



empowering empowering HVES

Sarcomere directed therapies

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Our Mission

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



Achieve regulatory approvals for at least two drugs arising from our pipeline

Build commercial capabilities to market and sell our medicines reflective of their innovation and value

Generate sustainable and growing revenues from product sales

• Double our development pipeline to include ten therapeutic programs

• Expand our discovery platform to muscle energetics, growth and metabolism

Be the science-driven company people want to join and partner with

Our vision is to be the

leading muscle biology

biopharma company that meaningfully improves the lives of patients with diseases of impaired muscle function through access to our

pioneering medicines

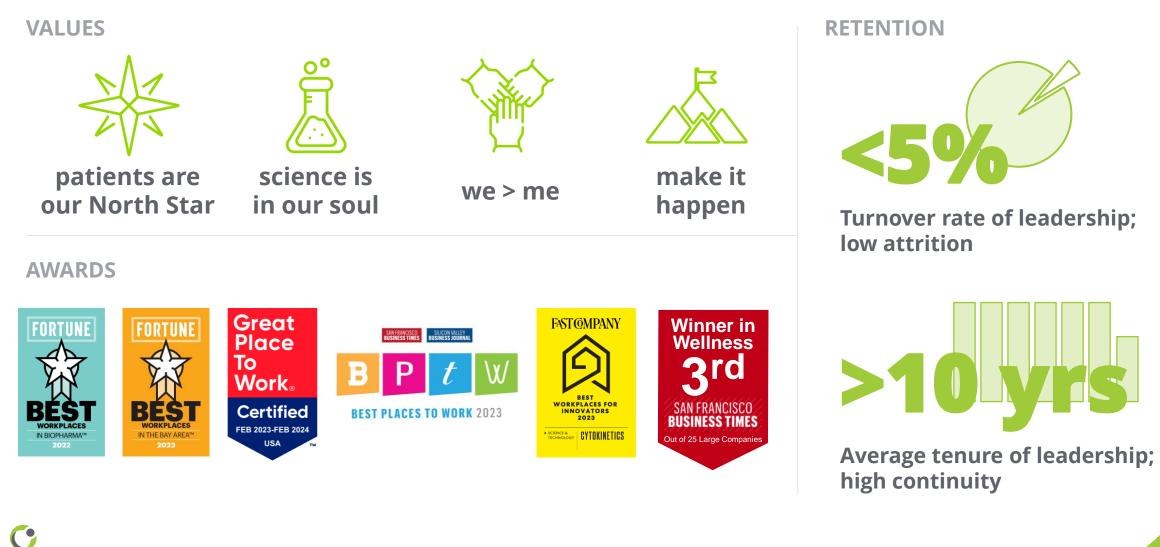
2025 Leading with Science, Delivering for Patients

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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

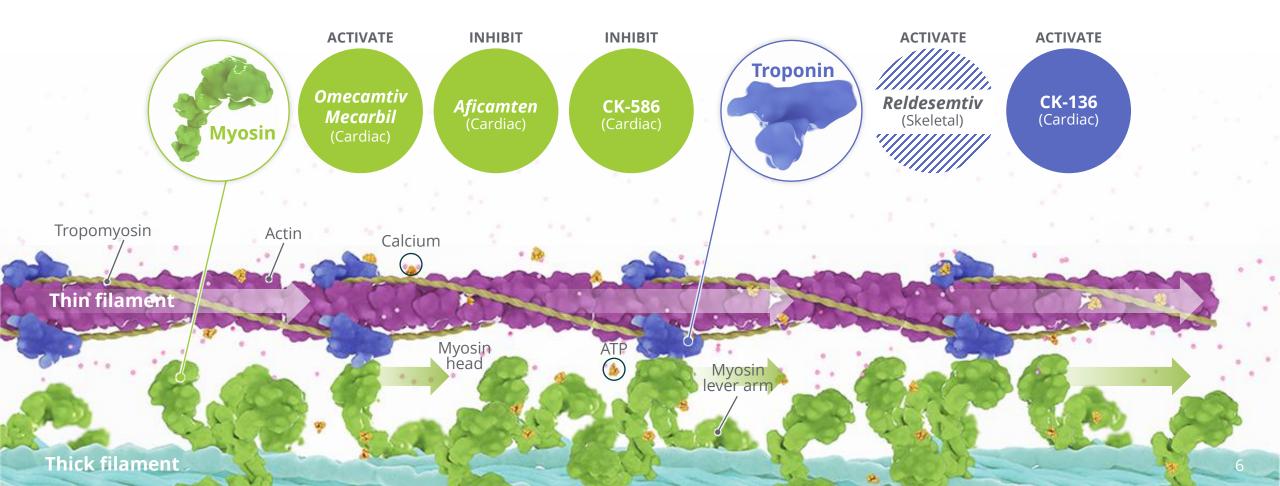
A Great Place to Work; Uncommon Continuity of Team



Cytokinetics

Sarcomere Directed Drug Development

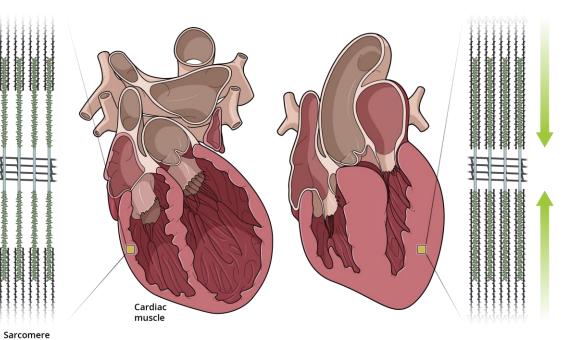
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables myocytes to contract and generate force



