Actual patient who consented to use of their name, image, and condition.

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 to Cytokinetics' research and development activities; clinical trial initiation, design, enrollment, conduct, progress, continuation, completion, timing and results; regulatory submissions, review processes, approval timing and outcomes, including with respect to supplemental applications and approvals in jurisdictions outside the United States; the scope, expansion, modification, durability or continuation of labeling and promotional claims; commercial readiness, launch timing, market access and reimbursement; anticipated patient, prescriber and payer adoption; expectations regarding market opportunity, growth and market share; pipeline development and expansion into additional indications or geographies; access to and use of capital; and Cytokinetics' business strategy, objectives and future plans.

Such statements are based on management's current expectations and assumptions; however, actual results may differ materially due to various risks and uncertainties, including, but not limited to, uncertainties inherent in drug development and commercialization; the timing, conduct and outcomes of clinical trials; regulatory review and approval processes in the United States and other jurisdictions; differences in regulatory requirements, labeling, market access or promotional restrictions across jurisdictions; the ability to obtain, expand, maintain or continue desired labeling, promotional claims or commercial positioning for approved products; potential legal, intellectual property or regulatory constraints affecting commercialization and marketing claims; patient and prescriber acceptance of MYQORZO as compared to alternative therapies; the availability and terms of reimbursement from commercial and government payers; manufacturing, supply and distribution risks; competition; and the availability of sufficient capital to execute Cytokinetics' business plans. 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").

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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.

MYQORZO™
(aficamten) 5·10·15·20 mg tablets

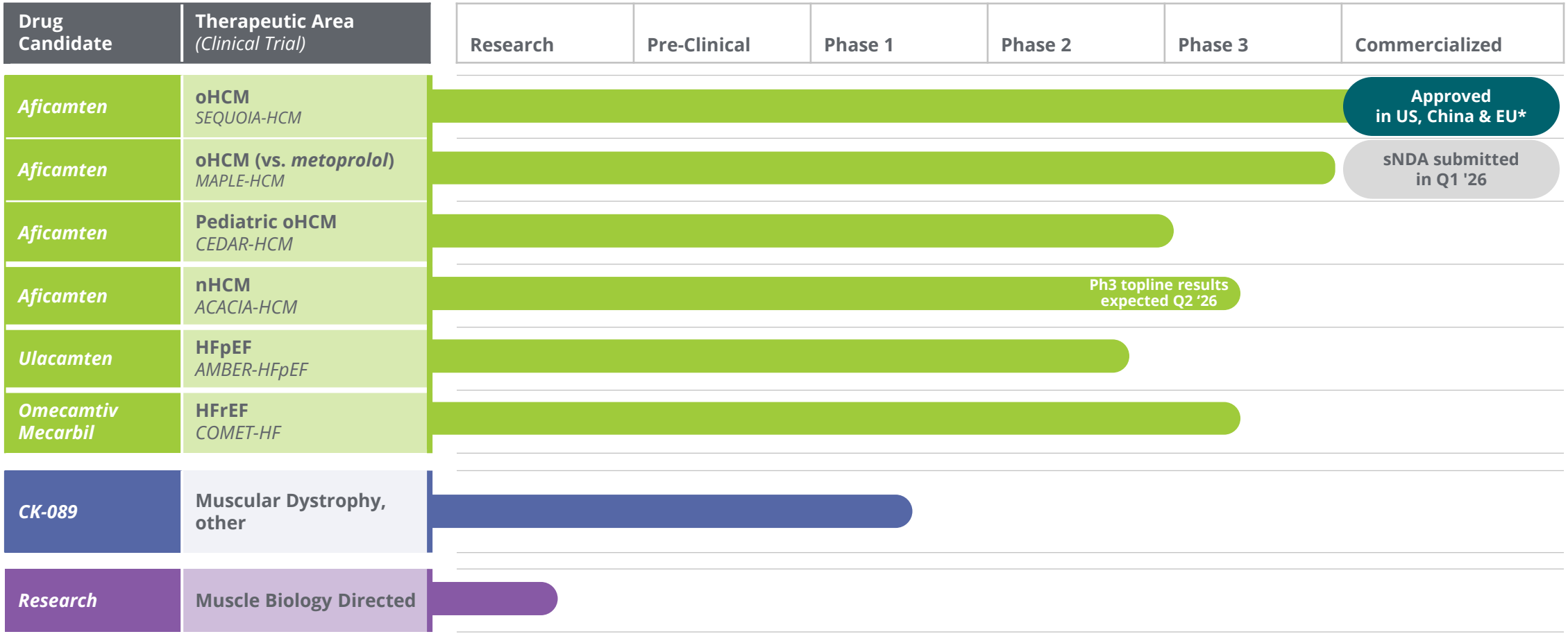
Now Available

FDA-approved for the treatment of adults with symptomatic oHCM to improve functional capacity and symptoms

FDA: U.S. Food & Drug Administration; oHCM: obstructive hypertrophic cardiomyopathy
Please see full Prescribing Information, including Boxed WARNING and Medication Guide

Cytokinetics®

A Commitment to Muscle-Directed Cardiac Medicines



oHCM: obstructive hypertrophic cardiomyopathy; nHCM: non-obstructive hypertrophic cardiomyopathy; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reserved ejection fraction; sNDA: Supplemental New Drug Application
MYQORZO is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.
Ulacamten, omecamtiv mecarbil and CK-089 are investigational agents and have not been approved for use by any regulatory agency. Their safety and efficacy has not been established.

Cytokinetics®

Positioned for Launch Velocity & Sustainable Growth

COMMERCIAL

Approved for the treatment of adults with symptomatic oHCM to improve functional capacity and symptoms in U.S., China & Europe

RESEARCH & DEVELOPMENT

Muscle-directed platform with multi-program pipeline

Specialty Cardiology Franchise

sNDA for *aficamten* submitted in Q1 2026 based on superiority results from MAPLE-HCM vs. *metoprolol**

Expansion & breadth: topline results from **ACACIA-HCM** (nHCM Ph3) Q2 2026, **CEDAR-HCM** (pediatric) enrolling, **FOREST-HCM** (OLE) ongoing

Building specialty cardiology pipeline:

Omecamtiv mecarbil: Ph3 confirmatory trial enrolling (**COMET-HF**)

Ulacamten: Ph2 trial enrolling (**AMBER-HFpEF**)

STRONG FINANCIAL POSITION

~$1.22B
cash & cash equivalents (as of 12/31/25)

Access to further capital:

- Eligible to draw up to **$175M** from tranche 7 loan provided by Royalty Pharma
- Up to **$150M** funding of a pivotal trial of *ulacamten* by Royalty Pharma at its option

**The results of MAPLE-HCM showed that the mean change in pVO_2 from baseline to Week 24 for aficamten was +1.1 mL/kg/min and -1.2 mL/kg/min for metoprolol (least-squares mean (LSM) difference between groups of 2.3 mL/kg/min (p<0.0001)*

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VISION2030

Empowering Muscle, Empowering Lives

To be the leading muscle-focused specialty biopharma company intent on meaningfully improving the lives of patients through global access to our innovative medicines

INNOVATION
Advance 2 approved products across 3 indications and 10 NMEs in our pipeline

IGNITION
Achieve broad access and rapid use of our medicines in >15 countries throughout North America and Europe

IMPACT
Reach >100,000 patients globally with our medicines

INSPIRATION
Foster a patient-centric culture with emphasis on equitable access

INGENUITY
Extend leadership in muscle biology deploying multiple therapeutic modalities

The company's Vision 2030 statements are a statement of goals and there can be no assurance that the goal indicated will be achieved or, if achieve, will be achieved on this timeline.

