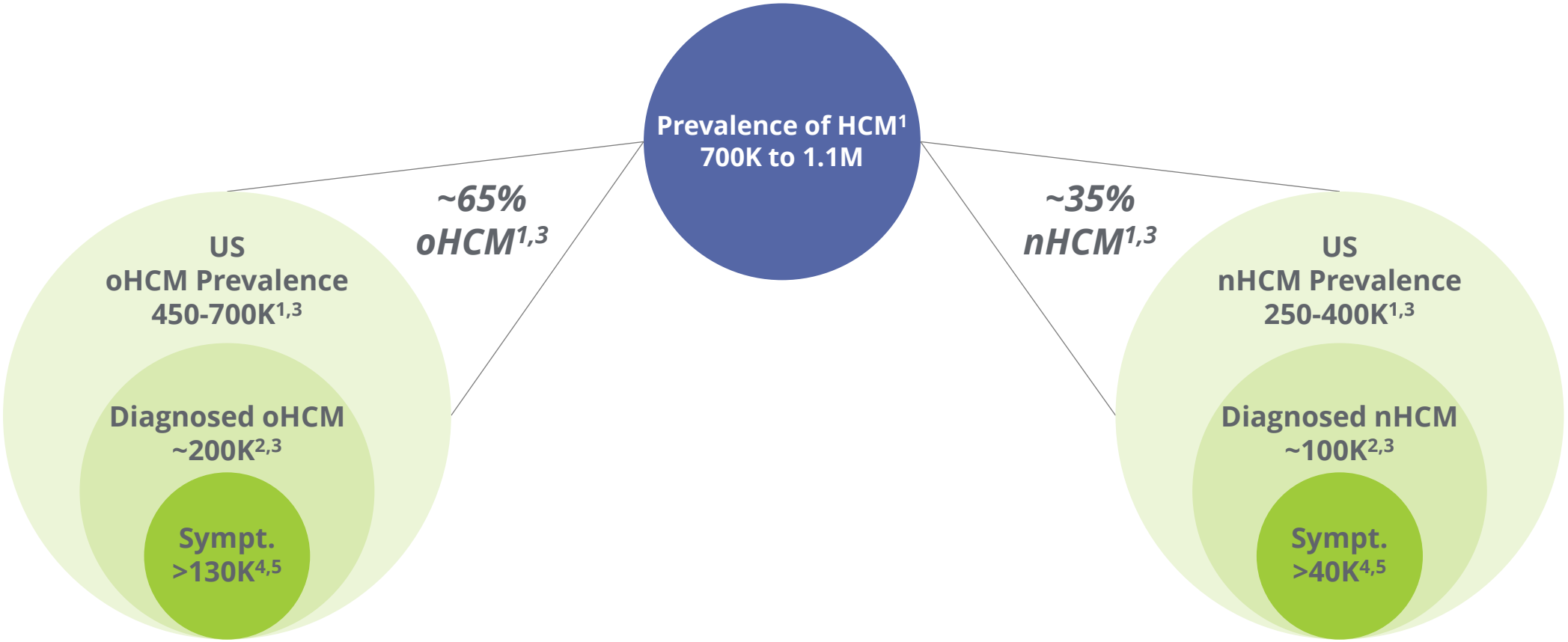
HCM True Patient Prevalence (Est. 2021)



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

Opportunity for CMIs in Diagnosed, Symptomatic HCM Patients

Potential for nearly 200K patients eligible for CMIs in 2025



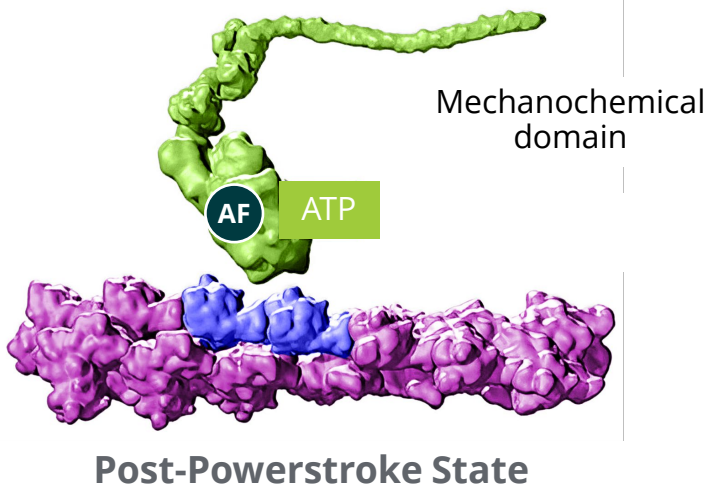
Projections and forecasts for illustration.

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.

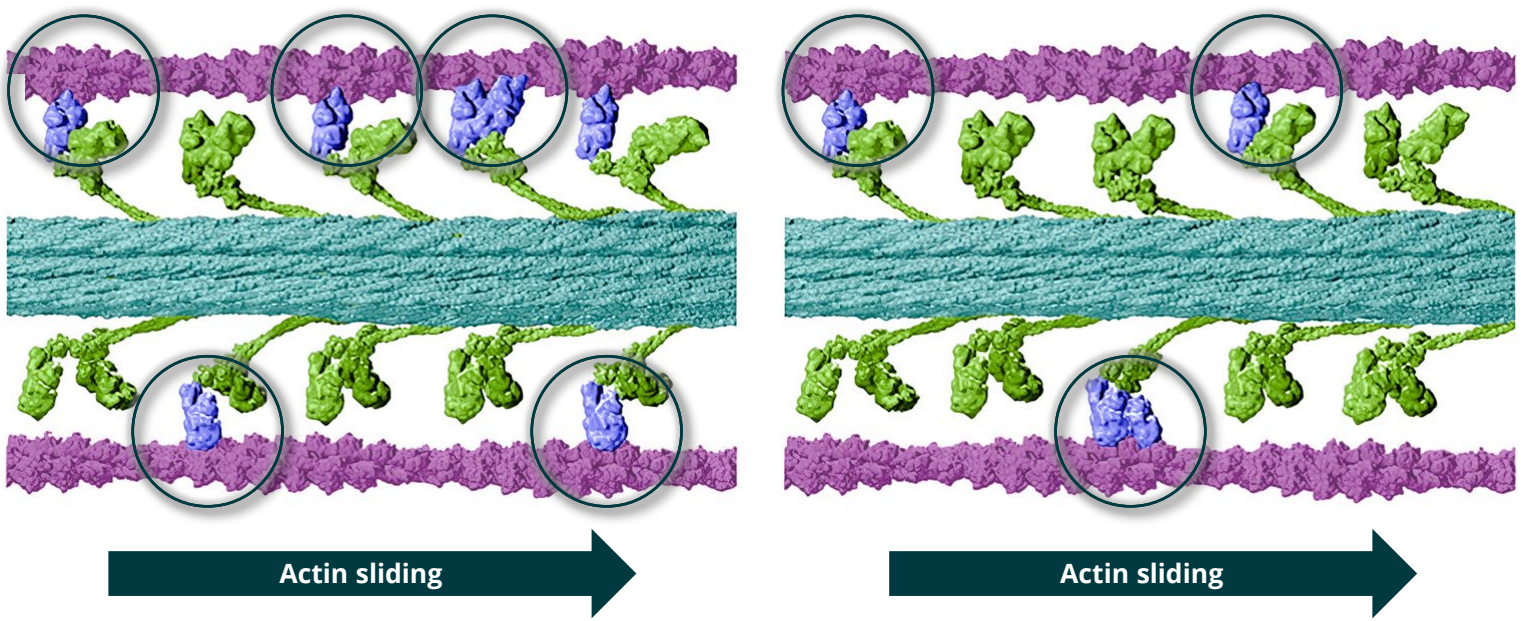
Cytokinetics®

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 agent and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Cytokinetics®

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

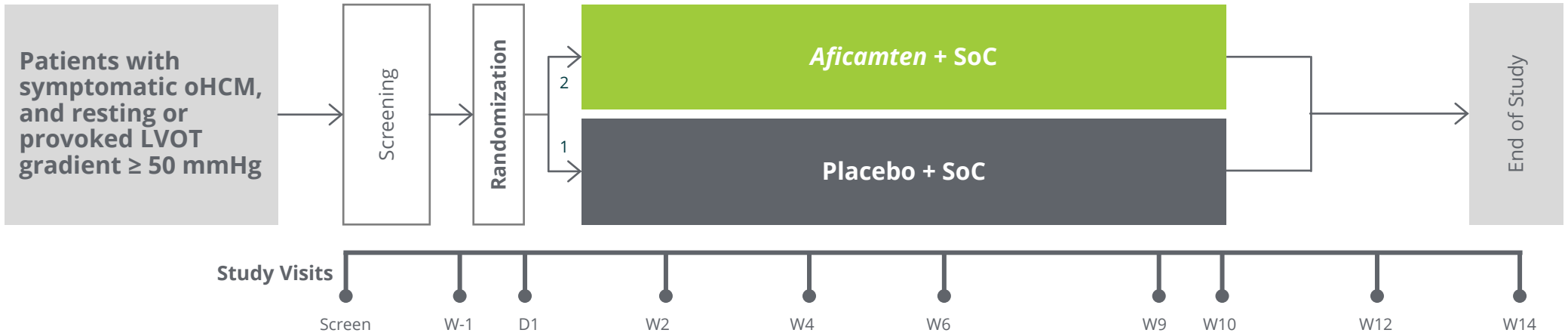
Aspirational information. Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Cytokinetics®

REDWOOD-HCM: Cohorts 1 & 2

Patients with symptomatic oHCM on background therapy excluding *disopyramide*

Two sequential dose-finding cohorts



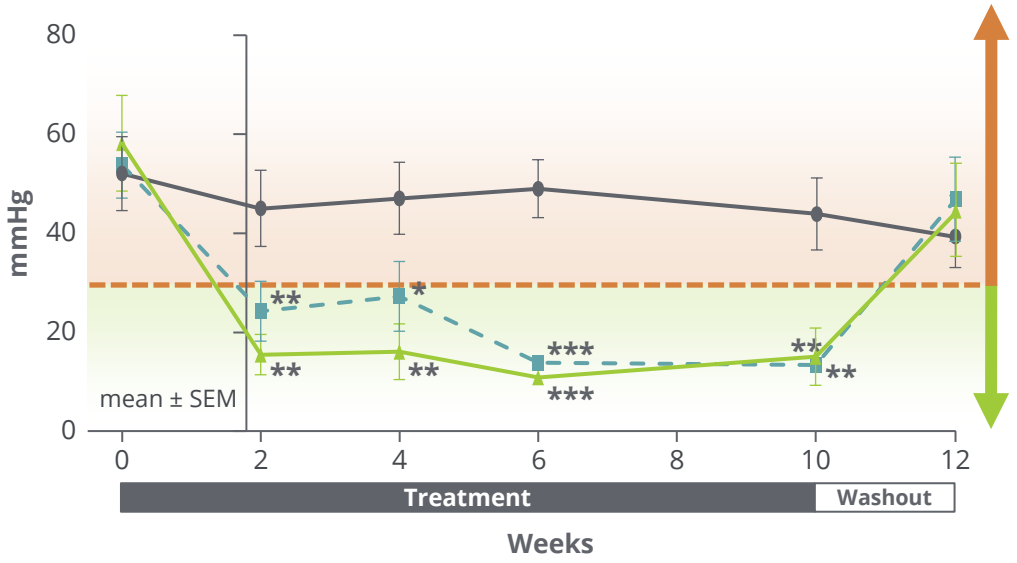
	Dose 1	Dose 2	Dose 3
Cohort 1	5 mg	10 mg	15 mg
Cohort 2	10 mg	20 mg	30 mg