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

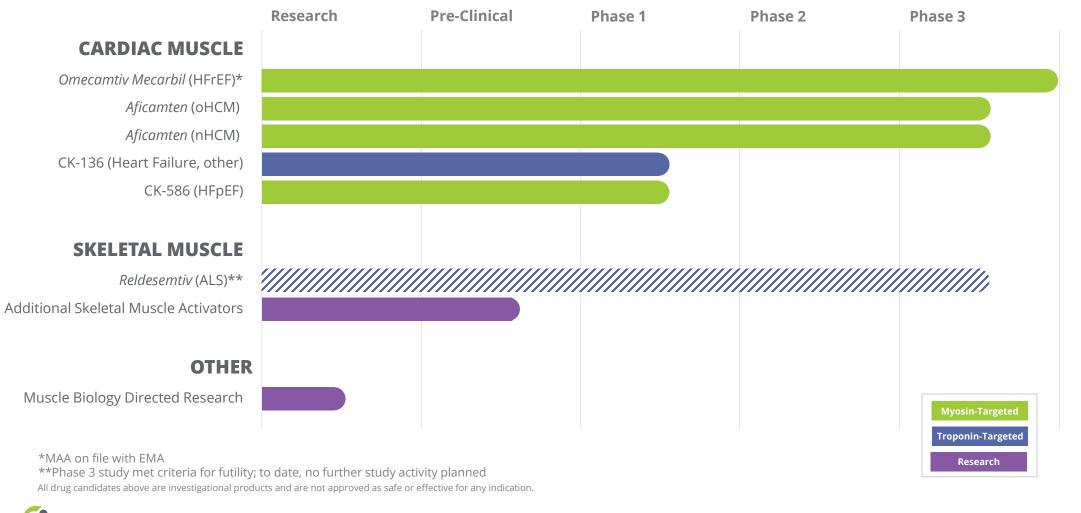


Increased / Preserved Cardiac Contractility

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



Pipeline of Novel Muscle-Directed Drug Candidates



Sarcomere Directed Drug Development

Specialty Cardiovascular Portfolio

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



Omecamtiv mecarbil , aficamten, CK-136 and CK-586 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.

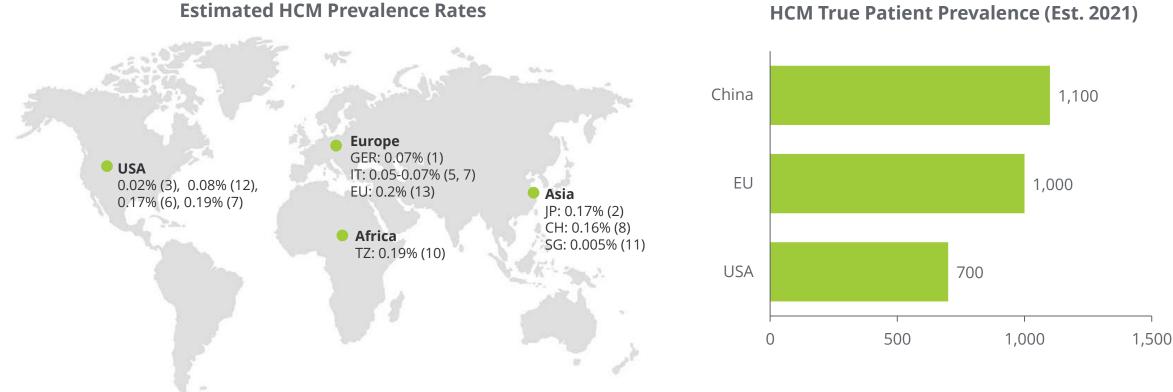
Aficamten



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

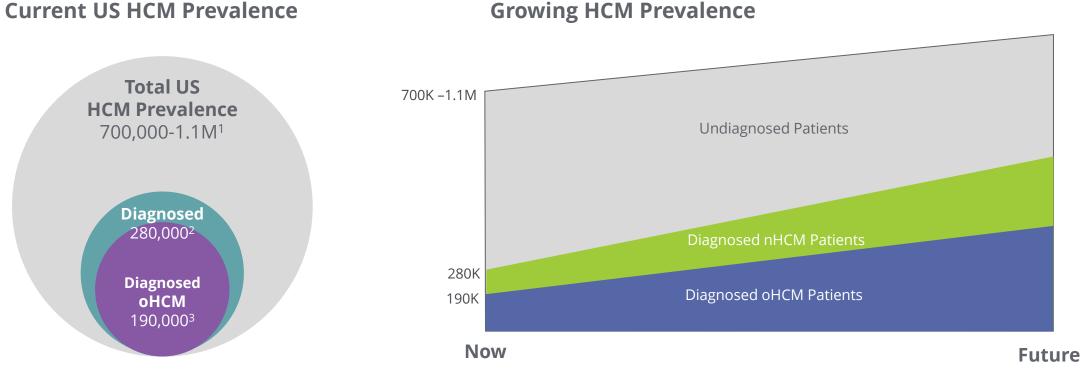
HCM prevalence estimates vary across geography and over time



Source: 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



In US, Large HCM Population With Many Undiagnosed 280K Diagnosed HCM Patients; Estimated 400-800K Undiagnosed



Growing HCM Prevalence

nHCM: non-obstructive HCM: oHCM: obstructive HCM

1. CVrg: Heart Failure 2020-2029, p 44; Maron et al. 2013 DOI: 10.1016/S0140-6736(12)60397-3; Maron et al 2018 10.1056/NEJMra1710575

2. Symphony Health 2016-2021 Patient Claims Data DoF;

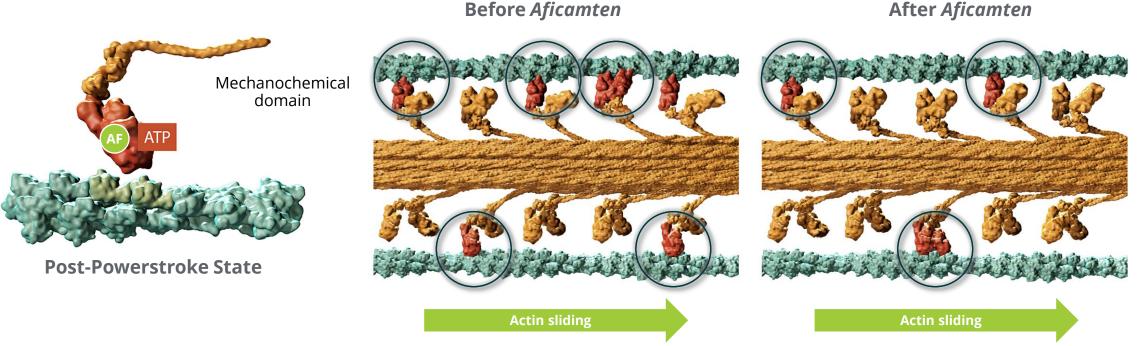
Maron MS, Hellawell JL, Lucove JC, Farzaneh-Far R, Olivotto I. Occurrence of Clinically Diagnosed Hypertrophic Cardiomyopathy in the United States. Am J Cardiol. 2016; 15;117(10):1651-1654.