Building a Specialty Cardiology Franchise

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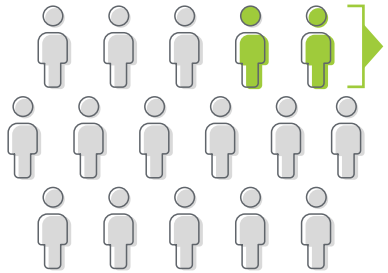
The following slides contain information about investigational agents that have not been approved by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and efficacy of these investigational agents have not been established.

Building Specialty Cardiology Business for High ROI

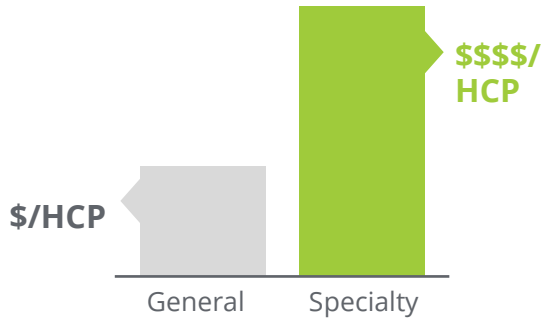
Concentrated Prescribers

~80K cardiologists/PCPs treat CV diseases



~10K
cardiologists treat ~80% HCM

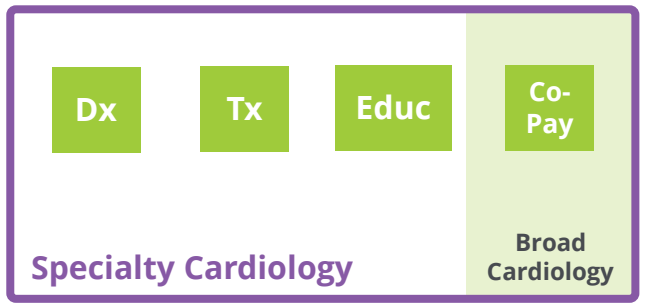
Higher Revenue Per Prescriber



Opportunity To Grow Market Through Diagnosis

Distribution Limited to Specialty Retailers

Differentiated Patient Experience



Path to Reimbursement

Broad Cardiology
High Rebates
Winners/loser

Specialty Cardiology
Access to Label

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Addressing Difficult to Treat Populations Within Heart Failure

Specialty cardiology franchise strategy applies to markets with similar characteristics

HCM

Opportunity for MYQORZO™ (*aficamten*) as the anchor

- ✓ Few available therapies
- ✓ Significant unmet need
- ✓ Concentrated market
- ✓ Tractable customer base
- ✓ Payors manage to label

HFrEF
Severely reduced EF

Expanding into adjacent population*

- ✓ Few available therapies
- ✓ Significant unmet need
- ✓ Concentrated market
- ✓ Tractable customer base
- ✓ Payors manage to label

HFpEF
Supranormal EF

Addressing underserved segment of HF market*

- ✓ Few available therapies
- ✓ Significant unmet need
- ✓ Concentrated market
- ✓ Tractable customer base
- ✓ Payors manage to label

** Subject to future regulatory approval*

MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

Ulacamten, omecamtiv mecarbil and CK-089 are investigational agents and have not been approved for use by any regulatory agency. Their safety and efficacy has not been established.

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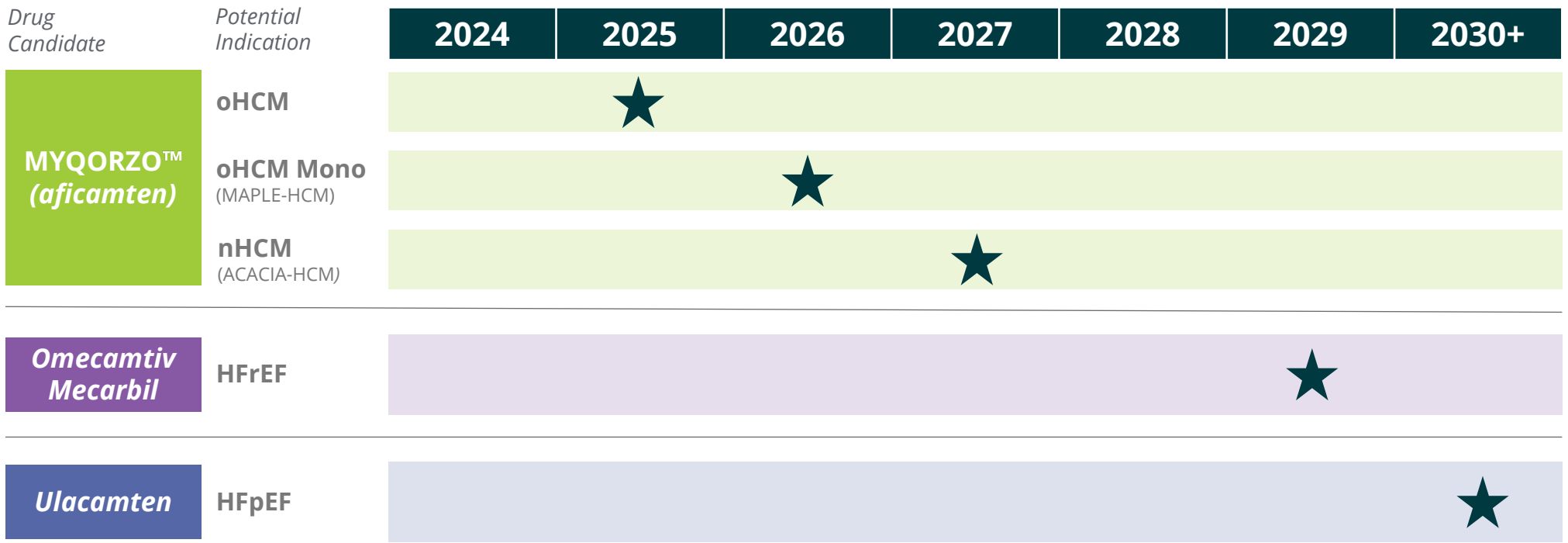
Potential for Multiple Specialty Cardiology Launches



Estimated date of potential future launch of each candidate for the respective indication. The estimated launch date requires positive clinical data and regulatory approval within projected timelines.
MYQORZO™ (aficamten) is only approved in the U.S. and China for the treatment of adults with symptomatic oHCM. Ulacamten and omecamtiv mecarbil are investigational drug candidates and are not approved as safe or effective for any indication.

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MYQORZO™ (*aficamten*)

Clinical Evidence

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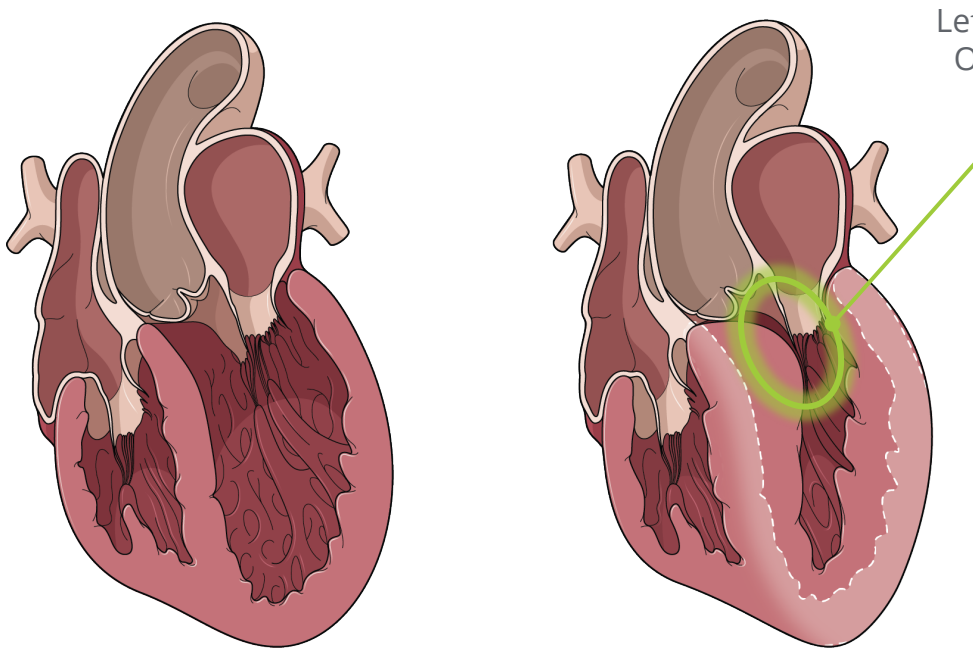
MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.
Please see full Prescribing Information, including Boxed WARNING and Medication Guide