REDWOOD-HCM: Robust Reduction of LVOT Gradients

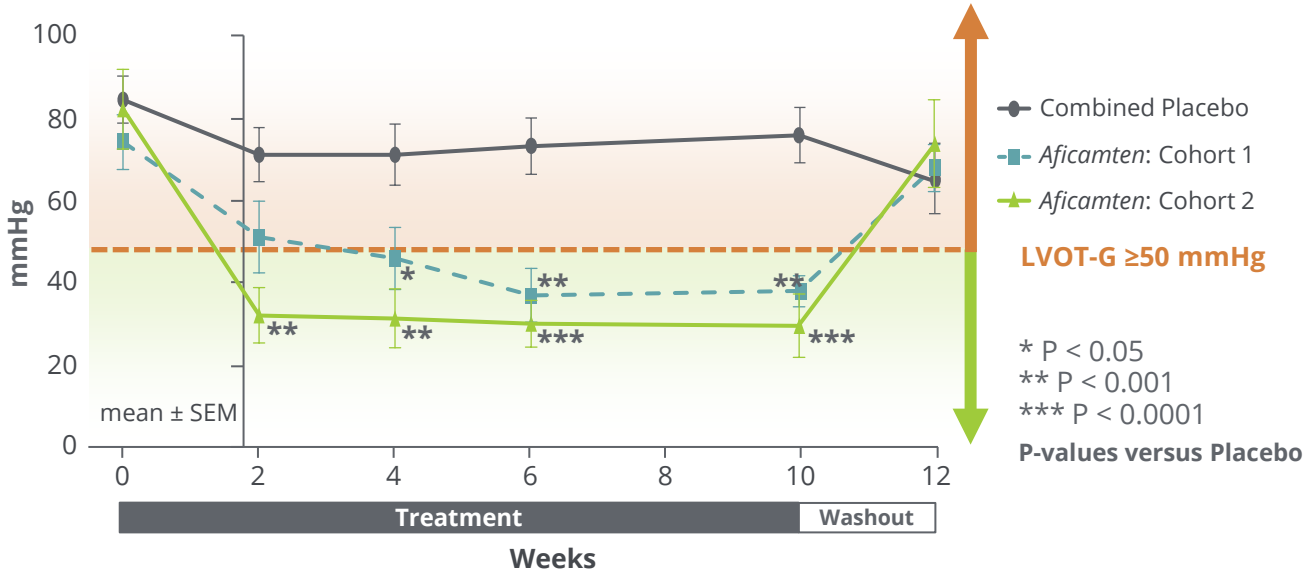
Cohorts 1 & 2

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

Resting LVOT-G



Valsalva LVOT-G



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

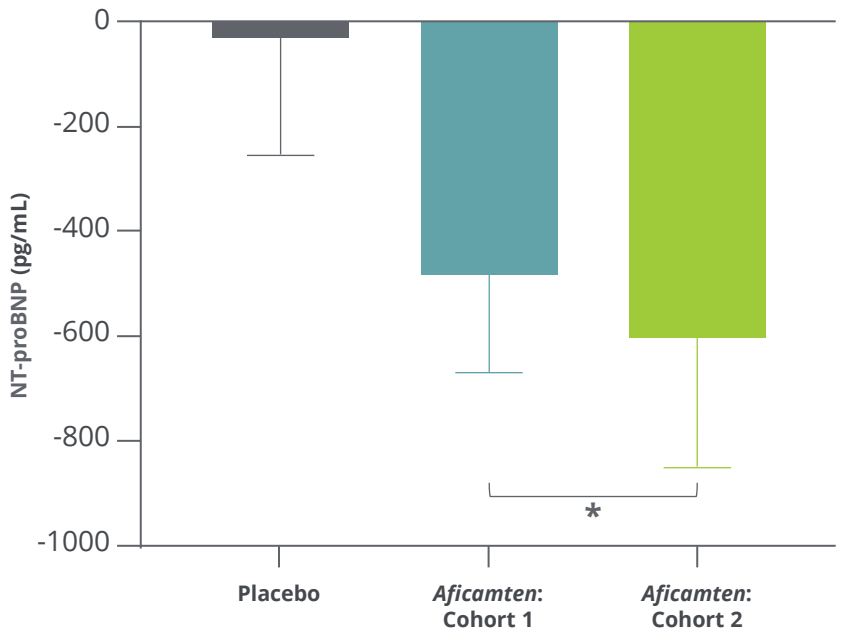
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

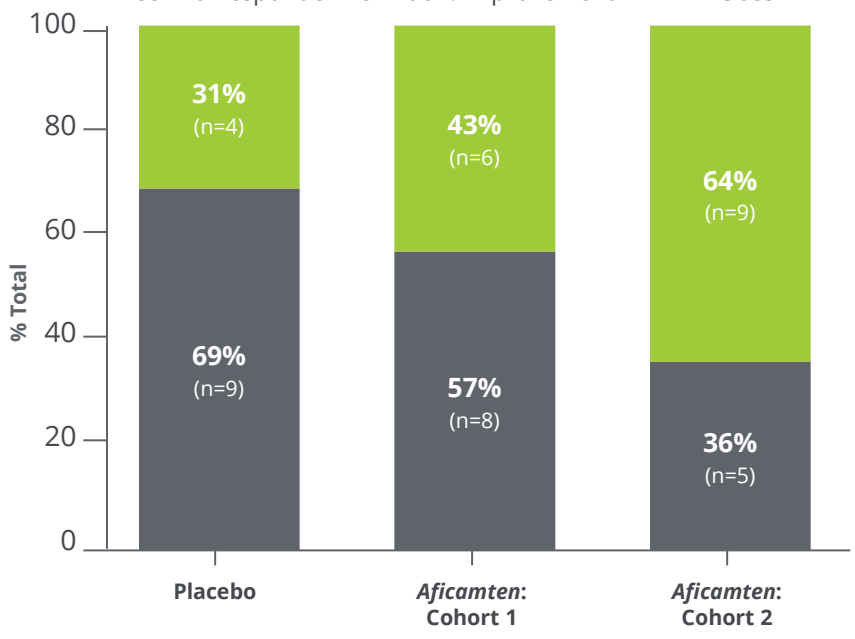


***p = 0.003 for Pooled Cohort 1 & 2 vs. Placebo**

- 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 agent and is not approved by any regulatory agency. Its safety and efficacy have not been established.

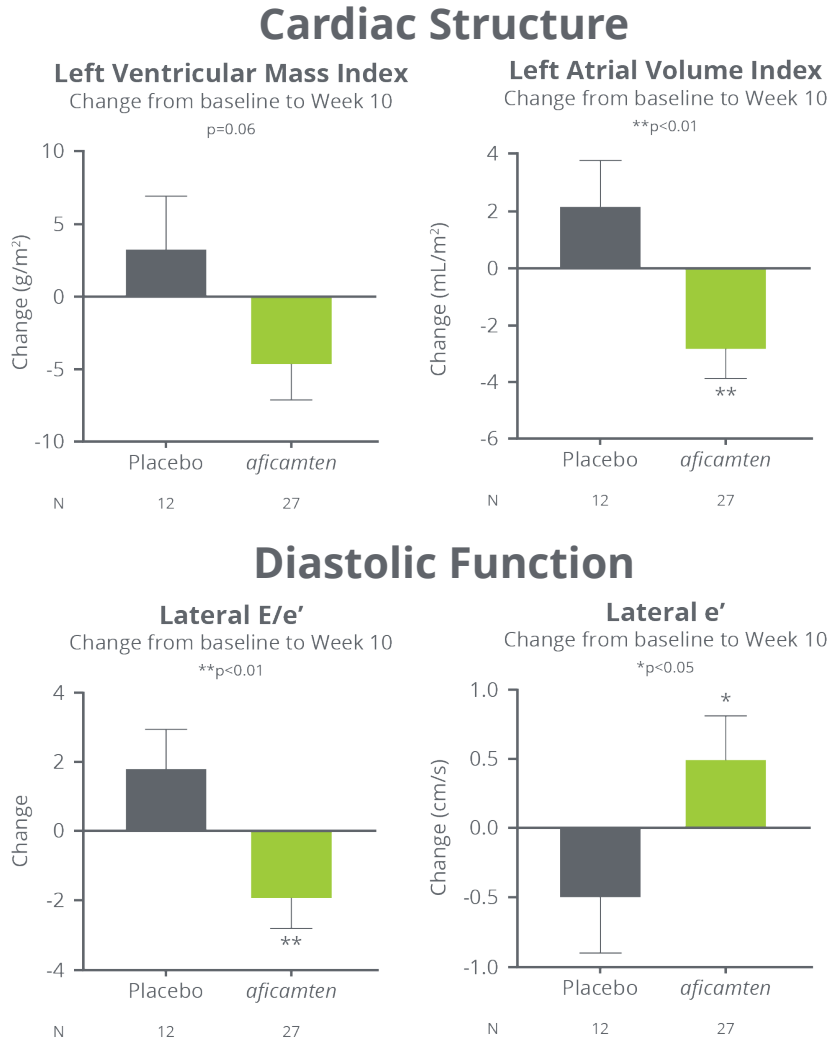
Maron M, Abraham T, Masri A, et al. "REDWOOD-HCM: A Randomized, Double-blind, Placebo-controlled, Dose-finding Trial of the Cardiac Myosin Inhibitor, Aficamten, In Obstructive Hypertrophic Cardiomyopathy". HFSA 2021.

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' ($p<0.05$))

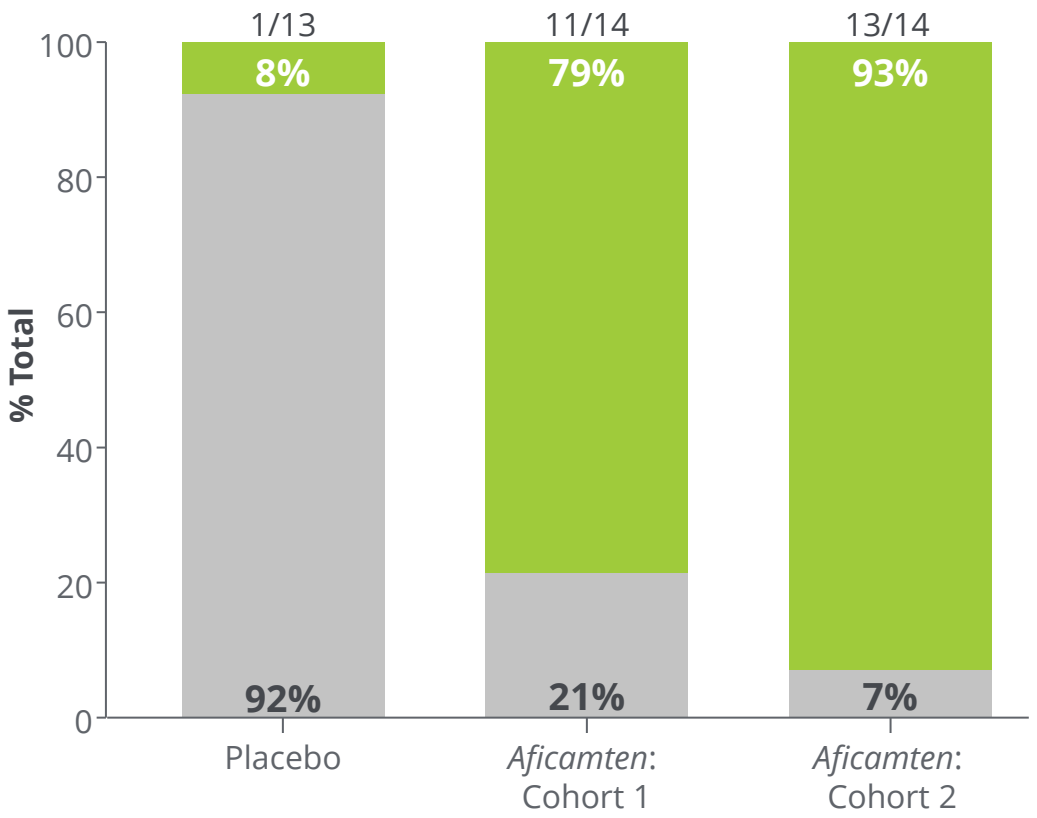


Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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.

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

Aficamten is an investigational agent 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

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

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

Cytokinetics®

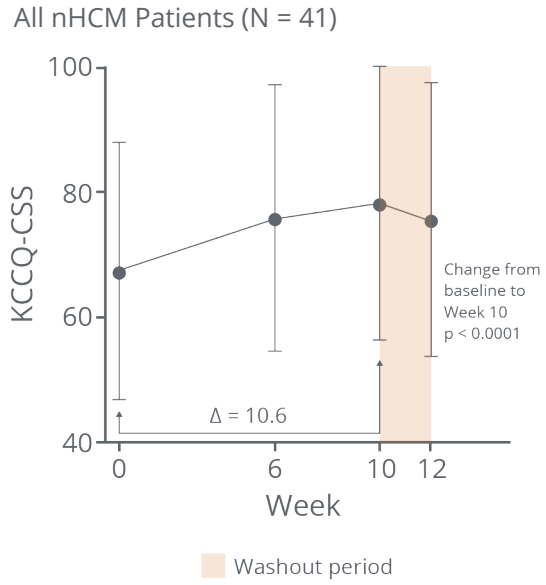
Significant Improvements in KCCQ & NYHA Class

Cohort 4

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

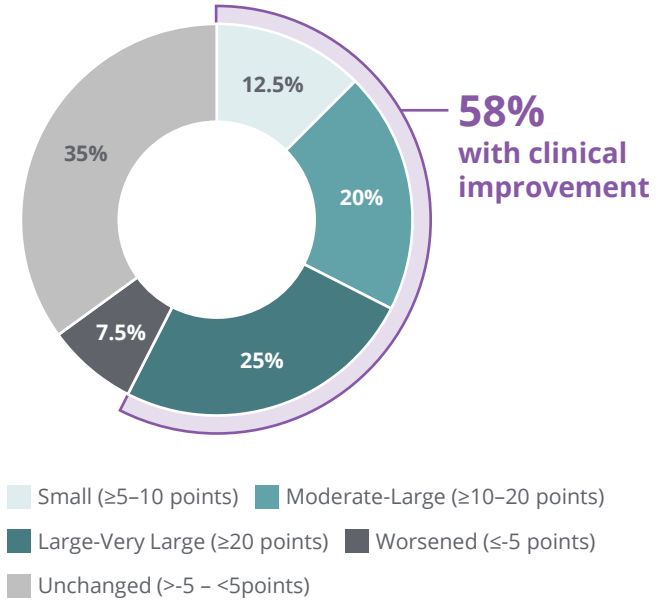
Kansas City Cardiomyopathy Questionnaire