Aficamten: 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.

Aficamten: Aspirational Target Profile Potential next-in-class cardiac myosin inhibitor

Rapid Onset	Precise Dosing	Simplicity of Use	Rapid Reversibility
Symptom relief as early as within 2 weeks initiation and dose adjustment possible biweekly if indicated	Echo guided dose titration allows both dose increases and decreases at the patient visit	No off-target effects and use in combination with β-blockers, CCB, Disopyramide, and/or Ranolazine	Washout of pharmacodynamic effect within 2 weeks

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

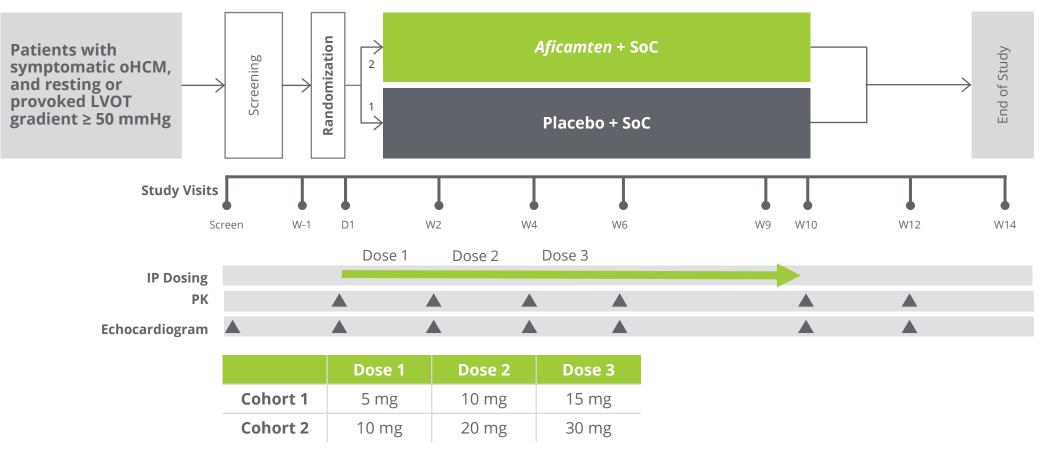


REDWOOD-HCM: Cohorts 1 & 2



Patients with symptomatic oHCM on background therapy excluding disopyramide

Two sequential dose-finding cohorts



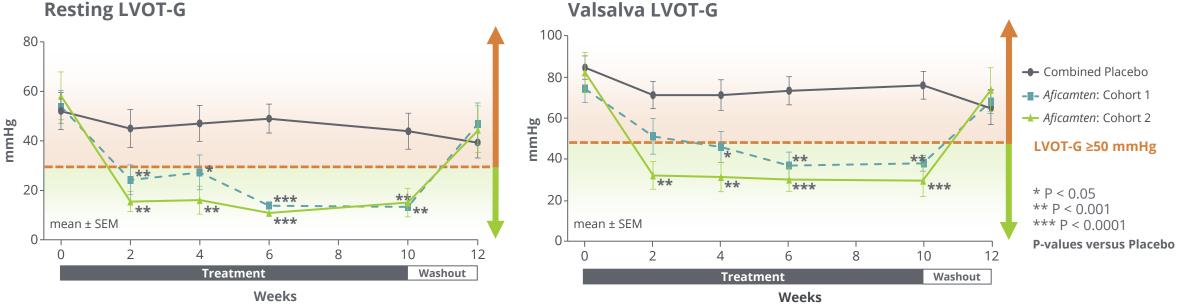


REDWOOD-HCM: Efficacy Cohorts 1 & 2



Results published in JACC in January 2023

Resting LVOT-G

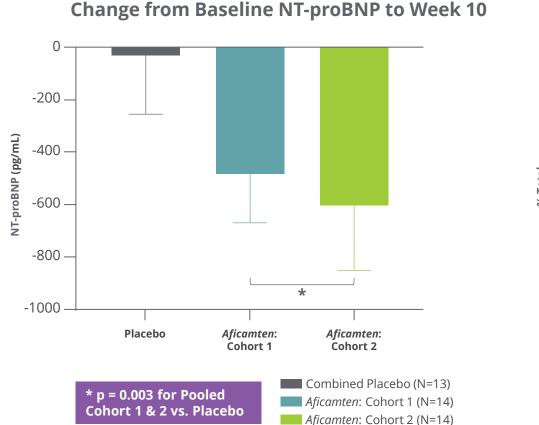


Dose finding study Cohort 1 (n=21), Cohort 2 (n=20)

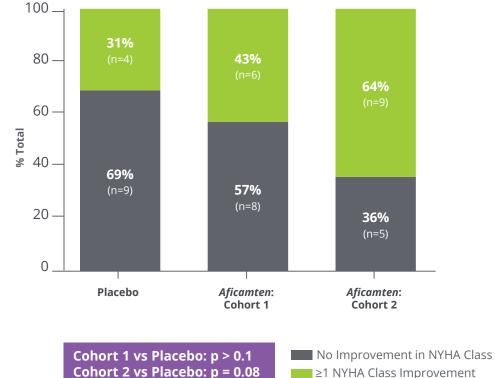
Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established. Maron M, et. al. Phase 2 Study of Aficamten in Patients With Obstructive Hypertrophic Cardiomyopathy. JACC. January 2023.

Change from Baseline in NT-proBNP & NYHA Class Cohorts 1 & 2





Improvement in Heart Failure Symptoms (NYHA Class)



Week 10 Responder Definition: Improvement in NYHA Class ≥1

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.