About oHCM



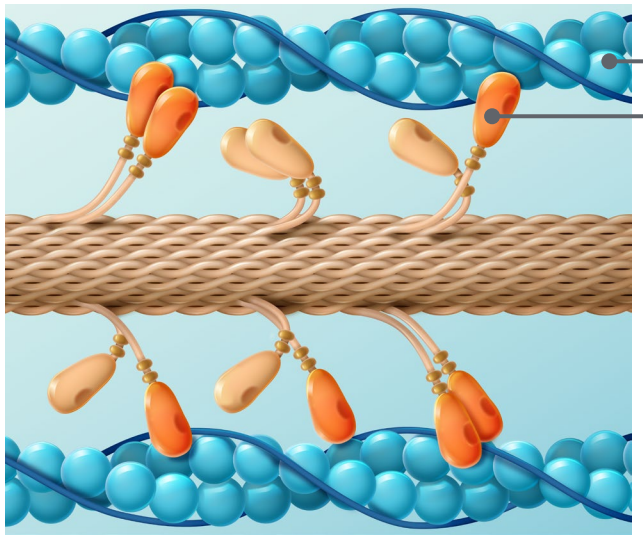
- HCM causes the heart muscle to **abnormally thicken**.
- In obstructive HCM (oHCM), the thickened muscle causes the left ventricle to become **smaller, stiffer** and **less able to relax and fill with blood**.[1–4]
- In oHCM, **obstruction of the LVOT**, blocks blood flow and **limits the heart's pumping function**, leading to reduced exercise capacity and a variety of symptoms.
- People with HCM report that it can limit their physical activities, cause feelings of **anxiety or depression** and impact their work.[5]

HCM: hypertrophic cardiomyopathy; oHCM: obstructive hypertrophic cardiomyopathy

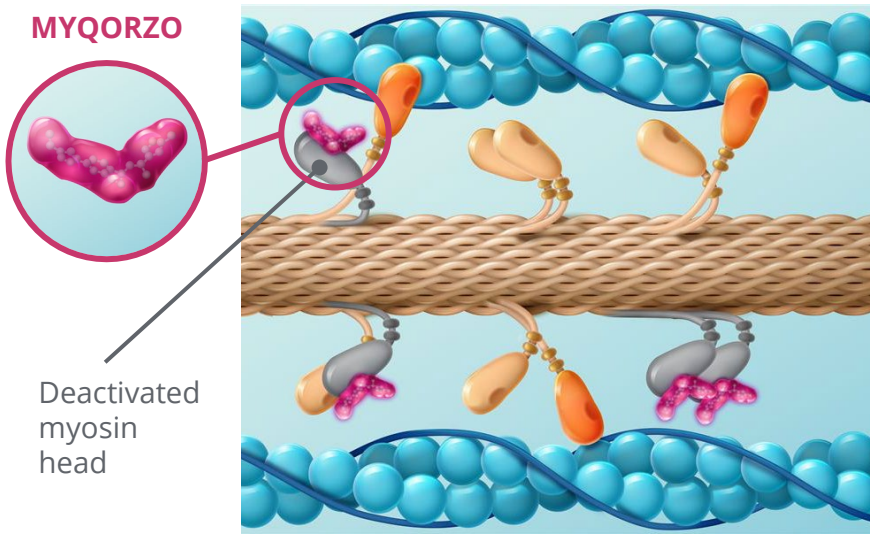
1. Naidu SS, Sutton MB, Gao W, et al. Frequency and clinicoeconomic impact of delays to definitive diagnosis of obstructive hypertrophic cardiomyopathy in the United States. J Med Econ. 2023;26(1):682-690. doi:10.1080/13696998.2023.2208966
2. Argulian E, Sherrid MV, Messerli FH. Misconceptions and Facts About Hypertrophic Cardiomyopathy. Am J Med. 2016;129(2):148-152. doi:10.1016/j.amjmed.2015.07.035
3. Ommen SR, Ho CY, Asif IM, et al. 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. Circulation. 2024;149(23):e1239-e1311. doi:10.1161/CIR.0000000000001250
4. Maurizi N, Olivotto I, Maron MS, et al. Lifetime Clinical Course of Hypertrophic Cardiomyopathy: Outcome of the Historical Florence Cohort Over 5 Decades. JACC Adv. 2023;2(4):100337. doi:10.1016/j.jacadv.2023.100337
5. Zaiser E, Sehnert AJ, Duenas A, Saberi S, Brookes E, Reaney M. Patient experiences with hypertrophic cardiomyopathy: a conceptual model of symptoms and impacts on quality of life. J Patient-Rep Outcomes. 2020;4(1):102. doi:10.1186/s41687-020-00269-8

MYQORZO™ Inhibits Cardiac Myosin Motor Activity

oHCM causes cardiac hypercontractility,
impaired cardiac relaxation &
increased energy consumption



MYQORZO binds to and inhibits cardiac myosin,
reducing cardiac contractility
& LVOT obstruction



oHCM: obstructive hypertrophic cardiomyopathy; LVOT: left ventricular outflow tract
Please see full Prescribing Information, including Boxed WARNING and Medication Guide

Cytokinetics®

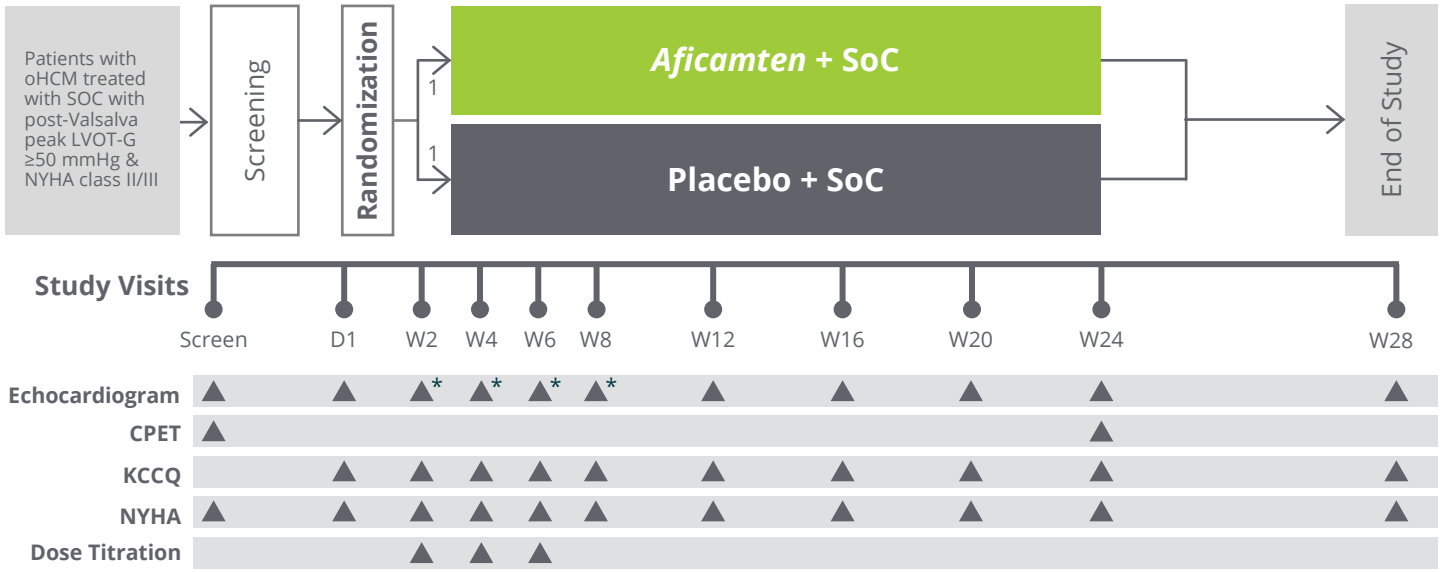
SEQUOIA-HCM: Pivotal Phase 3 Trial

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



Dose Options (Dose optimization completed by Week 8)