Mean improvement in KCCQ of 10.6 points



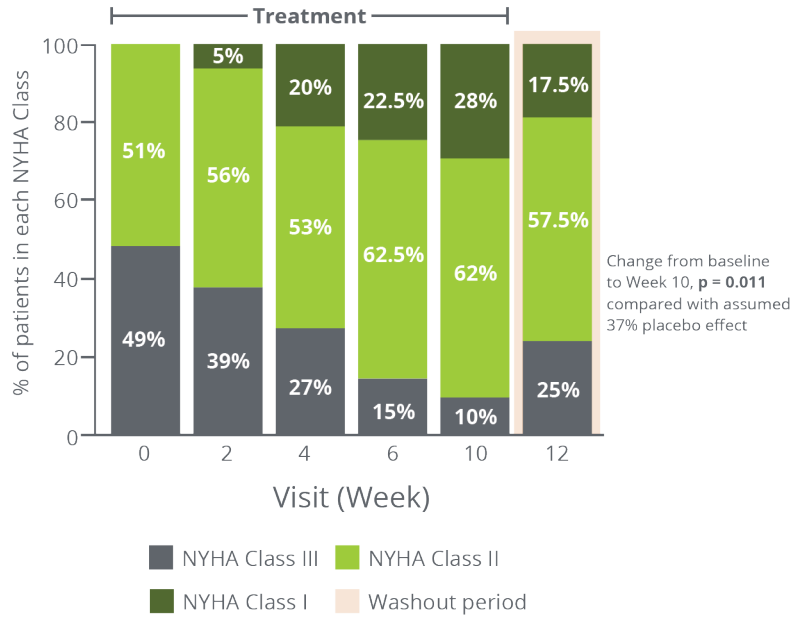
Data presented as mean and standard deviation

Categorical Changes at Week 10 in KCCQ-CSS



NYHA Functional Class

56% of patients improved by ≥1 NYHA class



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

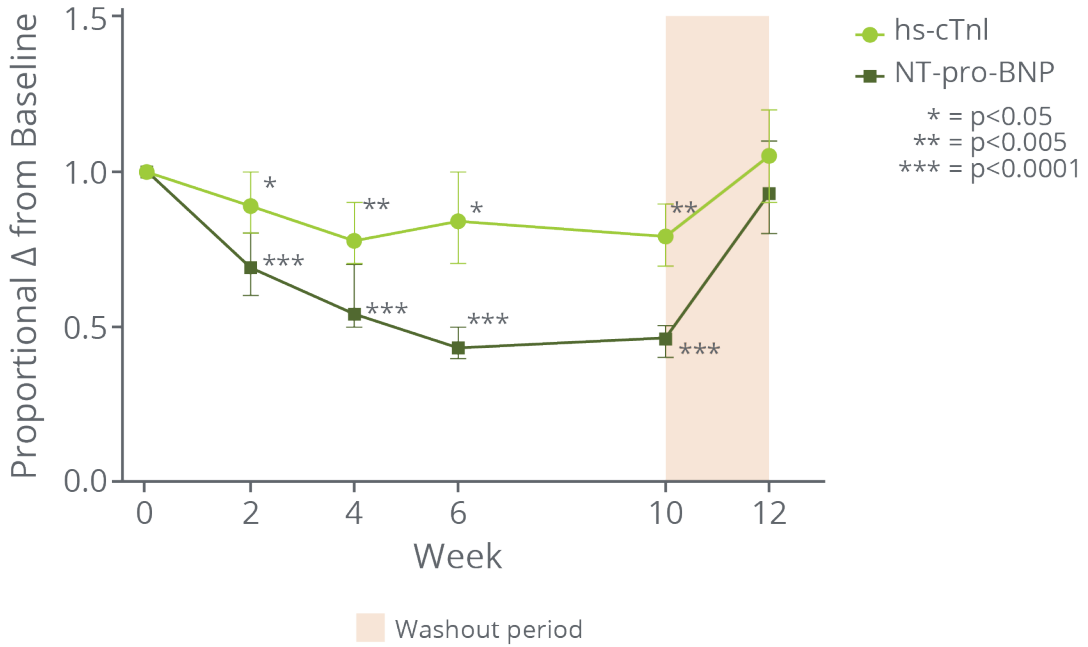
Masri A. et al. "*Aficamten* in Patients with Symptomatic Non-Obstructive Hypertrophic Cardiomyopathy (REDWOOD-HCM Cohort 4)". ESC HF 2023.

Change in Baseline in Biomarkers & Angina Frequency

Cohort 4

Proportional Change from Baseline in Cardiac Biomarkers

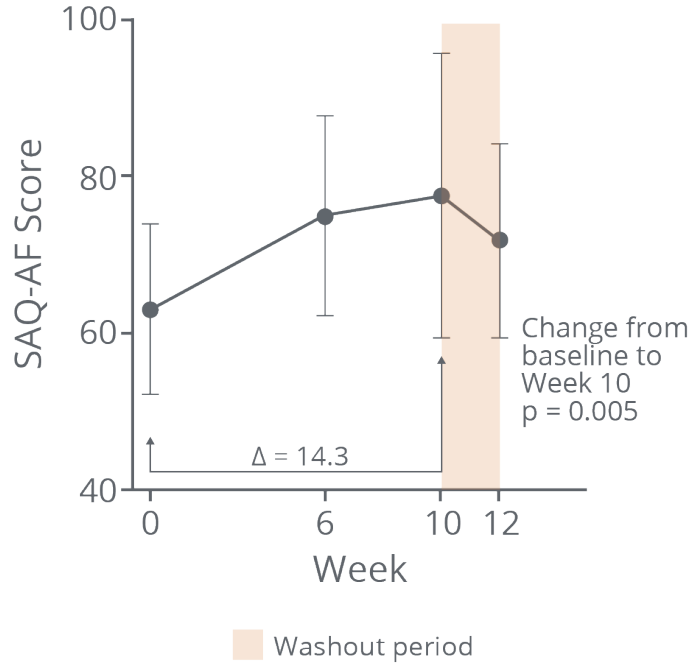
Mean reduction in high-sensitivity cardiac troponin of 21%
Mean reduction in NT-proBNP of 55%



Data presented as the mean proportional change and 95% CI

Seattle Angina Questionnaire Angina Frequency (SAQ-AF)

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



Data presented as mean and standard deviation

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

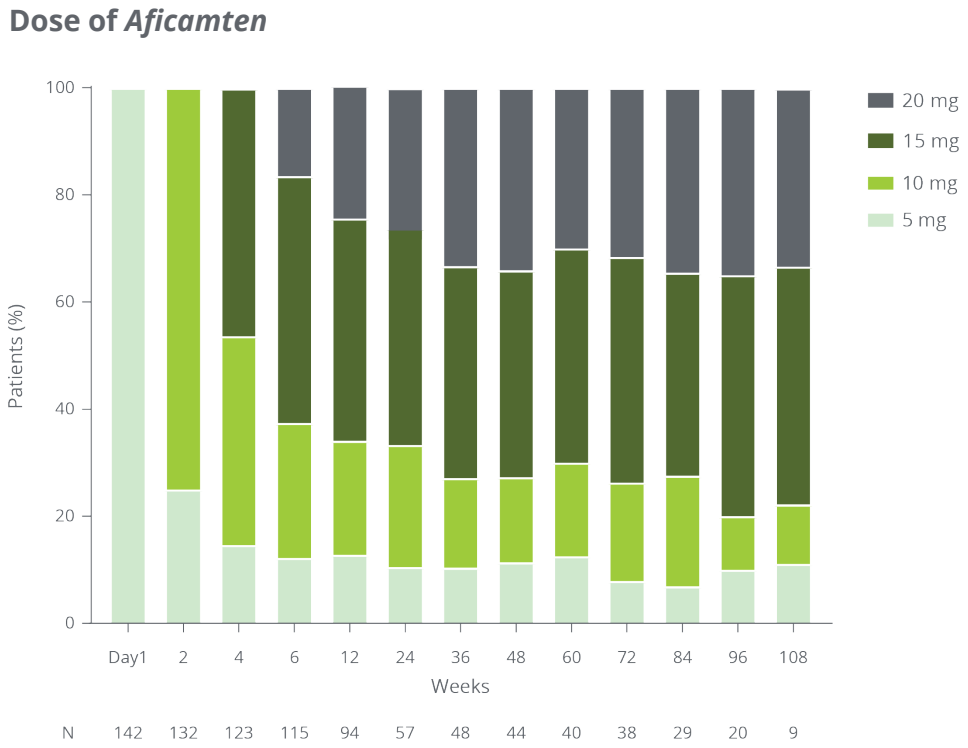
Masri A. et al. "*Aficamten* in Patients with Symptomatic Non-Obstructive Hypertrophic Cardiomyopathy (REDWOOD-HCM Cohort 4)". ESC HF 2023.

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/m2), 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)



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

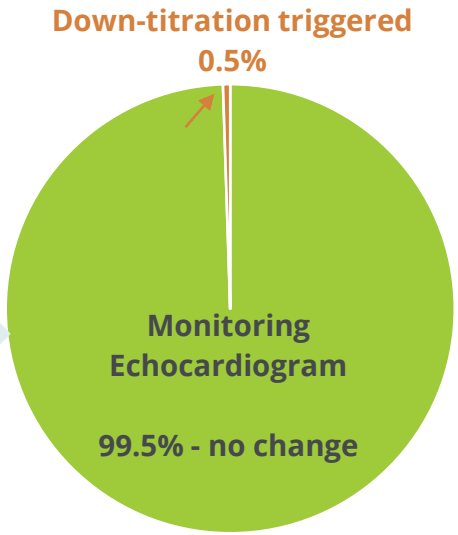
Few Dose Reductions During Maintenance

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.*

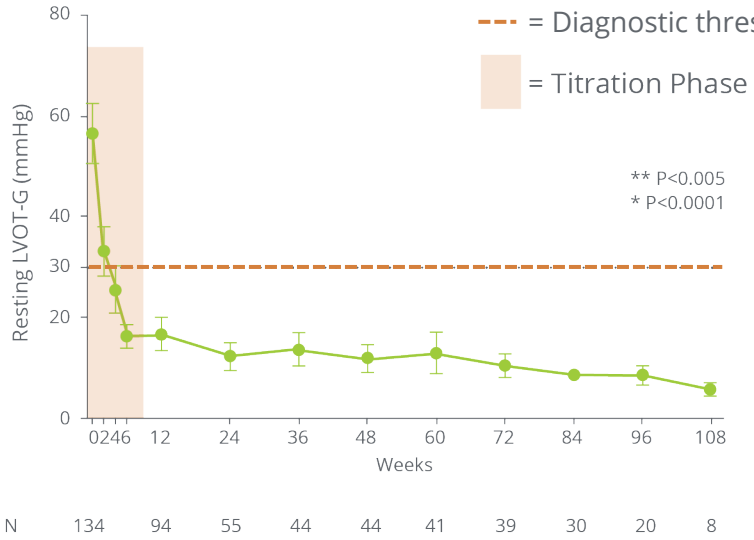
Cytokinetics®

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

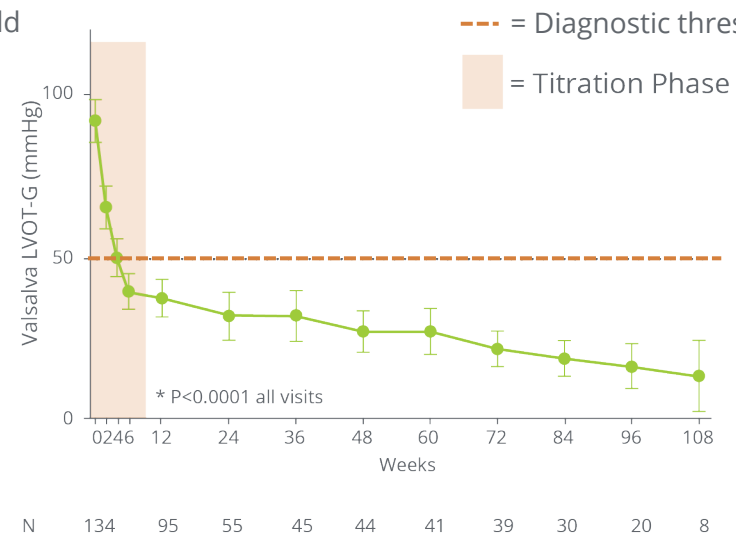
FOREST-HCM data cut as of September 15, 2023