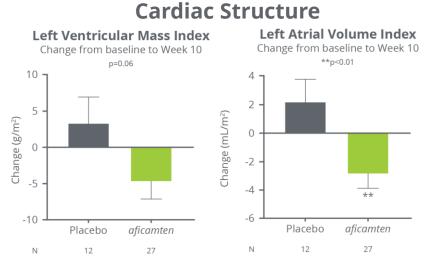
Improved Cardiac Structure and Diastolic Function



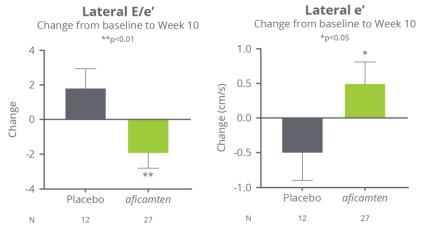
Cohorts 1 & 2: Early signs of improvement in cardiac structure and myocardial relaxation

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))



Diastolic Function

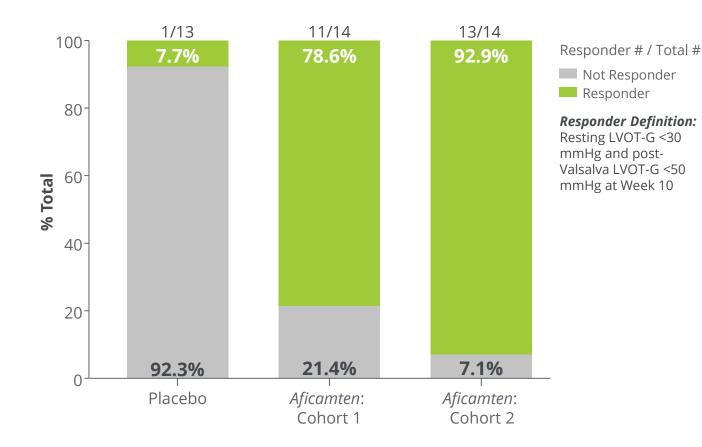


Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established. Abraham T. et al. "Early Cardiac Structural and Functional Reverse Remodeling in Obstructive Hypertrophic Cardiomyopathy after 10 Weeks of *Aficamten* Therapy: Analyses from REDWOOD-HCM". ASE 2022.



Response Rates on Treatment with *Aficamten*





- 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 ESC Heart Failure 2023



Cytokinetics

Significant Improvements in KCCQ & NYHA Class Cohort 4

35%

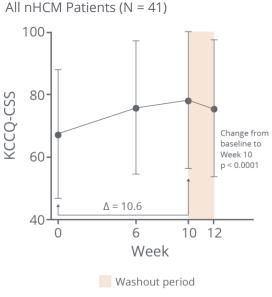
7.5%

Unchanged (>-5 – <5points)



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

12.5%

25%

Small (\geq 5–10 points) Moderate-Large (\geq 10–20 points) Large-Very Large (\geq 20 points) Worsened (<-5 points)

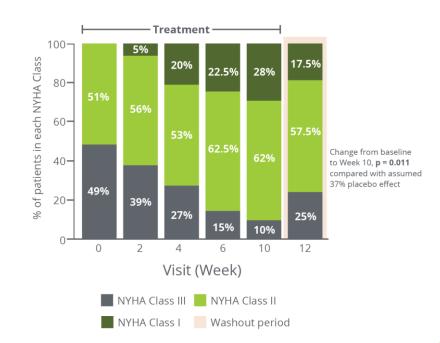
20%

58%

with clinical

improvement

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

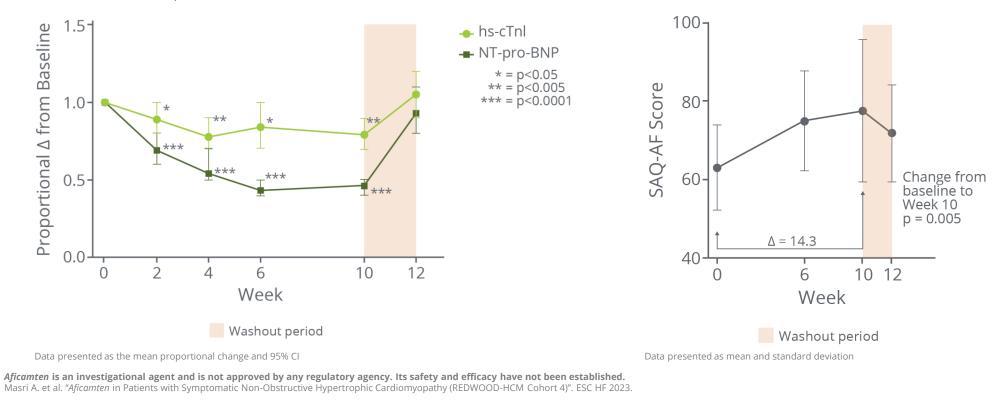


Mean reduction in high-sensitivity cardiac troponin of 21% Mean reduction in NT-proBNP of 55%

Seattle Angina Questionnaire Angina Frequency (SAQ-AF)

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

REDWOOD

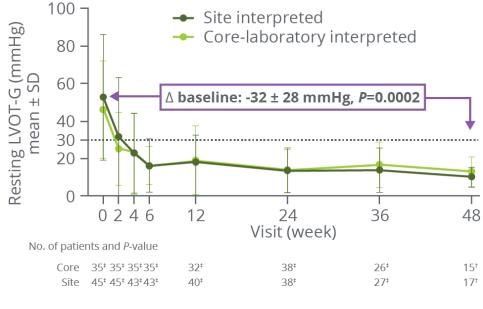




FOREST-HCM: Open Label Extension

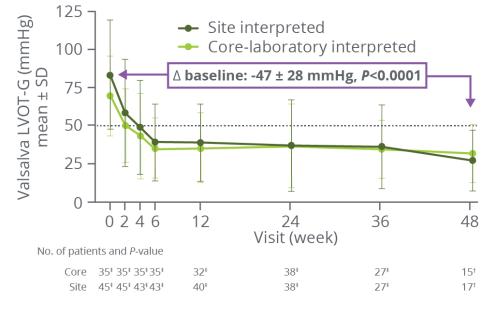


Long-term treatment shows sustained improvement in LVOT-G



48 Weeks: Resting LVOT Gradient

48 Weeks: Valsalva LVOT Gradient



[†]P<0.001; [‡]P<0.0001

[†]*P*<0.001; [‡]*P*<0.0001

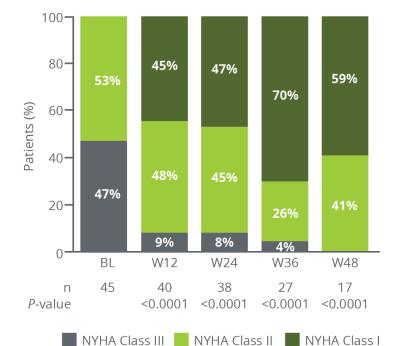
Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established. Saberi et al. "Long-Term Efficacy and Safety of *Aficamten* in Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy". ACC 2023.