5 mg QD	10 mg QD	15 mg QD	20 mg QD

SOC: standard of care
** Focused echocardiogram*
Please see full Prescribing Information, including Boxed WARNING and Medication Guide

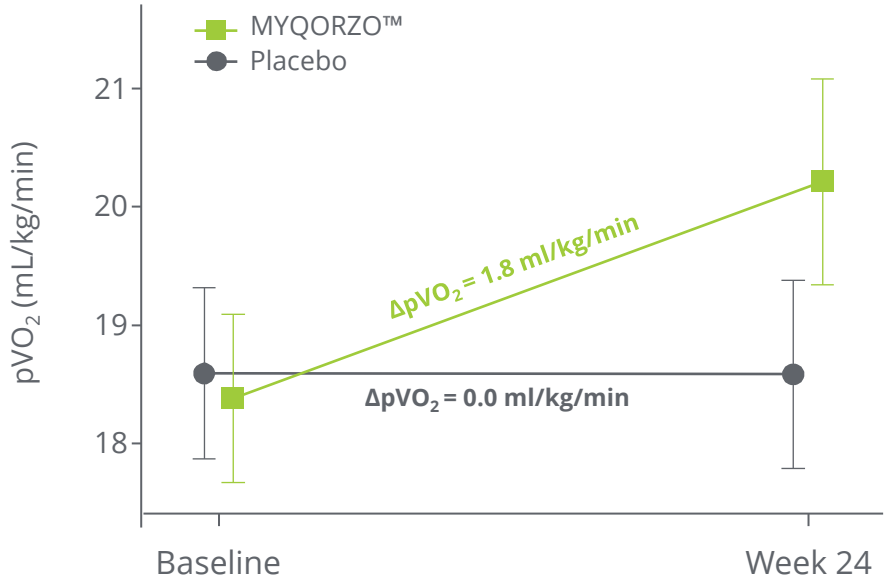
Cytokinetics®

SEQUOIA-HCM: Pivotal Phase 3 Trial in oHCM

Significant improvement in exercise capacity and symptoms compared to placebo

The NEW ENGLAND JOURNAL of MEDICINE

Absolute Change from Baseline to Week 24



pVO_2: peak oxygen uptake; LS: least squares; SE: standard error; LVOT-G: left ventricular outflow tract gradient; KCCQ-OSS: Kansas City Cardiomyopathy Questionnaire Overall Summary Score; SAQ7-SS: Seattle Angina Questionnaire Summary Score, NYHA: New York Heart Association; NT-pro-BNP: N-terminal prohormone of brain natriuretic peptide: hs-cTnI: high-sensitivity cardiac troponin I; LV: left ventricular

Sources:
1. Maron M. Aficamten for Symptomatic Obstructive Hypertrophic Cardiomyopathy. N Engl J Med 2024 May 30;390(20):1849-1861
2. Sherrod C, et al. Effect of Aficamten on Health Status Outcomes in Obstructive Hypertrophic Cardiomyopathy: Results from SEQUOIA-HCM. JACC. 2024.
3. Coats CJ, et al. Cardiac Biomarkers and Effects of Aficamten in Obstructive Hypertrophic Cardiomyopathy: The SEQUOIA-HCM Trial. Eur Heart J. 2024
4. Hegde S, et al. Impact of Aficamten on Echocardiographic Cardiac Structure and Function in Symptomatic Obstructive Hypertrophic Cardiomyopathy. JACC. 2024.

Please see full Prescribing Information, including Boxed WARNING and Medication Guide

Treatment with MYQORZO for 24 weeks also significantly improved:

Gradients

-50 mmHg placebo-corrected change in post-Valsalva LVOT-G ($p<0.0001$)[1]

Symptoms

+7.9 points in KCCQ-OSS ($p<0.0001$)[2]

+7.8 points in SAQ7-SS ($p<0.0001$)[2]

34% of patients had ≥1 class improvement in NYHA Class ($p<0.0001$)[1]

Disease Status

78 fewer days eligible for septal reduction therapy ($p<0.0001$)[1]

Biomarkers

80% reduction in NT-proBNP ($p<0.001$)[1]

43% reduction in hs-cTnI ($p<0.001$)[3]

Structure, Function & Remodeling

Improvements in maximal wall thickness, septal wall thickness, inferolateral wall thickness, LV mass index, LV end systolic volume index, left atrial volume index, lateral e' velocity, lateral E/e' (all $p<0.01$)[4]

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SEQUOIA-HCM: Safety Data

AEs with ≥5% incidence

There were no serious adverse cardiovascular events associated with MYQORZO™ treatment in SEQUOIA-HCM

Event, n (%)	MYQORZO (n=142)	Placebo (n=140)
Overall AEs	105 (73.9)	99 (70.7)
Headache	11 (7.7)	10 (7.1)
Hypertension	11 (7.7)	3 (2.1)
Palpitations	10 (7.0)	4 (2.9)
Upper respiratory infection	9 (6.3)	12 (8.6)
COVID-19	8 (5.6)	9 (6.4)
Dyspnea	8 (5.6)	8 (5.7)
SAEs	8 (5.6)	13 (9.3)
Cardiac AEs	24 (16.9)	21 (15.0)
Discontinuations	5 (3.5)	4 (2.9)
New-onset atrial fibrillation (AF)	1 (0.7)	1 (0.7)
Appropriate ICD shock	0	1 (0.7)
LVEF <50% by core laboratory[a]	5 (3.5)	1 (0.7)
Dose reduction based on site-read LVEF <50%	7 (4.9)	1 (0.7)

[a] 1 placebo- and 1 MYQORZO-treated patient overlap with dose reduction based on site-read LVEF <50%.