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

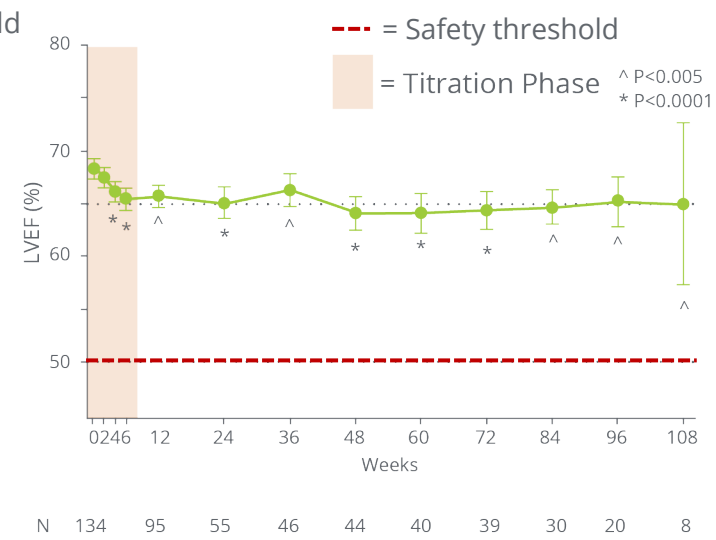
Resting LVOT Gradient



Valsalva LVOT Gradient



LVEF

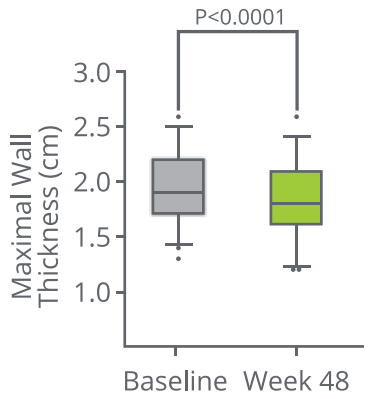


Aficamten **is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.**

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

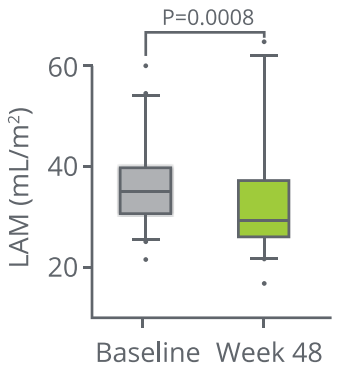
Maximal Wall Thickness

Data cut as of October 31, 2023



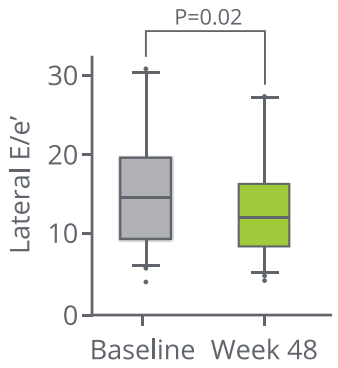
LA Volume Index

Data cut as of October 31, 2023



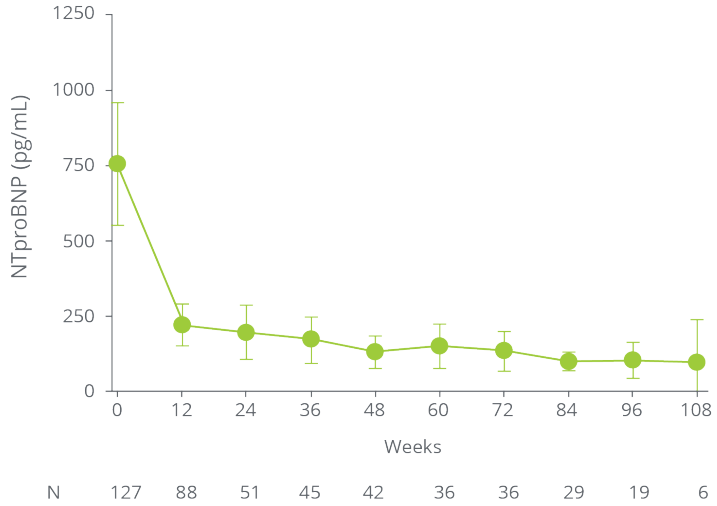
Lateral E/e'

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.**

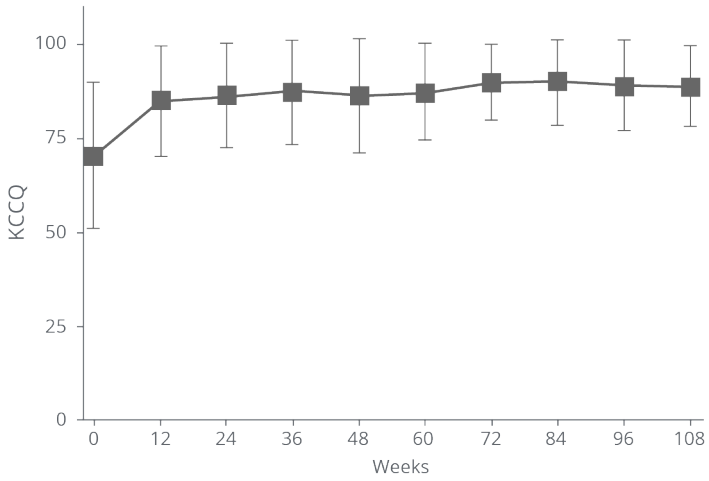
Observed Durable Effects of *Aficamten* on Clinical Endpoints

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

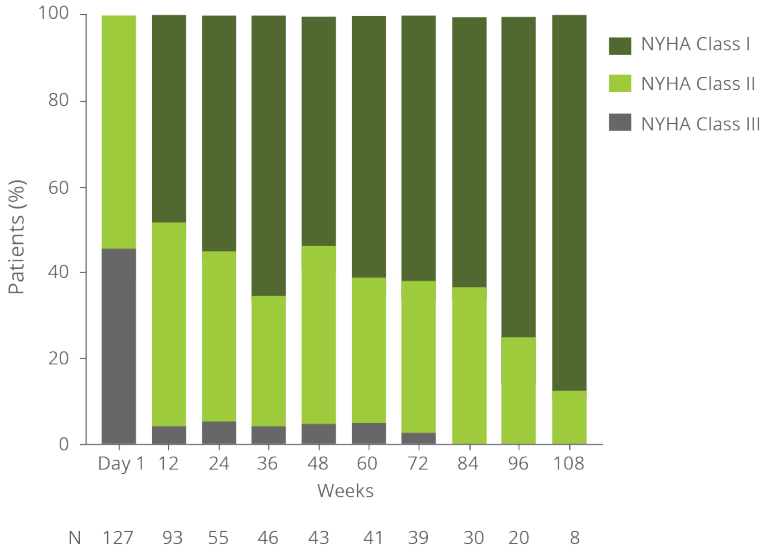


NYHA Class

Data cut as of September 15, 2023

~50% of patients were asymptomatic at 1 year

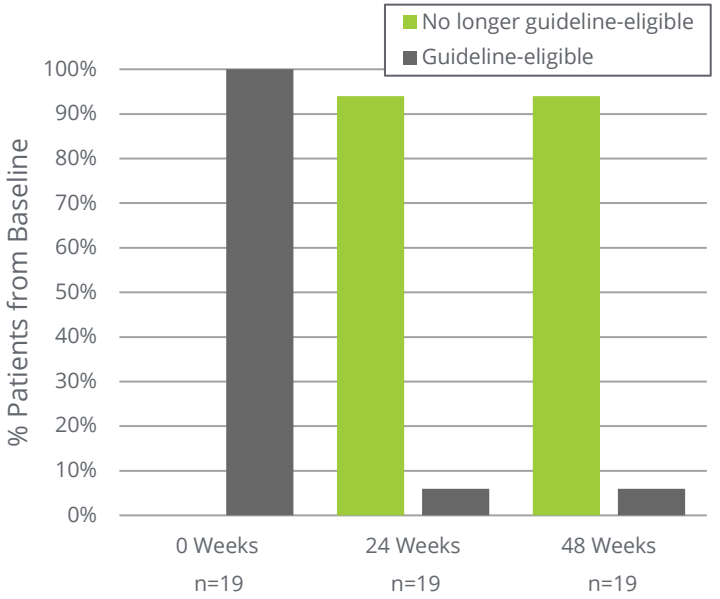
>80% of patients improved ≥1 NYHA Class at every visit after initiation of *aficamten*



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.**

Cytokinetics®

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

- **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

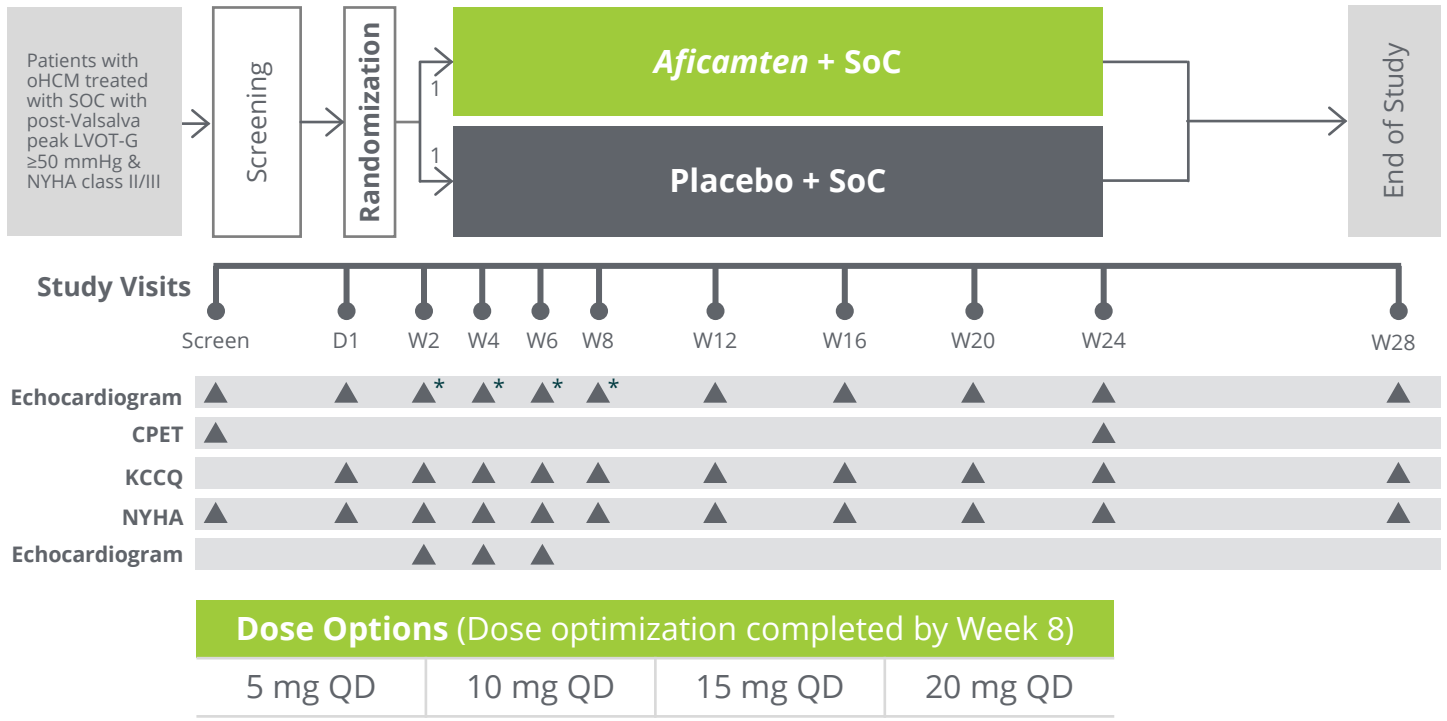
Announced positive topline results in December 2023; expect to present primary results in Q2 2024

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**

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*

Cytokinetics®

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 pVO_2 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**

SEQUOIA-HCM: Probability Values (p-value)

Endpoints	p-value
Primary Endpoint	
pVO_2 change from baseline to Week 24	<0.0001
Secondary Endpoints	
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

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]
Demographics	
Age, years	59.1 (12.9)
Female	114 (40.4)
Race/ethnicity[b]	
White	222 (78.7)
Black	3 (1.1)
Asian	53 (18.8)
Hispanic	9 (3.2)
Other	4 (1.4)
Region	
United States	94 (33.3)
China	46 (16.3)
Europe and Israel	142 (50.4)
Vital Signs	
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)
HCM History	
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]
HCM Medical Therapies	
Beta-blocker	172 (61.0)
Non-dihydropyridine calcium channel blocker	75 (26.6)
Disopyramide	36 (12.8)
HCM Symptoms	
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)
Comorbidities	
Hypertension[d]	136 (48.2)
Diabetes[e]	24 (8.5)
Permanent atrial fibrillation	1 (0.4)
Paroxysmal atrial fibrillation	40 (14.2)
CPET Metrics	
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)
Biomarker	
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
CCB, calcium channel blocker; DM, diabetes mellitus, including types 1 and 2; IQR, interquartile range