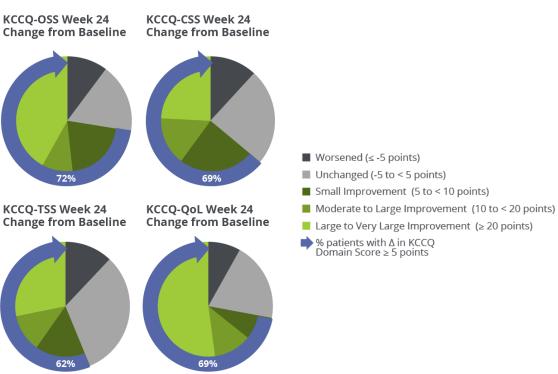
FOREST-HCM: Open Label Extension



Long-term treatment shows sustained improvement NYHA class and KCCQ



48 Weeks: Improvement in NYHA Class



24 Weeks: Change from Baseline KCCQ Scores

Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established. 1. Saberi et al. "Long-Term Efficacy and Safety of *Aficamten* in Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy". ACC 2023.

2. Saberi et al. "Improvement in KCCQ Scores in Patients with Obstructive Hypertrophic Cardiomyopathy Treated with Aficamten in the REDWOOD-HCM OLE Study." HFSA 2022.



24

Safety Data: Phase 2 & OLE



• <u>oHCM</u> → <u>Cohorts 1, 2, & 3:</u> 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

<u>nHCM</u> → <u>Cohort 4</u>: After 10-weeks of treatment

Cvtokinetics

- 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, NTproBNP was lower and plasma concentration of *aficamten* was within the expected range



- <u>oHCM</u> → FOREST-HCM: 45 patients and up-to 12months of treatment (as of Q1 2023)
 - No SAE's related to *aficamten* treatment
- One treatment interruption in the setting of alcoholrelated atrial fibrillation with a transient decrease in LVEF to <50% (as of Q1 2023)

SEQUOIA-HCM: Phase 3 Trial



Completed enrollment; expect topline results in Q4 2023

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

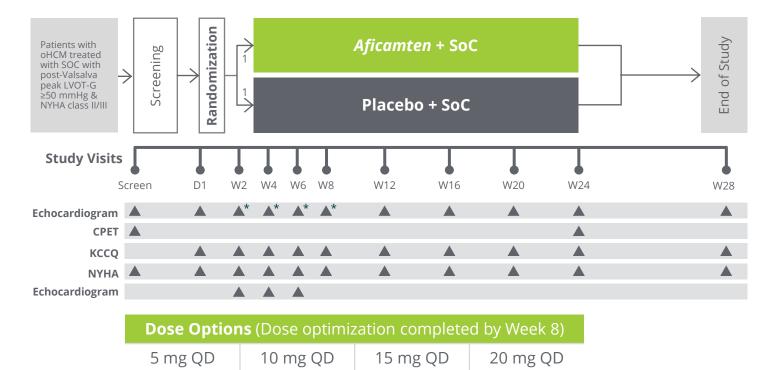
Enrolled 282 patients treated with standard of care with:

- 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

Cvtokinetics

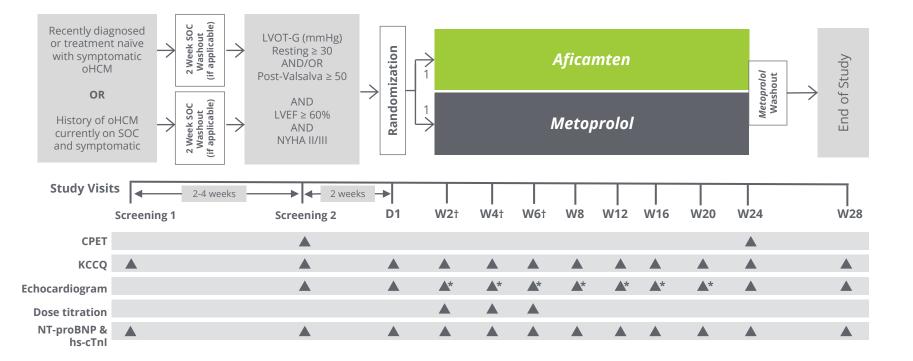


MAPLE-HCM: Phase 3 Monotherapy Trial Open to enrollment



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

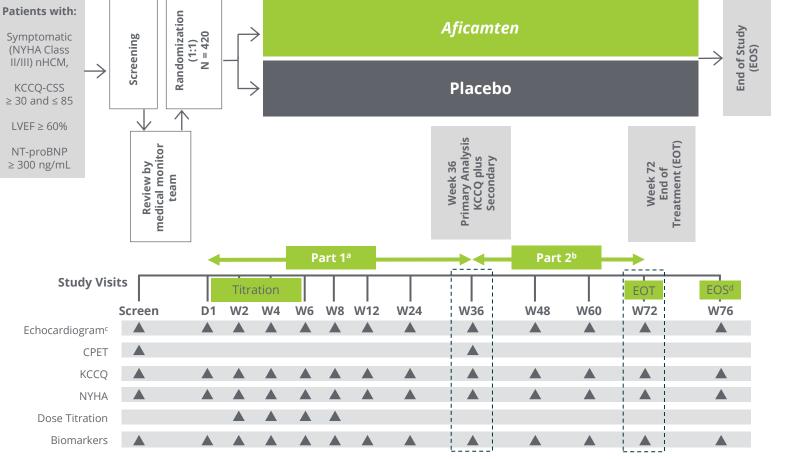
- Trial to enroll approximately 170 patients
- Primary endpoint: change in peak VO2, assessed by CPET from baseline to Week 24
- Secondary endpoints: change in NYHA class, KCCQ, NT-proBNP, and measures of structural remodeling