AE, adverse event; SAE, serious adverse event; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction

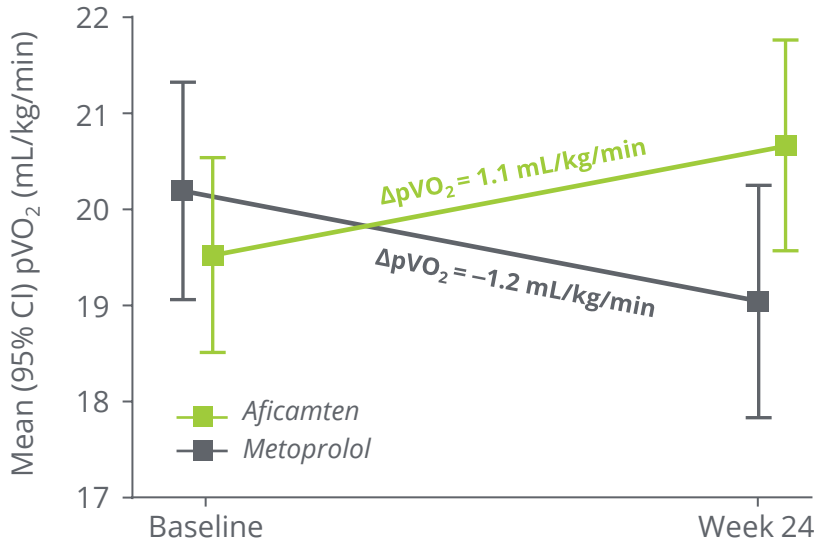
Coats CJ. Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy. J Am Heart Assoc 2024

MAPLE-HCM: Phase 3 Monotherapy Trial in oHCM

Aficamten superior to standard-of-care beta blocker metoprolol

The NEW ENGLAND JOURNAL of MEDICINE

Mean Change from Baseline to Week 24 in pVO_2



LSM difference (SE) vs. *metoprolol*
2.3 (0.39) mL/kg/min, *P*<0.0001

Relative to *metoprolol*, *aficamten* also improved:

Gradients

LSM difference of **-30 mmHg** in resting LVOT-G (p<0.0001)[1]
LSM difference of **-35 mmHg** in post-Valsalva LVOT-G (p<0.0001)[1]

Symptoms

LSM difference of **+6.9 points** in KCCQ-CSS (p<0.0001)[1]
51% of patients improved ≥1 NYHA FC (vs. 26% on *metoprolol)* (p<0.001)[1]

Biomarkers

-81% in NT-proBNP (-73% for *aficamten* vs. +42% for metoprolol) (p<0.001)[2]
-28% in hs-cTnI (-43% for *aficamten* vs. -17% for metoprolol) (p<0.001)[2]

Structure, Function & Remodeling

LSM difference of **-7.0 mL/m²** in left atrial volume index (p<0.0001)[1]

CI: Confidence interval; pVO_2, peak oxygen uptake; LSM: least squares mean; KCCQ-CSS: Kansas City Cardiomyopathy Questionnaire Clinical Summary Score; NYHA FC: New York Heart Association Functional Class; NT-pro-BNP: N-terminal prohormone of brain natriuretic peptide: hs-cTnI: high-sensitivity cardiac troponin I

1. Garcia-Pavia, P, et al. Aficamten or Metoprolol Monotherapy for Obstructive Hypertrophic Cardiomyopathy. N Engl J Med. 2025
2. Lakdawala, NK et al. The Effect of Aficamten vs. Metoprolol on Cardiac Biomarkers in Obstructive Hypertrophic Cardiomyopathy. AHA 2025.

MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

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MAPLE-HCM: Safety

	Aficamten (n=88)	*Metoprolol* (n=87)
Patients with any SAE	7 (8.0)	6 (6.9)
Patients with any AE that led to early treatment withdrawal of *aficamten* or *metoprolol*[a]	1 (1.1)	3 (3.4)
Patients with AE that led to temporary interruption of *aficamten* or *metoprolol*	1 (1.1)	1 (1.1)
Patients with dose reduction due to adverse events	1 (1.1)[b]	4 (4.6)[c]
Patients with ≥1 dose down-titration	4 (4.5)[d]	26 (29.9)[e]
Mean (SD) change in LVEF at Week 24 vs baseline	−5.3% (4.7)	−0.50% (3.7)
LVEF <50% by core lab	1 (1.1)[f]	0

Values are n (%).
[a] In the *aficamten* group, 1 patient had sudden death after a brief viral illness. In the *metoprolol* group, AEs leading to early treatment discontinuation are ischemic stroke, hypotension, and fractured humerus due to fall (n=1 each).
[b] In the *aficamten* group, 1 patient had a dose reduction due to an AE of dizziness.
[c] In the *metoprolol* group, 4 patients had dose reduction due to AEs of lightheadedness (n=2), bradycardia (n=1), and fatigue (metoprolol, n=1).
[d] In the *aficamten* group, 3 patients had 4 down-titration events based on site-read LVEF <50% (n=3) and due to an AE (n=1).
[e] In the metoprolol group, 26 patients had 31 down-titration events based on SBP <90 mmHg (n=5), HR <50 bpm (n=17), and AE (n=4).
[f] No associated AE with this LVEF <50%.

Garcia-Pavia, P. et al. Aficamten vs Metoprolol as Monotherapy for Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC 2025.
MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

Integrated Safety Analysis in oHCM

Analysis represents nearly 700 patient-years of exposure to *aficamten*

REDWOOD HCM | SEQUOIA HCM | MAPLE HCM | FOREST HCM

Safety Events of Interest

	Cumulative *aficamten* treated pool[a]		Placebo/*Metoprolol* pool[b]		
	Aficamten N=463		*Aficamten* N=258	Placebo N=153	*Metoprolol* N=87
	n (%)	EAIR[d]			
LVEF <50%[c]	19 (4.1)	2.8	12 (4.7)	1 (0.7)	0
LVEF <50% with clinical heart failure	3 (0.6)	0.6	1 (0.4)	1 (0.7)	0
Atrial Fibrillation					
New Onset	17 (3.7)	2.4	5 (1.9)	3 (2.0)	3 (3.4)
Recurrent	12 (2.6)	1.7	3 (1.2)	2 (1.3)	0
Heart Failure	13 (2.8)	1.9	5 (1.9)	2 (1.3)	1 (1.1)
Stroke	7 (1.5)	1.0	1 (0.4)	1 (0.7)	1 (1.1)
Myocardial Infarction	15 (3.2)	2.2	6 (2.3)	5 (3.3)	4 (4.6)
Syncope	10 (2.2)	1.4	4 (1.6)	3 (2.0)	3 (3.4)
Death	2 (0.4)	0.1	1 (0.4)	0	0

- ✓ **Low incidence of LVEF <50%;** no occurrences associated with clinical HF were corroborated by core lab, and all were successfully managed by dose reduction
- ✓ **Low incidence of new onset AF**, comparable to placebo/metoprolol
- ✓ **Incidence of syncope events comparable to placebo/*metoprolol*** despite much longer exposure to *aficamten*
- ✓ **No permanent discontinuations** related to *aficamten*
- ✓ Monitoring echo in the maintenance phase yielded **very few actionable results**

Masri A et al. Aficamten in Patients with Obstructive Hypertrophic Cardiomyopathy: An Integrated Safety Analysis. ESC 2025.

MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

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MYQORZO™ (*aficamten*)

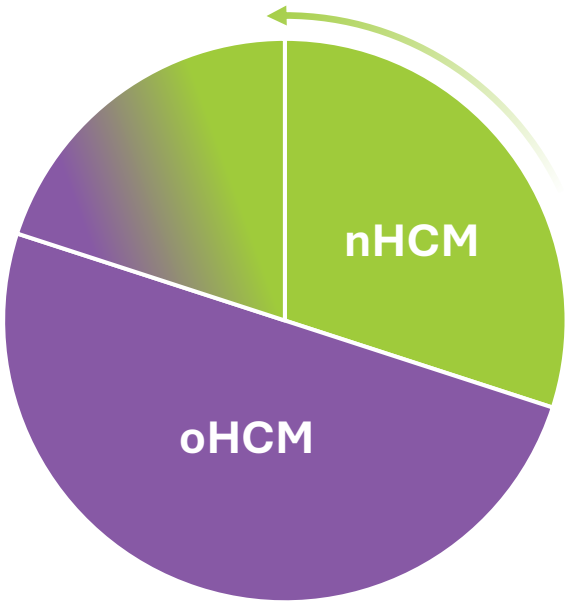
Commercial Launch

Cytokinetics®

MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.
Please see full Prescribing Information, including Boxed WARNING and Medication Guide