Preparing for Regulatory Submissions to FDA, EMA

SEQUOIA HCM

Positive Results from SEQUOIA-HCM

2024

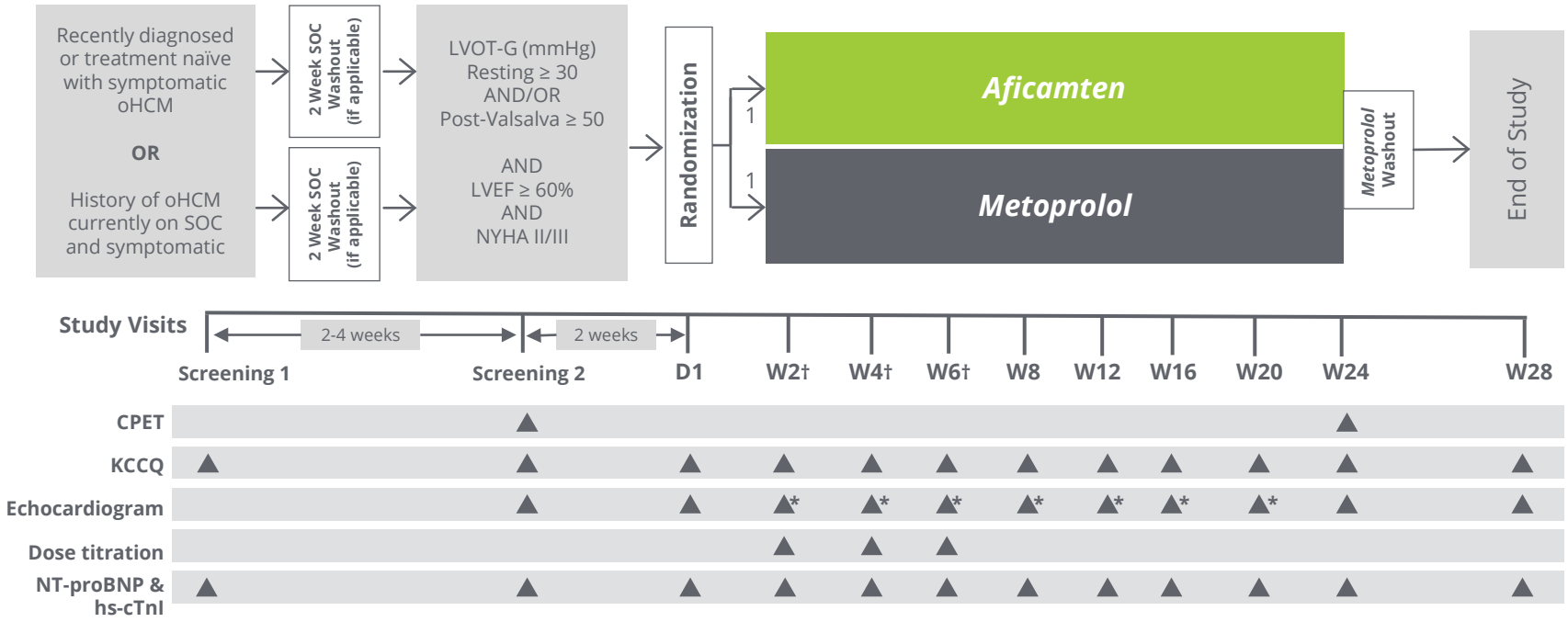
- **Met with FDA to review results from SEQUOIA-HCM** and **held pre-NDA meeting**
- **Meetings with EMA** in Q2 2024
- **Expect to submit NDA to FDA** in Q3 2024 and **MAA to EMA** in Q4 2024: development of all modules underway and manufacturing activities on track

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**

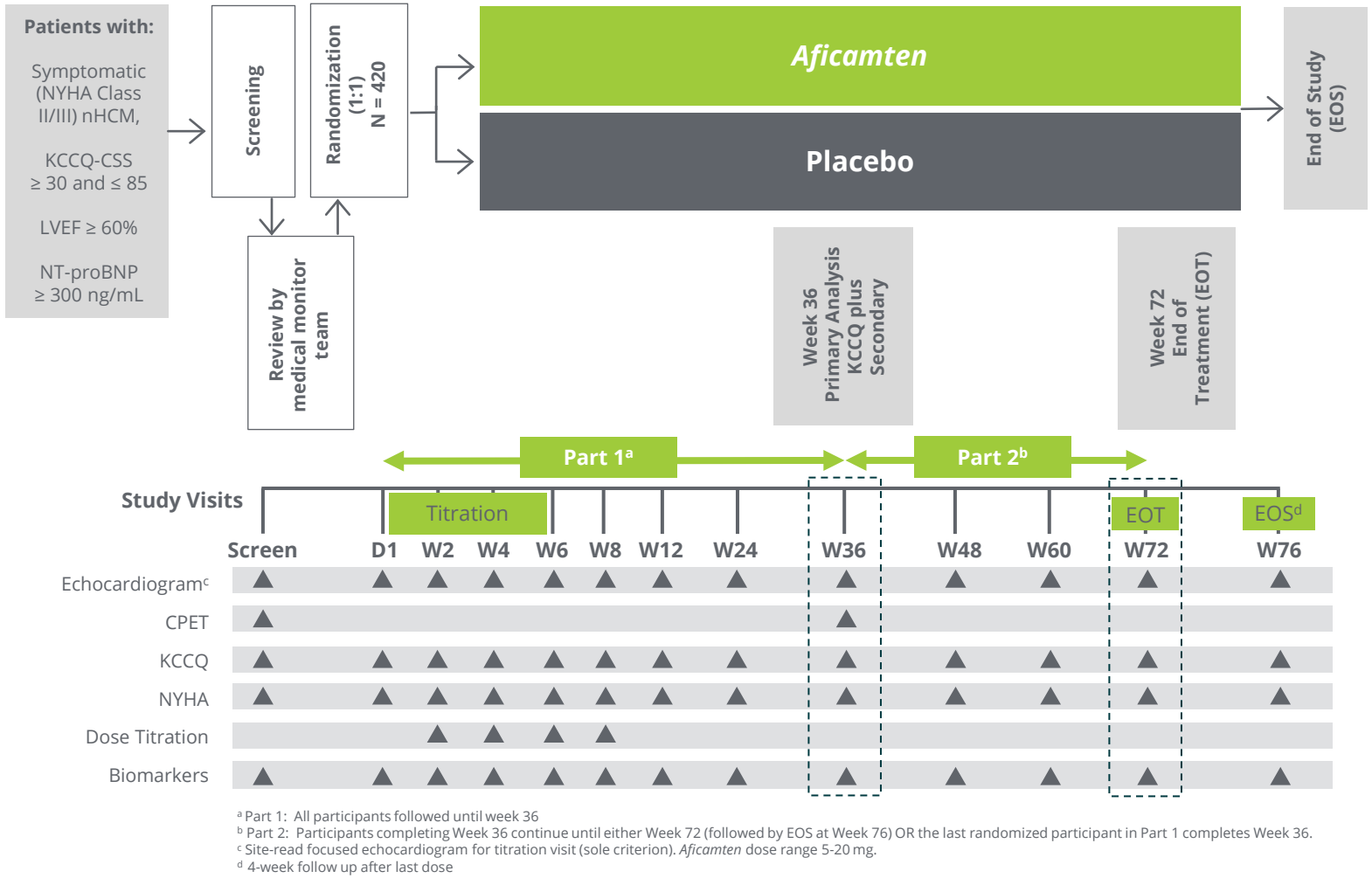


SOC: standard of care
** Focused echocardiogram*

ACACIA-HCM: Pivotal Phase 3 Trial in nHCM

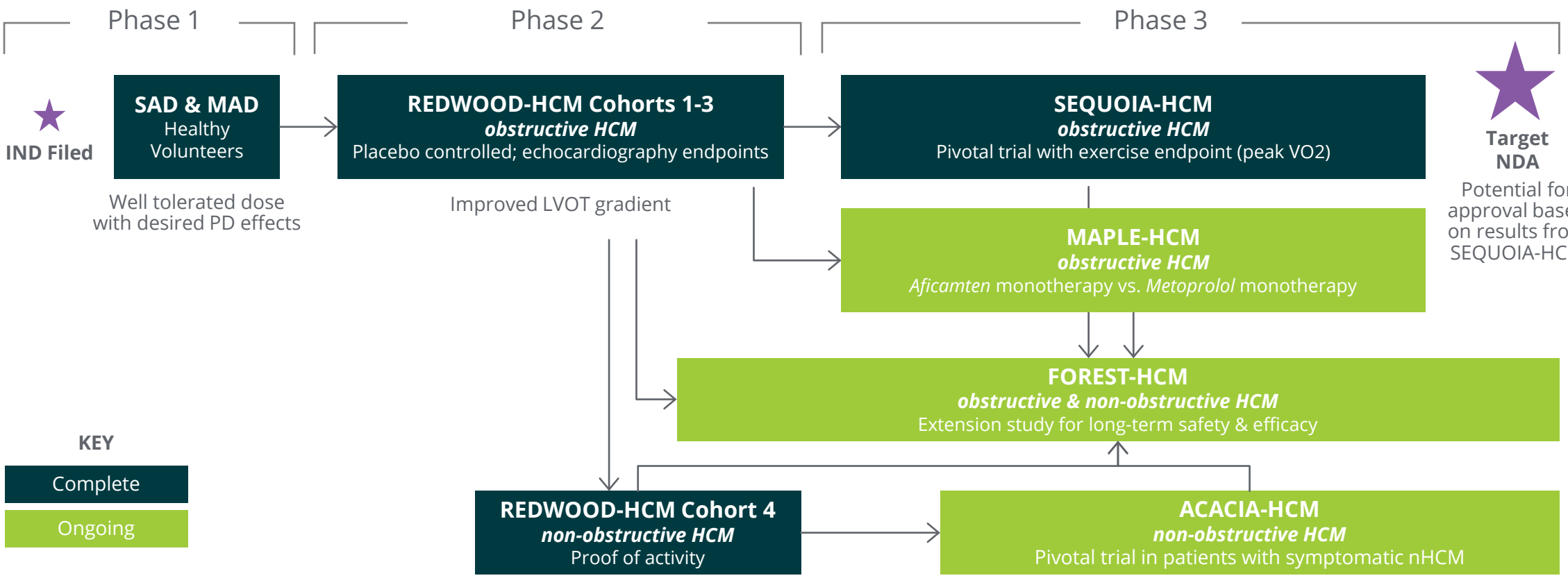
Currently enrolling

- 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



[a] Part 1: All participants followed until week 36
[b] Part 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.
[c] Site-read focused echocardiogram for titration visit (sole criterion). *Aficamten* dose range 5-20 mg.
[d] 4-week follow up after last dose

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.**

Cytokinetics®

Aficamten: Planned Commercial Approach

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

Learn	Design	Build
Leverage **deep understanding** of patients, HCPs, payers, and community	Engage with all stakeholders to design **an optimal customer experience**	Tap into deep functional experience to build **operational excellence** across launch functions