SOC: standard of care * Focused echocardiogram

Not for Promotional Use, For Investors Only OVERVIEW AFICAMTEN OMECAMTIV MECARBIL EMERGING PIPELINE CORPORATE PROFILE

- ACACIA-HCM: Pivotal Phase 3 Trial in nHCM Open to enrollment
- Trial to enroll approximately 420 symptomatic nHCM patients
- Primary endpoint: change in KCCQ Clinical Summary Score from baseline to Week 36
- Secondary endpoints: change in pVO2, Ve/VCO2, left atrial volume index (LAVI), NT-proBNP and the proportion of patients with ≥1 class improvement in NYHA from baseline to Week 36, as well as time to first cardiovascular event



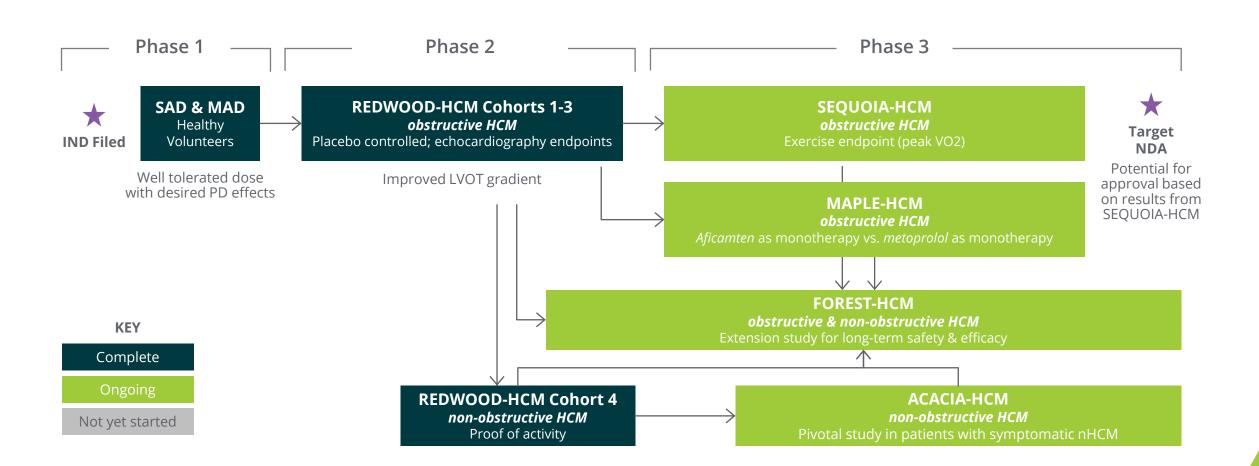
^a Part 1: All participants followed until week 36

^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). Aficanten dose range 5-20 mg.
 ^d 4-week follow up after last dose