Opportunity for CMIs to Treat Symptomatic oHCM Patients

Evolving Understanding of Prevalence Rates for HCM Subtypes: oHCM and nHCM



- ✓ HCM estimated prevalence ~0.3% in the general population ~850k (approximately 1 in 350 individuals)[1]
- ✓ Two HCM subtypes: obstructive HCM (oHCM) and nonobstructive HCM (nHCM)[2]
  - oHCM has historically represented ~65% of cases
  - nHCM diagnosis has been increasing
  - **roughly 50-50 split between HCM subtypes[3]**
- ✓ >100K oHCM patients are eligible for CMI treatment [4,5]

HCM: hypertrophic cardiomyopathy; oHCM: obstructive hypertrophic cardiomyopathy; nHCM: non-obstructive hypertrophic cardiomyopathy; CMI: cardiac myosin inhibitor

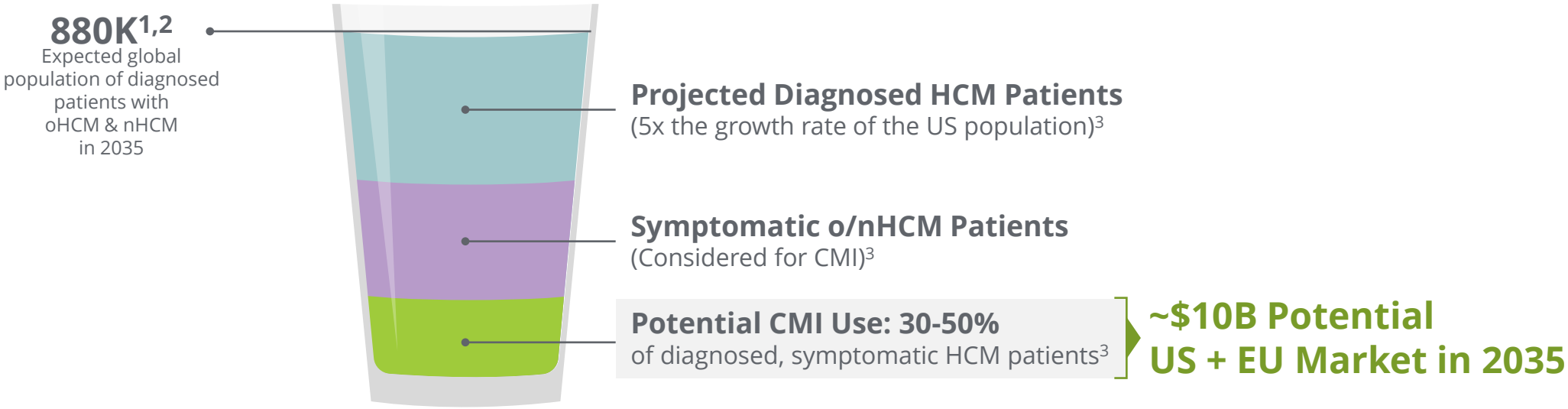
1. Semsarian C, et al. J Am Coll Cardiol. 2015;65(12):1249-1254. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ: et al:: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, Circulation 1995;92;785-789
2. Zaiser E, et al. J Patient Rep Outcomes. 2020;4(102).
3. Butzner M, et al. Epidemiology of Hypertrophic Cardiomyopathy in the United States From 2016 to 2023. JACC Adv. 2026. 2026;5(2):102552. doi:10.1016/j.jacadv.2025.102552
4. Lu DY, et al. J Am Heart Assoc. 2018;7.
5. DoF: SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the year June 2022-May 2023)

$10B Potential Market of CMI-Eligible Patients

Diagnosis of HCM anticipated to grow 5x the rate of the general U.S. population

US and EU HCM Patients in 2035

Illustrative

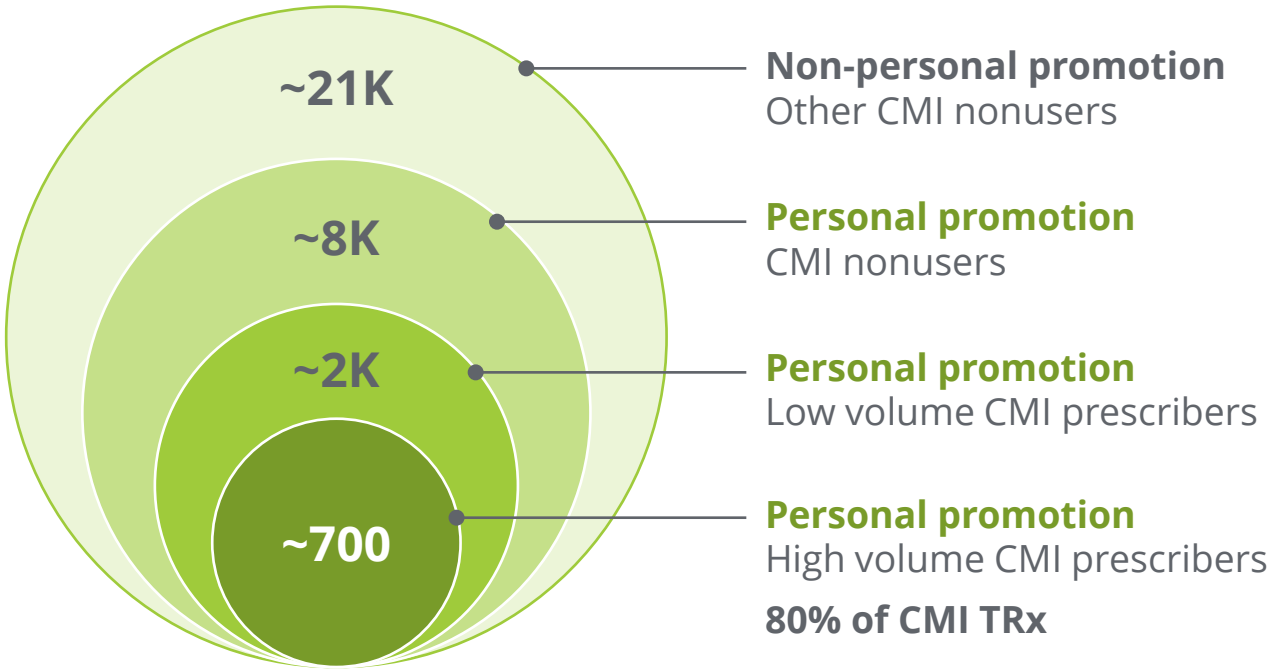


1. DoF: SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023);
2. Butzner et al 2021 estimated a 8% growth rate in diagnosed HCM patients between 2013-2019 https://www.ajconline.org/article/S0002-9149(21)00783-9/fulltext; CYTK is forecasting an average growth rate of 5% over the coming decade and a more conservative 4% growth rate in Europe due to a lack of growth of the overall population in EU5 countries.
3. Internal forecasts

Cytokinetics®

Driving Breadth & Depth Among Concentrated Cardiologist Prescribers

HCPs for Personal and Non-Personal Contact



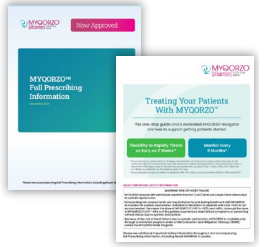
- ✓ **Our field team is sized to cover ~10,000 HCPs** who are treating at least 80% of oHCM patients among cardiologists
- ✓ At launch, we intend to **focus on the top CMI prescribers for depth of prescribing and drive growth by expanding the prescriber base of CMIs**
- ✓ Clinical differentiation drives breadth & depth of prescribing among HCPs

HCP: healthcare provider; oHCM: obstructive hypertrophic cardiomyopathy; CMI: cardiac myosin inhibitor; TRx: total prescriptions