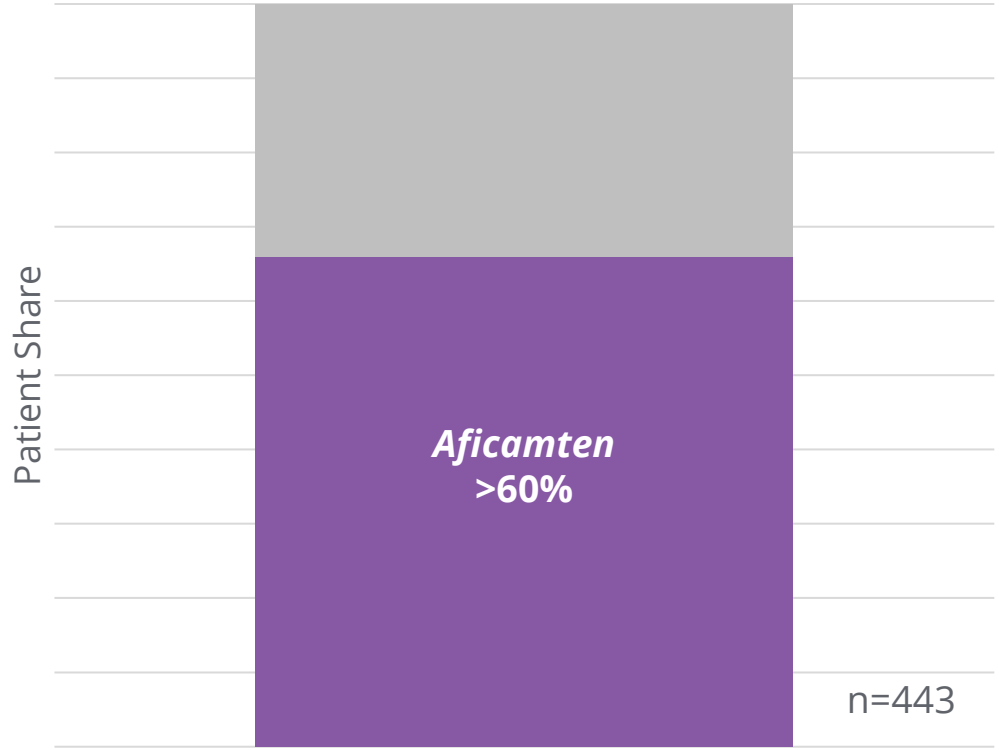
Our Focus in 2023 → **Our 2024 Focus**

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

Cytokinetics®

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

oHCM CMI Preference Shares in Eligible Patient Population*

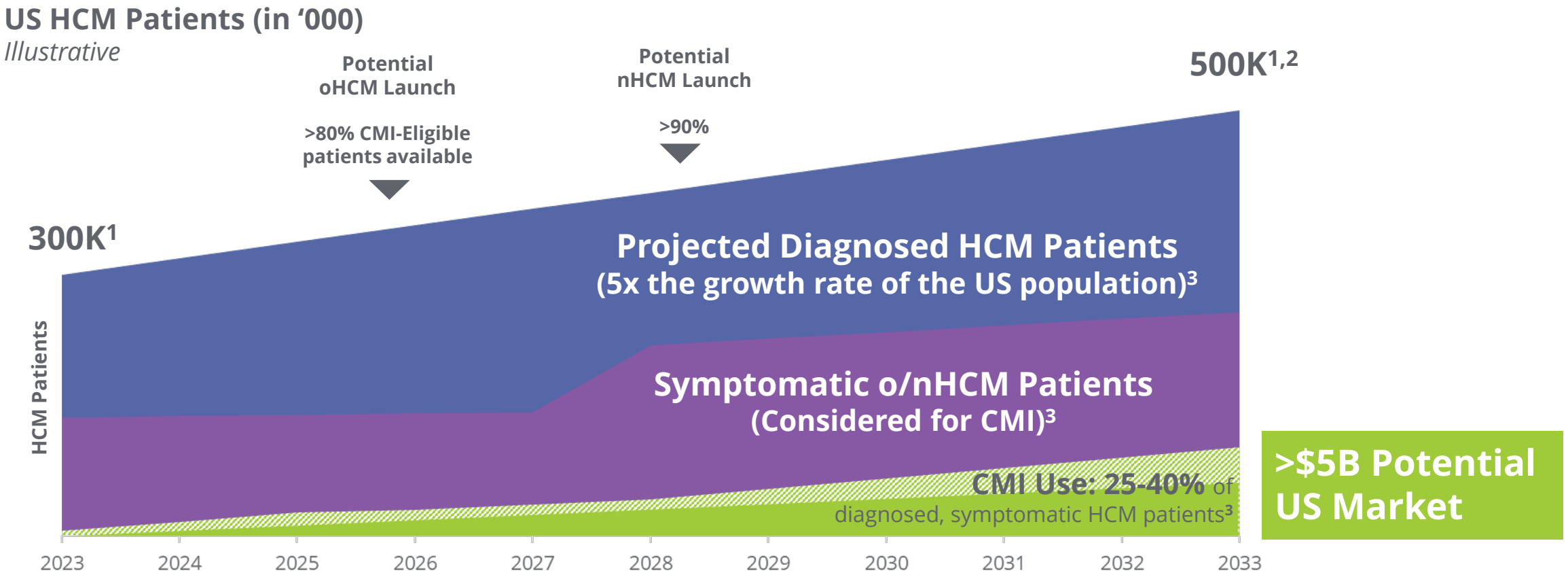


- Potential target product profile for *aficamten* interest creates **share opportunity** in newly treated CMI patients
- *Aficamten* is **also expected to expand the total CMI market**
- Key attributes that may drive preference include the potential for:
  - LVOT gradient reduction
  - Change in NYHA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

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

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



***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

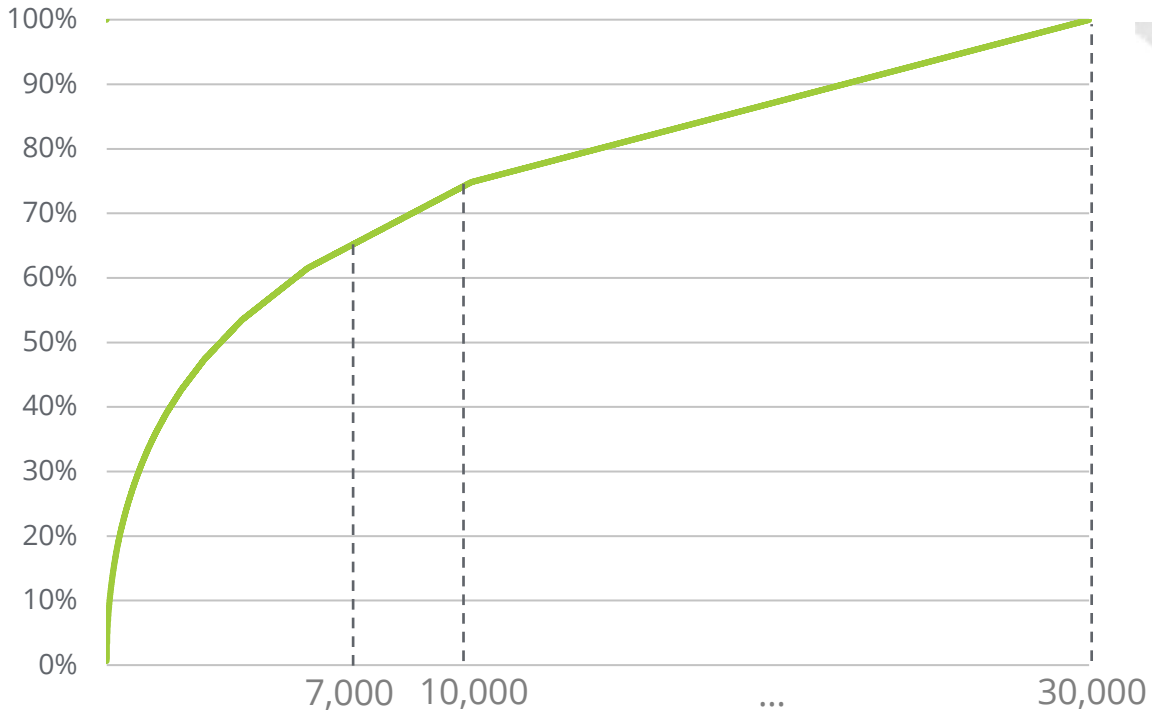
1. DoF: SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023);
2. Butzner et al 2021 estimated a 8% growth rate in diagnosed HCM patients between 2013-2019 https://www.ajconline.org/article/S0002-9149(21)00783-9/fulltext; CYTK is forecasting an average growth rate of 5% over the coming decade;
3. Internal forecasts

Cytokinetics®

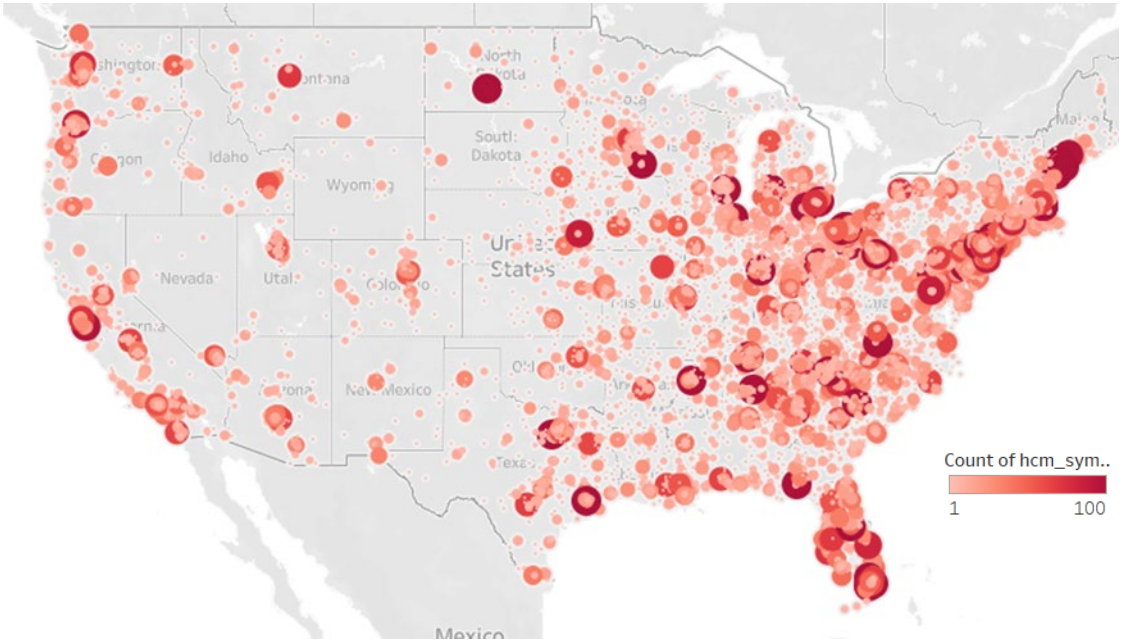
Cardiologists Located in Concentrated Geographic Clusters Across the US

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

HCM Patient Concentration by Cardiologist



Geographic Distribution of HCM Patients



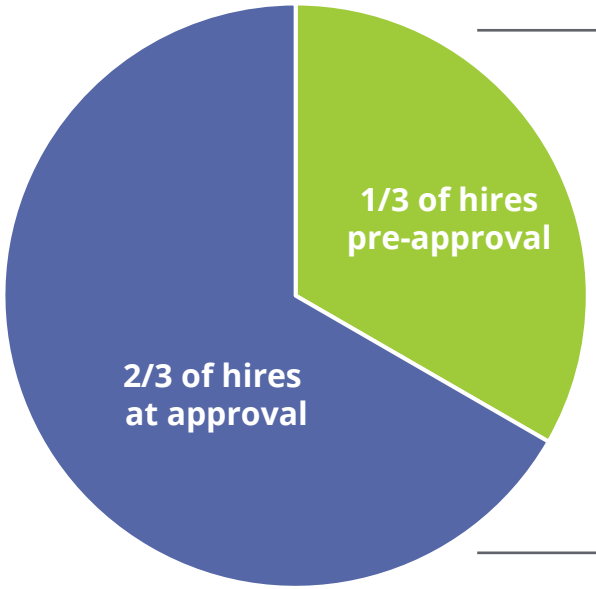
Aficamten **is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.**
Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients
Source: Symphony PTD (Patient Transaction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

Cytokinetics®

Gated Build of Commercial Infrastructure

Majority of spending to occur closer to approval in 2025

2/3 of hiring to occur at-approval



Commercial leadership
Marketing
HEOR
Patient services
Access & distribution
Field operations
Commercial learning & development
Sales team leadership

Sales representatives

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

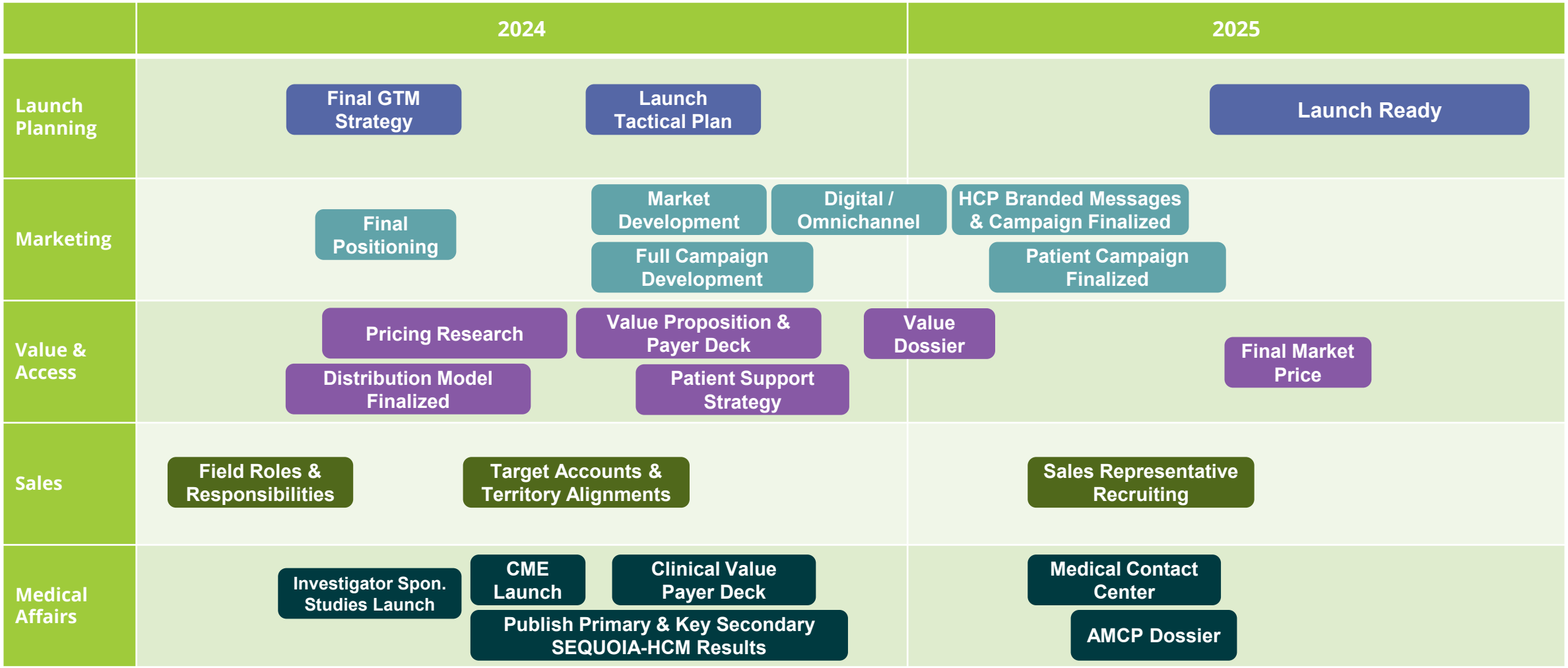
Media purchases
Patient support programs
Peer to peer engagement
HCP Omnichannel launched