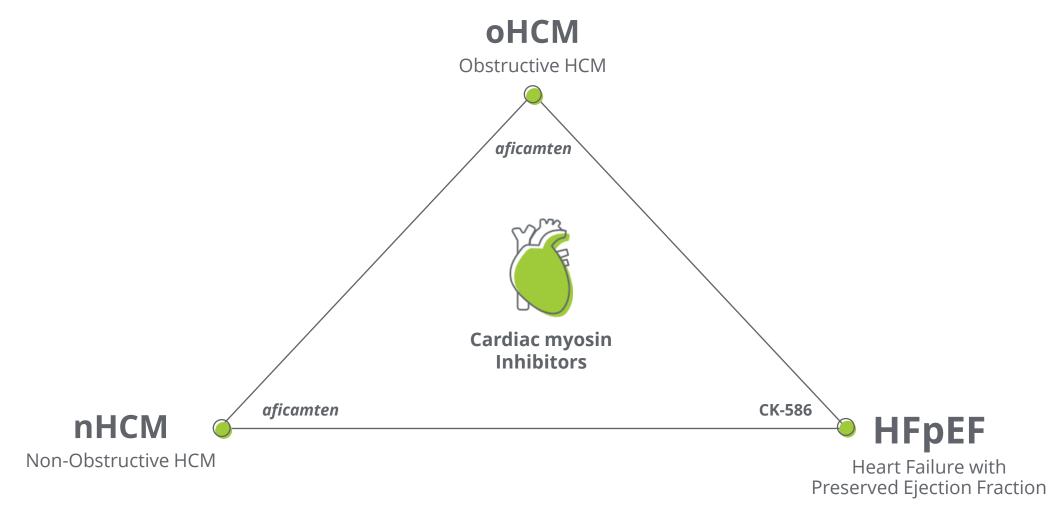


Aficamten: Clinical Development Plan for HCM





Novel Approach May Address Multiple Unmet Patient Needs



Cytokinetics

Aficamten: Targeting Patients with Unmet Need

Positive HCP Anticipation for *Aficamten*

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

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

Characteristics of the Ideal US HCM Patient for *Aficamten*

• Symptomatic, uncontrolled (nonresponsive, refractory) to standardof-care

or

 Contra-indication for standard-ofcare or other cardiac myosin inhibitors

or

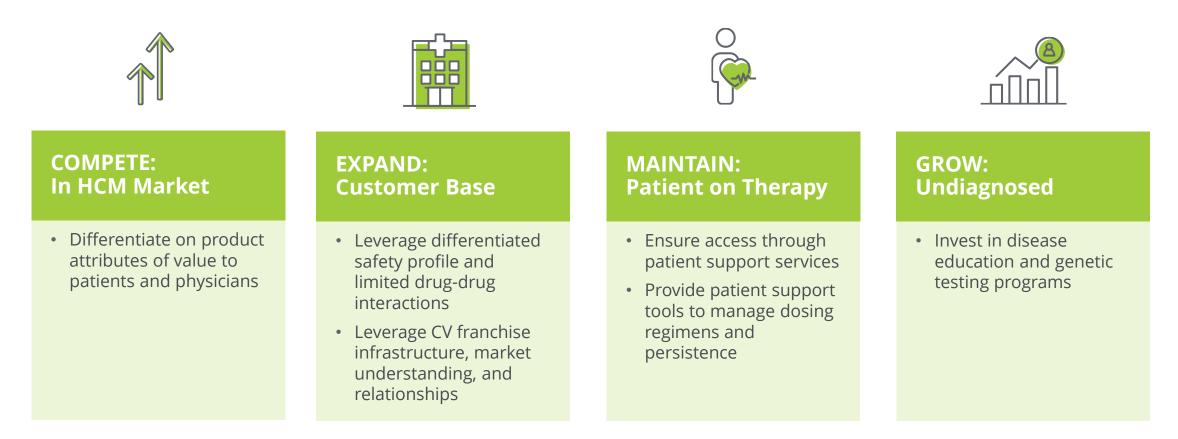
Newly diagnosed patients

Aficamten is an investigational agent and is not approved by any regulatory agency. Its safety and efficacy have not been established. Cogent Primary Mkt Research, USA 2022 (n = 150)



Aficamten: Brand Strategy

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



Aficamten: Market Access Strategy







Get rapid and parity access

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

Clear pricing based on benefit

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

Develop value proposition and value story

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



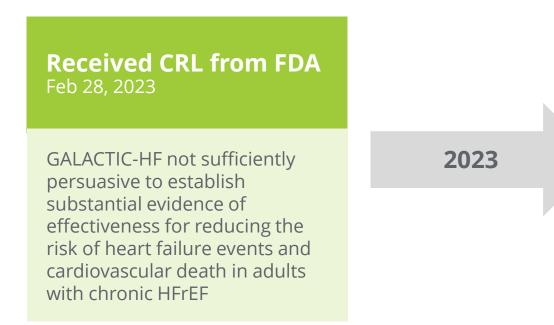
Omecamtiv Mecarbil



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

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



- Engaged with FDA to understand the FDA's views related to the CRL
- Continue to pursue **international approvals** of *omecamtiv mecarbil*
 - MAA on file with EMA
 - NDA on file with NMPA's CDE
- Continue to seek partnerships in Europe and Japan



Emerging Cardiovascular Pipeline CK-136 & CK-586



CK-136 and CK-586 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.

Early Development Supports Cardiovascular Portfolio

CK-136

Cardiac troponin activator

for the potential treatment of patients with heart failure with reduced ejection fraction (HFrEF) and other types of heart failure, such as right ventricular failure, resulting from impaired cardiac contractility

CK-586

Cardiac myosin inhibitor designed to potentially reduce the hypercontractility associated with heart failure with preserved ejection fraction (HFpEF)

Additional Research

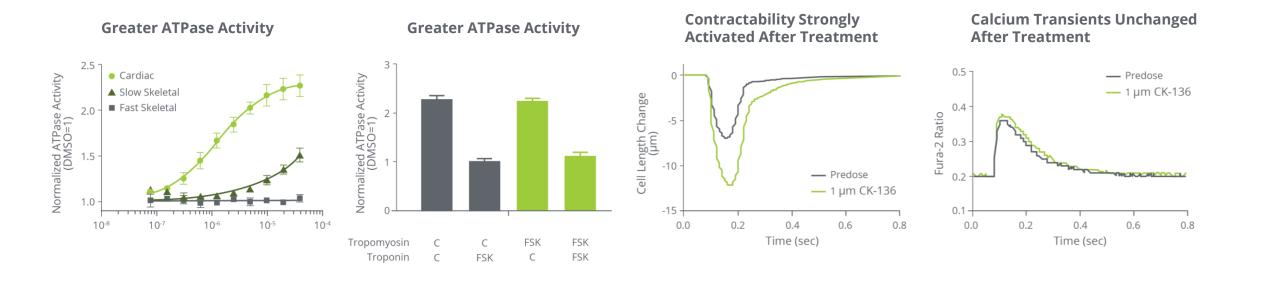
Advancing pre-clinical research in the mechanics of muscle contractility as well as energetics, growth and metabolism



CK-136: Mechanism of Action

Key biochemical and cellular features

The first selective cardiac troponin activator



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.