HCP & Patient-Directed Promotional Campaigns Activated

For HCPs

Office Resources



Non-Personal

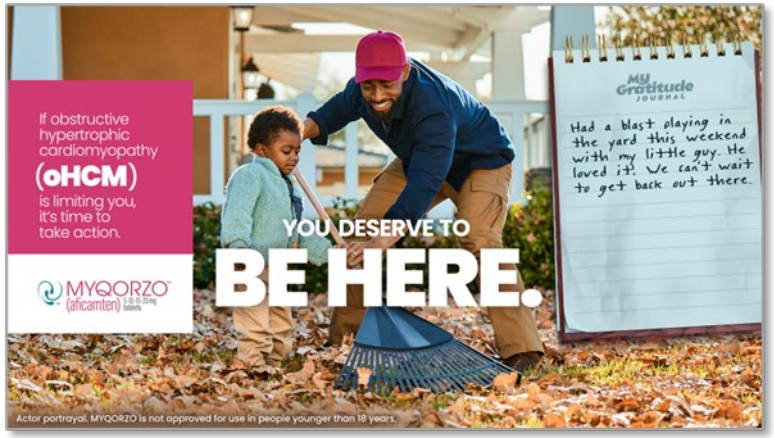
HCP Website

Digital Ads

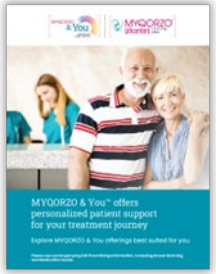
Email

Peer-to-Peer

For Patients

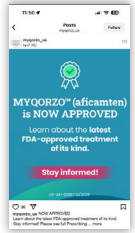


Patient Support Materials



In-Office Patient Materials

Social



Patient Website

Highly Experienced Sales Team Deployed

125 experienced Cardiovascular Account Specialists and Area Business Managers

21

Average years of **industry experience**

14

Average years of **cardiovascular experience**

4

Average years **rare disease experience**

5

Average number of **President's Awards** for sales performance

Cytokinetics®

Key Launch Drivers to Achieve High Share and Grow Category

Clinical

Rapid & sustained
symptom improvement and reduction in obstruction

Flexibility to rapidly titrate
as early as 2 weeks, with flexible monitoring schedule

No treatment interruptions
or worsening HF events observed in patients with LVEF <50% in SEQUOIA-HCM

REMS

Flexibility to rapidly titrate as early as 2 weeks

- ✓ Dose may be titrated after each echocardiogram
- ✓ Echocardiogram assessment within 2 to 8 weeks
- ✓ No monthly DDI screens required with the pharmacy

Monitor every 6 months

- ✓ Echocardiogram every 6 mo. for patients with LVEF ≥55%
  - ✓ Every 3 mo. if LVEF is <55 & ≥50%
- ✓ No monthly DDI screens required with the pharmacy

Patient Support Services

1. Provide a ***compliant*** single point of contact model that is ***flexible and scalable***
2. Deliver a ***consistent but tailored user experience*** based on patient & provider preferences
3. Enable ***streamlined & seamless*** engagement with Cytokinetics systems & programs
4. Build ***empathetic connections*** with patients and providers

HF: heart failure; LVEF: left ventricular ejection fraction; REMS: Risk Evaluation and Mitigation Strategies; DDI: drug-drug interaction

Cytokinetics®

Key Features of REMS Monitoring Schedule for First Year of Therapy

Estimated Titration Regimen Across Dose Range

MYQORZO™ (aficamten)

Starting dose of 5 mg

Process Step [within 12 months]	5 mg	10 mg	15 mg	20 mg
Echocardiogram*	3	4	5	6
Patient Monitoring Form⁺*	3	4	5	6
Pharmacy DDI Checklist*	0	0	0	0
Required DDI Screen with Patient‡	0	0	0	0
Minimum # of Months to Reach Maintenance	0.5	1	1.5	2.0

CAMZYOS® (mavacamten)

Starting dose of 5 mg

Process Step [within 12 months]	5 mg	2.5 mg**	10 mg	15 mg
Echocardiogram*	5	6	7	8
Patient Status Form⁺*	5	6	7	8
Pharmacy DDI Checklist*	12	12	12	12
Required DDI Screen with Patient‡	12	12	12	12
Minimum # of Months to Reach Maintenance	3	4	6	9

There are no head-to-head studies between MYQORZO™ and CAMZYOS®; therefore, no comparisons between their safety and efficacy can be made.

	MYQORZO™	CAMZYOS®
Up-titration	Increase dose **after each echo,** as soon as **every 2 weeks.**	Increase dose **after Week 12** if LVEF ≥55% and Valsalva LVOT-G ≥30 mmHg.
Echo	Echocardiogram within 2 to 8 weeks of treatment initiation or dose adjustment.	Echocardiograms at Weeks 4, 8, & 12 to increase starting dose. Weeks 16 & 24 to increase dose. Weeks 28 & 36 to confirm maximum dose.
LVOT-G	**No down-titration required based on LVOT-G. Down-titration based on LVEF only.**	**Down-titration at Week 4 and Week 8 based on LVEF and if Valsalva LVOT-G <20 mmHg.**
Dispensing	Patients can be dispensed up to **90-day supply** in maintenance phase.	Patients are limited to **35-day supply** in maintenance phase for first 12 months of therapy.
DDI Calls	**No requirement for monthly DDI screen or checklist.**	**DDI screen required** between patient and pharmacy prior to each dispense.***

DDI: Drug-drug interaction; LVEF: left ventricular ejection fraction; LVOT-G: left ventricular outflow tract gradient.

¶CAMZYOS® is a trademark of MyoKardia, Inc., a Bristol Myers Squibb company.

‡Estimated titration timing assume echocardiograms are performed as early as possible and that no down-titration is required.

*Number includes eligibility echocardiogram and patient enrollment form.

**Patients are initiated at 5mg; lowest dose is 2.5 mg. An estimated 35% of patients down titrate to 2.5 mg after starting 5mg.

***Potentially every 3 months after first year on therapy depending on insurance coverage and dispensing schedule.

⁺Can be faxed, emailed, or uploaded to REMS portal; enables drug dispensing.

‡Assumes phone is answered on first call; calls are made per patient, not per prescriber's office. Occurs monthly for initial 12 months of therapy.

#Prescribers must submit a Patient Status Form (PSF) to the Camzyos REMS portal within 3 days of each scheduled echocardiogram.

Cytokinetics®

MYQORZO & You™: Bespoke Treatment Experience

MYQORZO & You™
PERSONALIZED PATIENT SUPPORT

Patient Activation & Engagement

Access & Reimbursement	Support investigating patient's health insurance benefits, OOP cost, Prior Authorization and/or Appeal criteria & submission
Free Trial Program	Free drug supply during trial period for eligible government-insured patients *Limited to one use per patient per lifetime. On-label use only. Age, financial need & residency criteria apply.*
Bridge Program	Free drug supply for up to 12 months for commercially insured patients due to coverage delay

Patient Affordability

Co-Pay Program	Financial assistance for commercially-insured patients to reduce out-of-pocket costs for MYQORZO and echocardiograms
Patient Assistance Program	Free supply of MYQORZO for eligible patients meeting financial criteria

OOP: out-of-pocket

Cytokinetics®

Personal, Timely, Empowering Treatment Experience

Dedicated single point of contact for patient & HCP creates clarity, continuity, trust throughout treatment journey

HCP/Office Experience*

MYQORZO & You™ Navigator

Communicates the "how"

Dedicated single point of contact for entire treatment journey: status of dispense, missing information, reimbursement support, Patient Support Services, support REMS certifications & address REMS related questions

Primarily communicates with office staff

Cardiovascular Account Specialist

Communicates the "why"

Overall account owner responsible for driving demand, educating about MYQORZO, REMS, Patient Support Services, and access

Primarily communicates with prescriber

Patient Experience

MYQORZO & You™ Navigator

Dedicated single point of contact

Support from time of Rx through ongoing treatment to help with access & affordability, Patient Support Services, and REMS education