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

Cytokinetics®

US Commercial Readiness Milestones for *Aficamten*

2024-2025



Cytokinetics®

Omecamtiv Mecarbil

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

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

2024

- Continue to pursue **approval** of *omecamtiv mecarbil* in Europe

Cytokinetics®

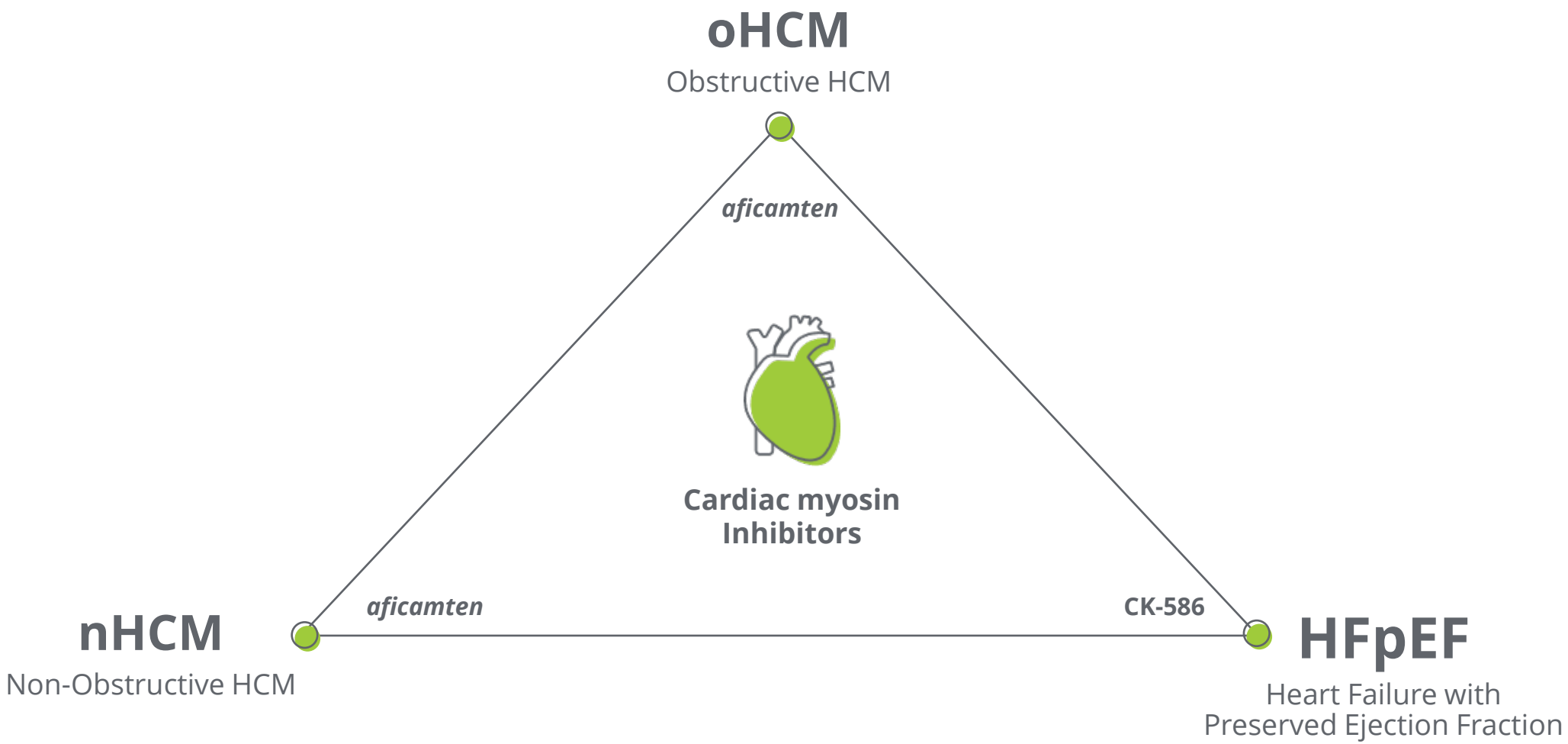
Emerging Cardiovascular Pipeline

CK-586 & CK-136

Cytokinetics®

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 products have not been established.

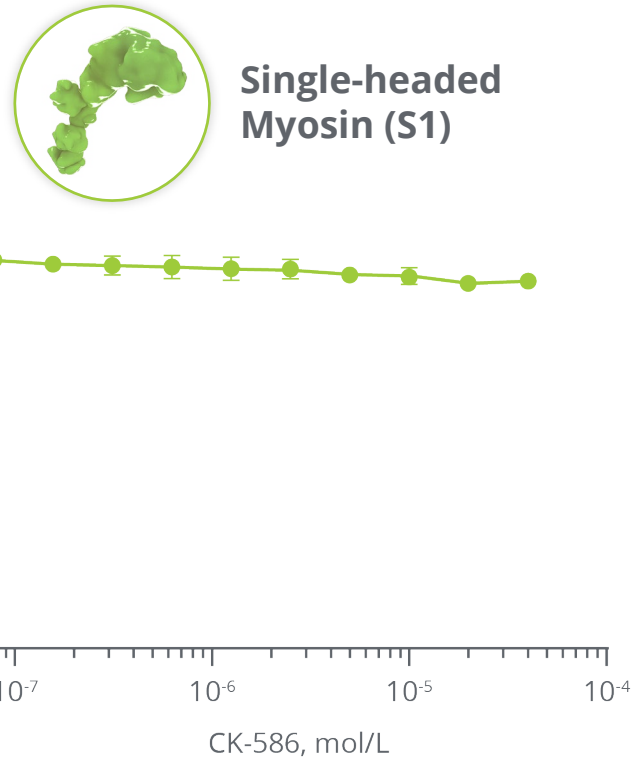
Novel Approach May Address Multiple Unmet Patient Needs

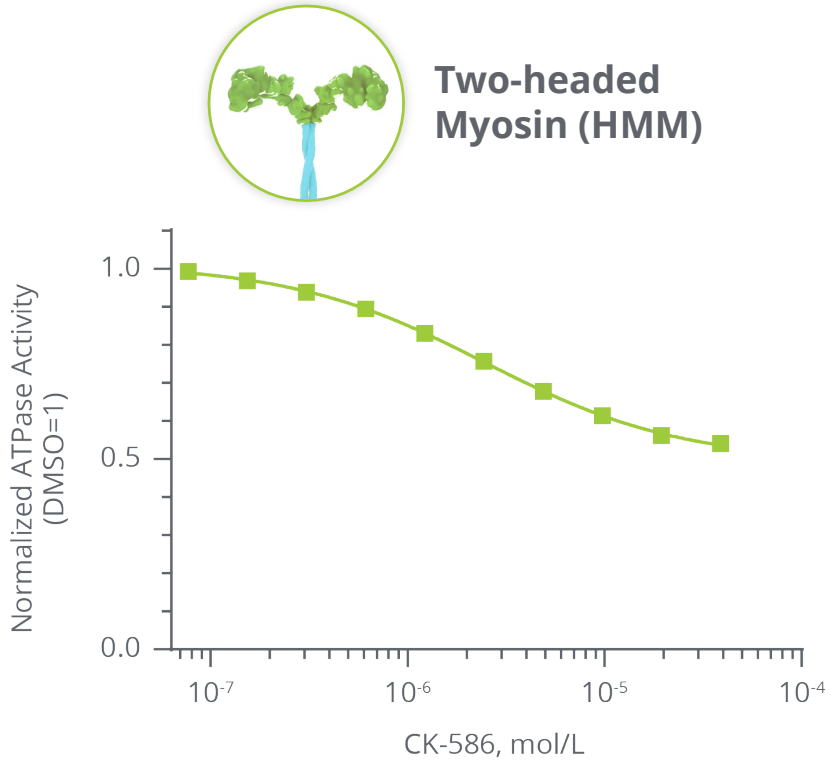


Cytokinetics®

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

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





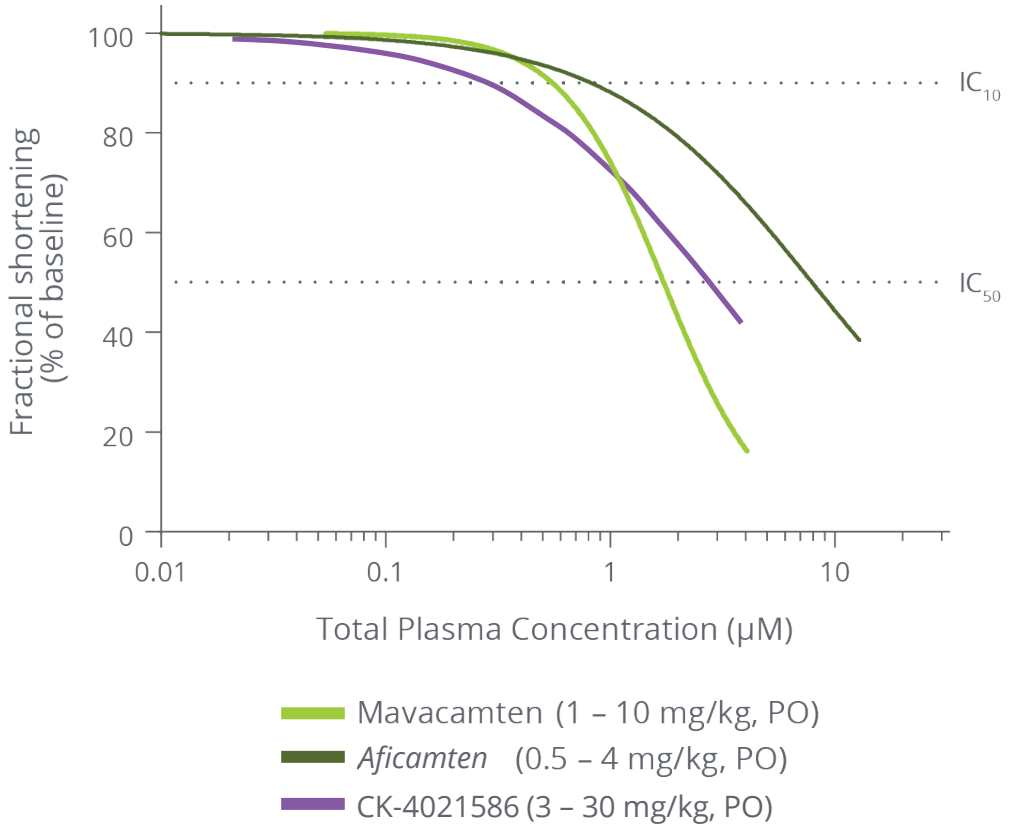
Based on preclinical testing

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

Cytokinetics®

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
aficamten	9.9x
CK-586	9.3x

IC_{10}: plasma concentration at 10% relative reduction in fractional shortening
IC_{50}: plasma concentration at 50% relative reduction in fractional shortening

Compound half-life in humans	Actual	Predicted
aficamten	~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.

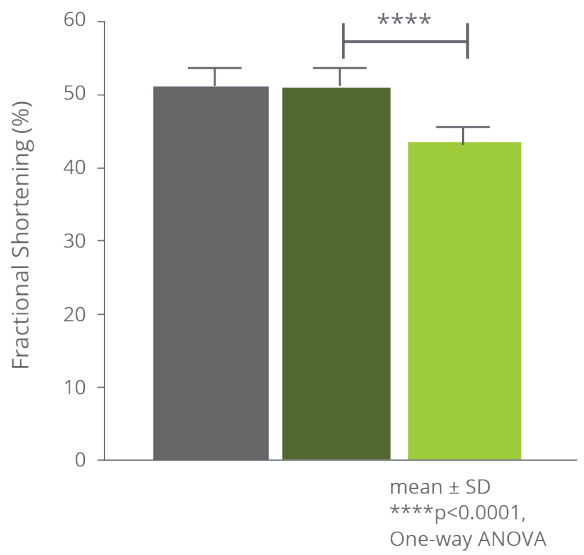
Cytokinetics®

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

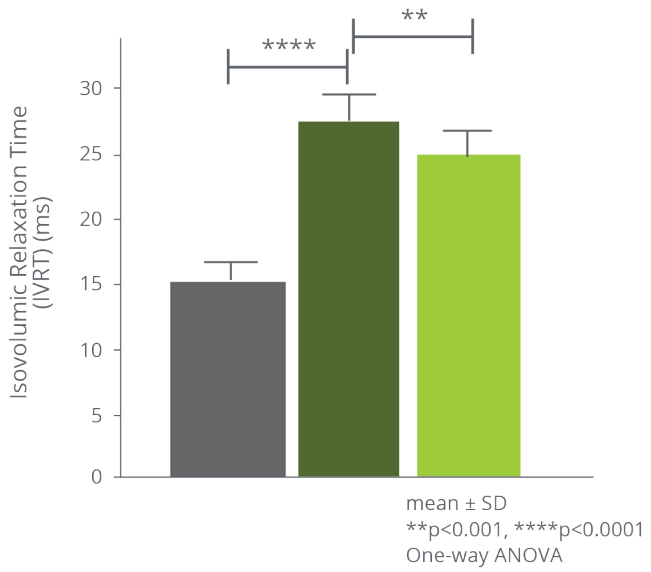
Model is representative of hypertensive, diabetic, metabolic aspects of HFpEF

10 weeks of treatment improved diastolic function and reduced cardiac fibrosis

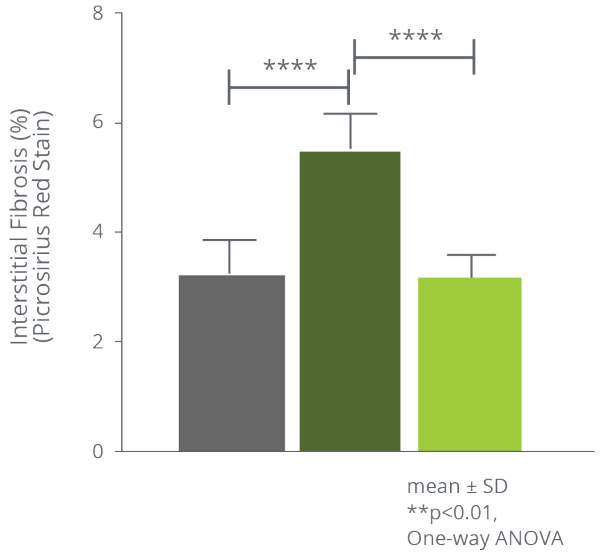
Reduced Fractional Shortening



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.