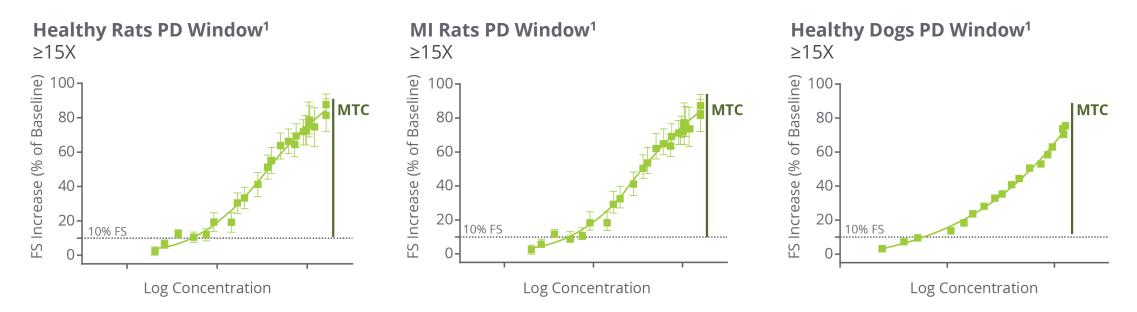


CK-136: Exposure Response Relationship

Exposure-response of troponin activator is shallower than myosin activator

Phase 1 study in progress

Animal Models of Cardiac Function

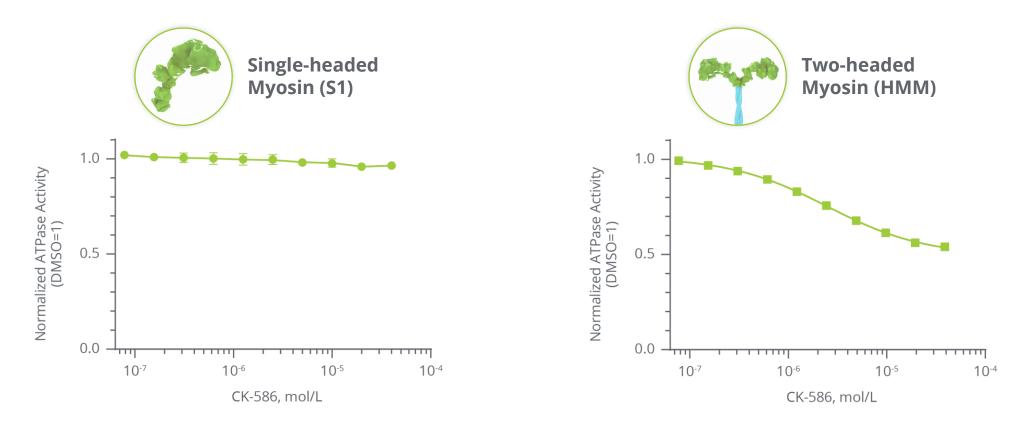


¹PD Window = Maximum Tolerated Concentration (MTC) / 10% increase in Fractional Shortening (FS)



CK-586: Distinct Mechanism of Action from Aficamten

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



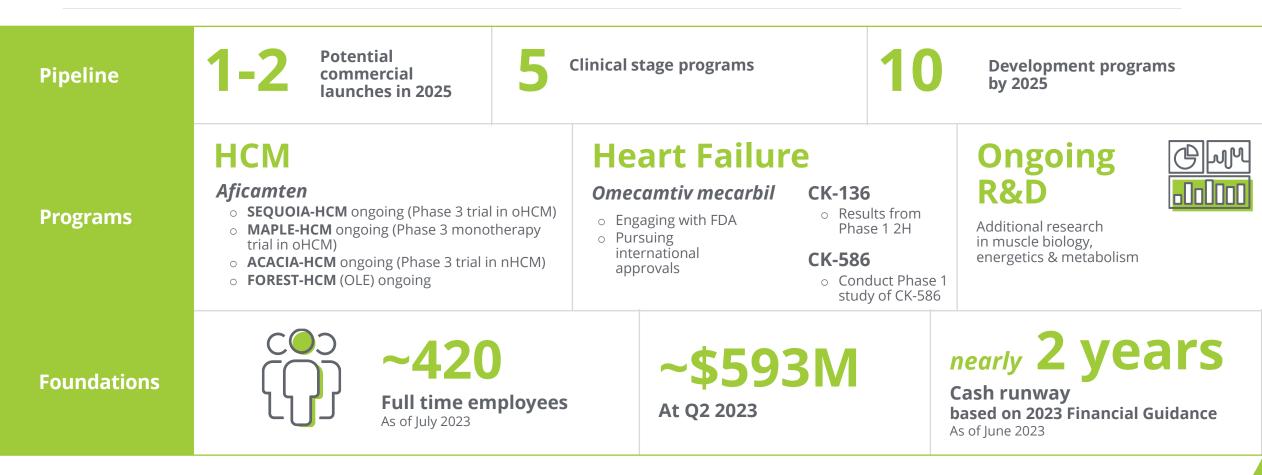
Based on preclinical testing

Sarcomere Directed Therapies

Corporate Profile



Robust Pipeline, Solid Financial Position



Timelines and milestones reflect Cytokinetics' current expectations and beliefs



Balance Sheet & Financial Guidance

Nearly 2 years cash runway based on 2023 guidance

2023 Condensed Balance Sheet

As of 6/30/2023	in millions
	Total
Cash and investments	\$592.6
Accounts receivable	\$1.0
PPE	\$77.2
Leased assets	\$80.9
Other assets	\$28.2
Total Assets	\$779.9
Convertible Debt	\$545.0
Liability related to sale of future royalties	\$313.2
Lease liability	\$123.8
Other liabilities	\$131.0
Total Liabilities	\$1,113.0
Working capital	\$521.0
Accumulated deficit	(\$1,845.9)
Stockholders' deficit	(\$333.1)
Wtd Avg Basic Shares Outstanding	95.8

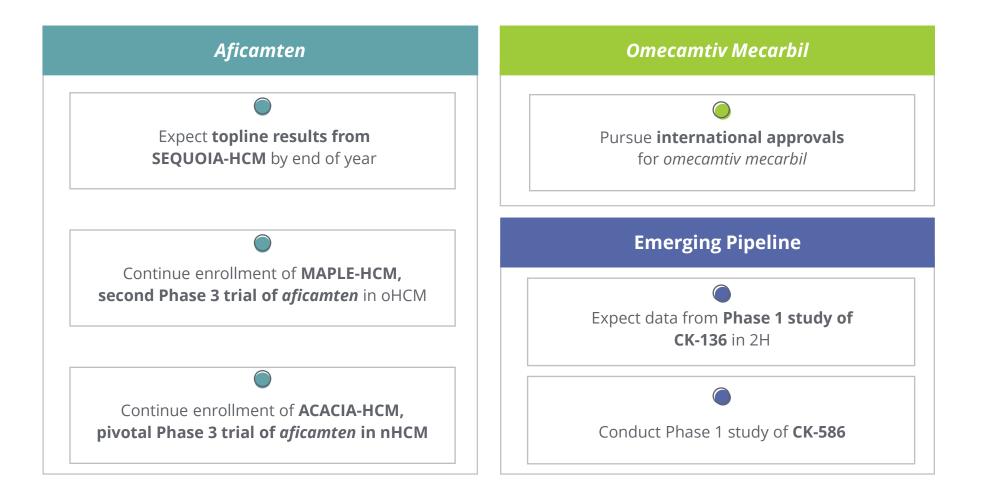
1. Cytokinetics internal planning data. Outside services spend for clinical trials, CMC and toxicology studies

2023 Financial Guidance

Net	~ \$310-320
Cash Operating Expenses	\$390-410
Cash Revenue	\$5
	Total



Expected 2023 Milestones





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Thank You

Sarcomere directed therapies



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