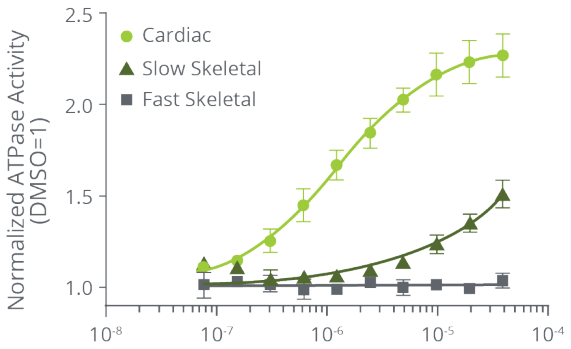
Cytokinetics®

CK-136: Mechanism of Action

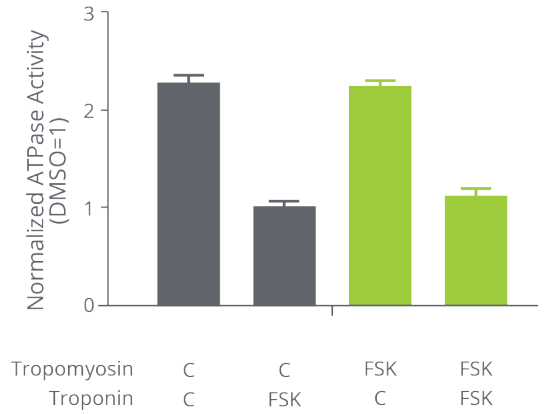
Key biochemical and cellular features

The first selective cardiac troponin activator

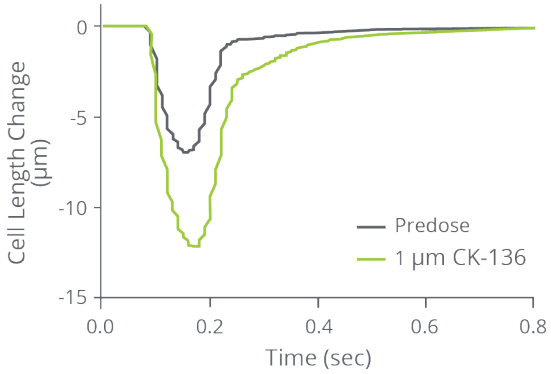
Greater ATPase Activity



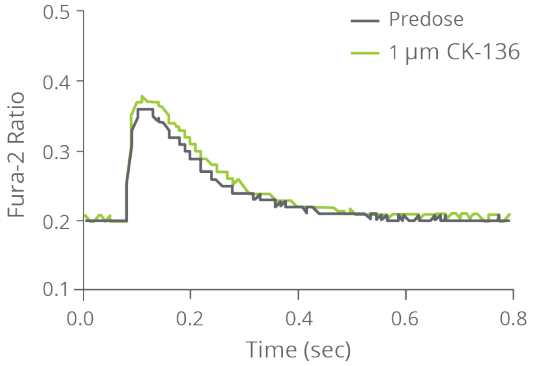
Greater ATPase Activity



Contractability Strongly Activated After Treatment



Calcium Transients Unchanged After Treatment



[1]PD 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.

Cytokinetics®

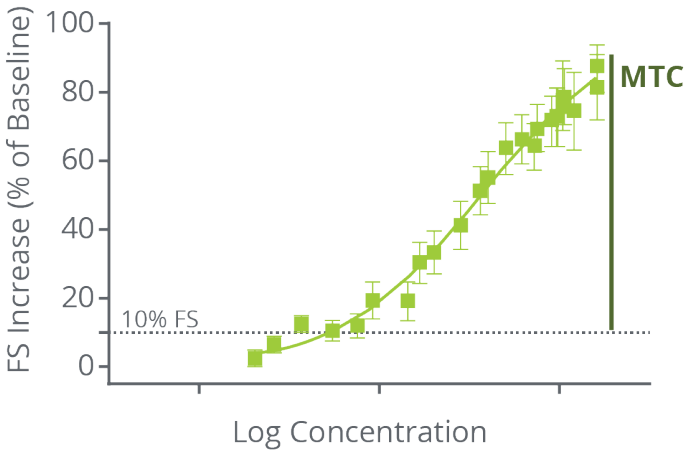
CK-136: Exposure Response Relationship

Exposure-response of troponin activator is shallower than myosin activator

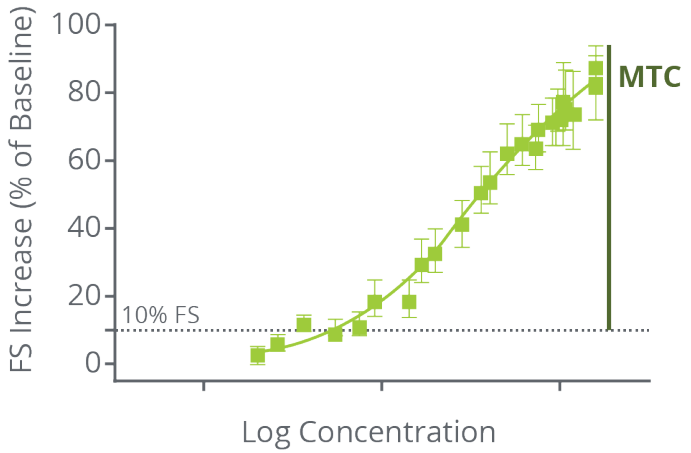
Analyzing single ascending dose data from Phase 1 study

Animal Models of Cardiac Function

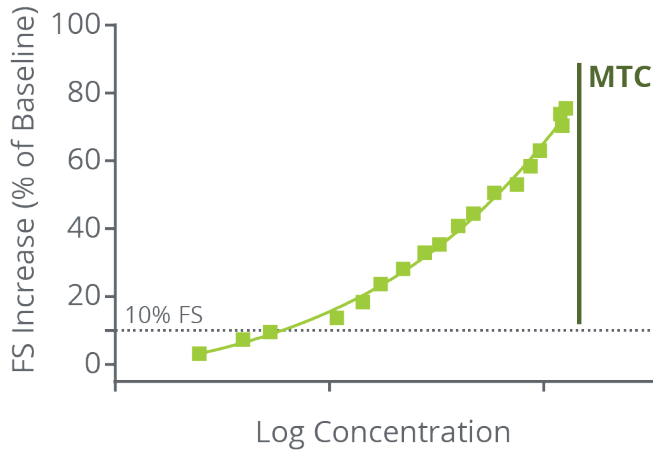
Healthy Rats PD Window[1]
≥15X



MI Rats PD Window[1]
≥15X



Healthy Dogs PD Window[1]
≥15X



[1]PD 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.

Cytokinetics®

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

- **SEQUOIA-HCM:** Positive Phase 3 results
- **MAPLE-HCM:** Phase 3 monotherapy trial in oHCM ongoing
- **ACACIA-HCM:** Phase 3 trial in nHCM ongoing
- **FOREST-HCM:** OLE ongoing

Heart Failure

Omecamtiv mecarbil

- Pursuing approval in Europe

CK-586

- Phase 1 study ongoing

CK-136

- Phase 1 study ongoing

Ongoing R&D

Additional research in muscle biology, energetics & metabolism

Foundations

~415

Full time employees

As of February 2024

~$655M*

At Q4 2023

***Approximately* 2 years**

of cash runway based on 2024 Financial Guidance

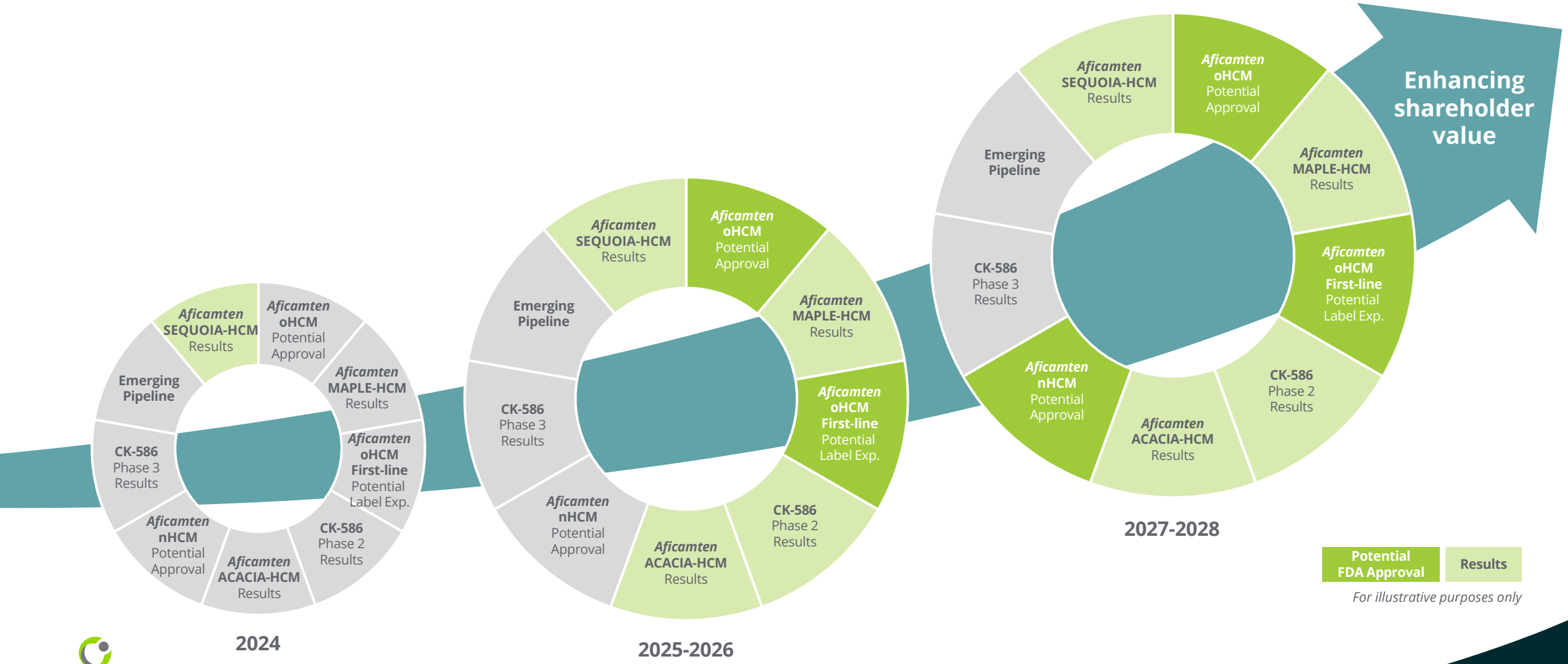
Timelines and milestones reflect Cytokinetics' current expectations and beliefs

**As of Q4 2023 10-K filing on 2/28/2024; not inclusive of net proceeds of $93.6 million from the issuance of 1,237,460 shares of our common stock under the Amended ATM Facility during the period January 1, 2024 through and inclusive of February 27, 2024*

Cytokinetics®

Expected Value Unlocked with Future Catalysts

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



Cytokinetics®

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

2023 Condensed Balance Sheet

As of 12/31/2023

in millions

	Total
Cash and investments	$655.4*
Accounts receivable	$1.3
PPE	$68.7
Leased assets	$79.0
Other assets	$19.9
Total Assets	**$824.3**
Convertible Debt, net	$549.0
Liability related to sale of future royalties	$380.0
Lease liability	$138.3
Other liabilities	$143.3
Total Liabilities	**$1,210.6**
Working capital	$525.4
Accumulated deficit	($2,112.2)
Stockholders' deficit	($386.3)
Wtd Avg Basic Shares Outstanding (million)	**96.5**

2024 Financial Guidance

in millions

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

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

**As of Q4 2023 10-K filing on 2/28/2024; not inclusive of net proceeds of $93.6 million from the issuance of 1,237,460 shares of our common stock under the Amended ATM Facility during the period January 1, 2024 through and inclusive of February 27, 2024*

Cytokinetics®

Expected 2024 Milestones

Aficamten

- **Present primary results from SEQUOIA-HCM** at HFA in Q2 2024
- **Submit NDA to FDA** in Q3 2024 and **MAA to EMA** in Q4 2024
- **Complete enrollment in MAPLE-HCM** in Q3 2024
- **Continue enrollment of ACACIA-HCM**

Omecamtiv Mecarbil

- Continue to **pursue approval** for *omecamtiv mecarbil* in Europe

Emerging Pipeline

- **Share data from Phase 1 study of CK-586** in Q2 2024
- **Initiate Phase 2 study of CK-586** in Q4 2024
- **Complete the Phase 1 study of CK-136** in Q1 2024

***Aficamten*, *omecamtiv mecarbil*, CK-586 and CK-136 are investigational drugs and have not been approved. *Their* safety and efficacy have not been established.**

Cytokinetics®

Cytokinetics®

thank you

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