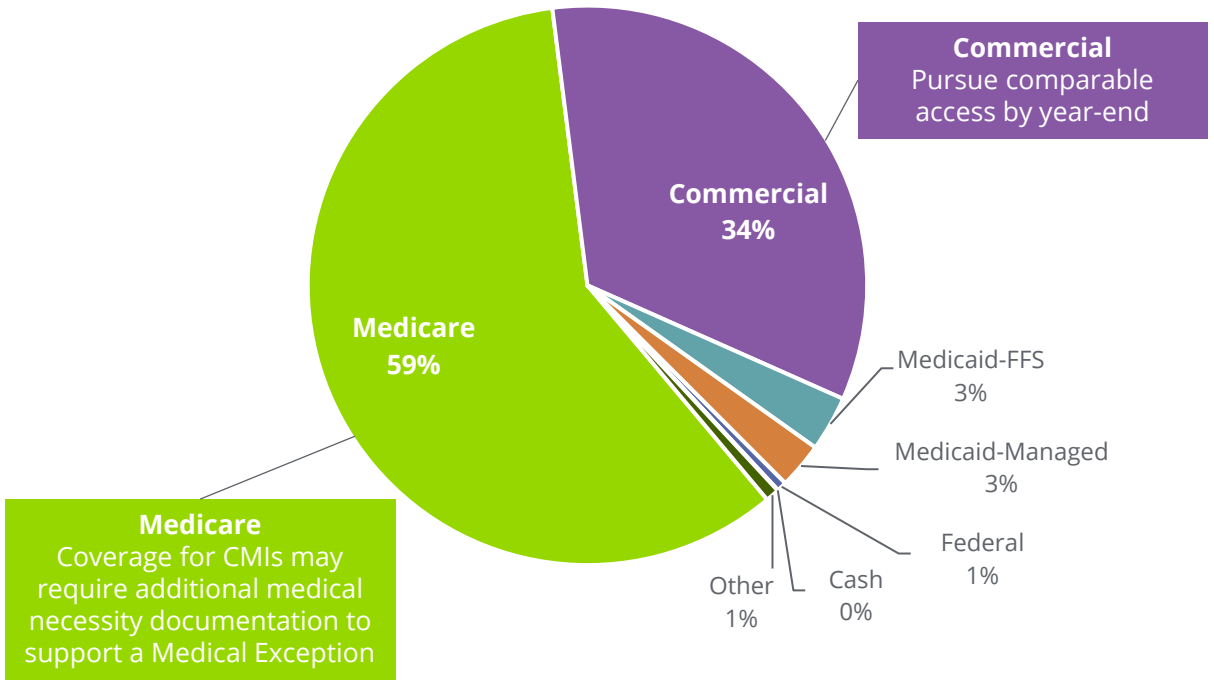
HCP: healthcare professional; REMS: Risk Evaluation and Mitigation Strategies; HCM: hypertrophic cardiomyopathy; PSS: Patient Support Services; Rx: Prescription
** The engagement will vary based on the Site of Care [COE vs. Community]*

Cytokinetics®

Market Access Strategy

Grow CMI class & compete via clinical differentiation, not price

CMI Q3 ’25 Payor Mix (TRx)



Goal to reach parity access with coverage criteria consistent with our clinical evidence. In 2026, plan to:

- **Continue engagement** with key payor accounts
- **Reinforce value proposition** based on clinical & HEOR evidence
- **Activate patient support services** for prior authorization & medical exception support

FFS: fee-for-service; HEOR: Health Economics & Outcomes Research. CMI: cardiac myosin inhibitor. TRx: total prescriptions
Source: Cytokinetics. DOF. Symphony PrescriberPayer – Camzyos claims

Measuring Launch Velocity: 3 Key Metrics

Potential to reach >50% share of new patients by the end of 2026

Breadth and depth of HCP prescribing of MYQORZO™

Number of HCPs
prescribing MYQORZO

Volume of MYQORZO prescriptions
each HCP writes

Volume of patients on MYQORZO

Volume of patients
on MYQORZO

HCP: healthcare provider
Please see full Prescribing Information, including Boxed WARNING and Medication Guide
Based on internal revenue forecast informed by demand studies

Cytokinetics®

MYQORZO™: Encouraging Early Engagement

Early launch metrics signal strong engagement and demand

Within first three weeks of drug availability
(Jan 26, 2026 – Feb 23, 2026)

>12,000

Customer engagements,
reaching over 95% of 700 HCPs who account for majority of CMI prescribing

Patients on therapy **within first week of availability**

>700

HCPs REMS certified
across HCM specialty centers and non-specialty centers

~90% of HCPs are aware of MYQORZO
on aided-basis in post-launch market research

Data as of February 24, 2026. MYQORZO was available in channel starting on January 26, 2026. Early metrics may not be indicative of long-term adoption or prescription trends.

Cytokinetics®

Precedents for Next-In-Class Success & Category Growth

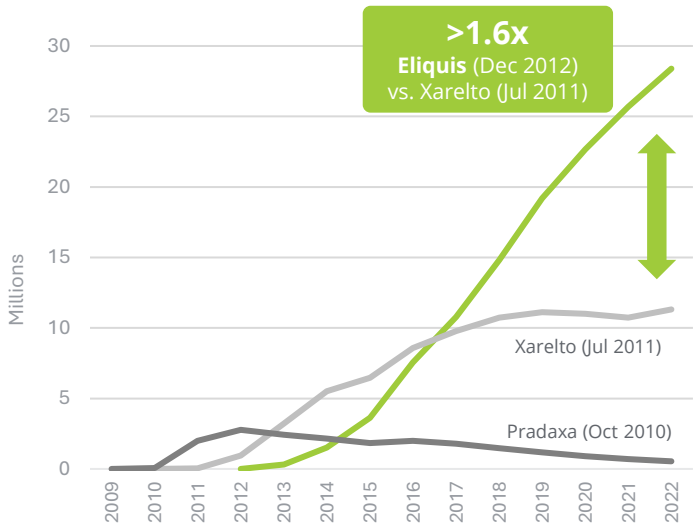
With differentiated product profile, Eliquis® generated 1.6x more prescriptions than Xarelto®

ATTR Class TRx has increased since Attruby™ launch

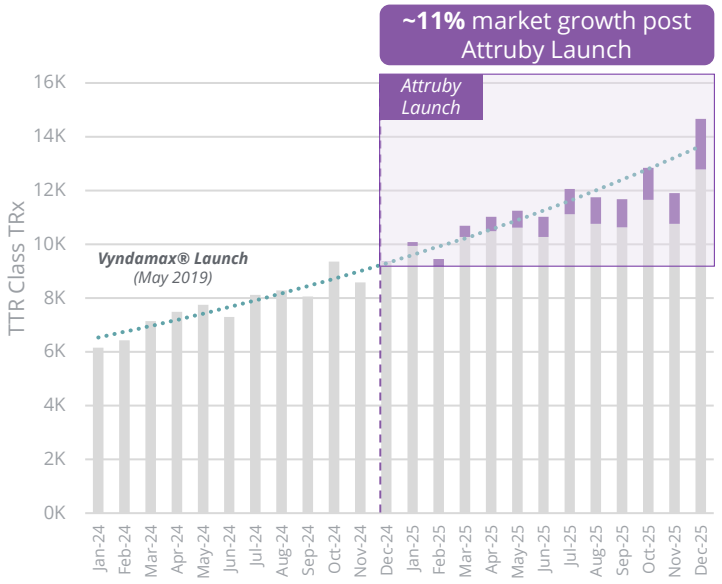
CMI market poised for growth[3]

Oral anticoagulants Pradaxa® (2010), Xarelto (2011), Eliquis (2012) approved over ~3 years

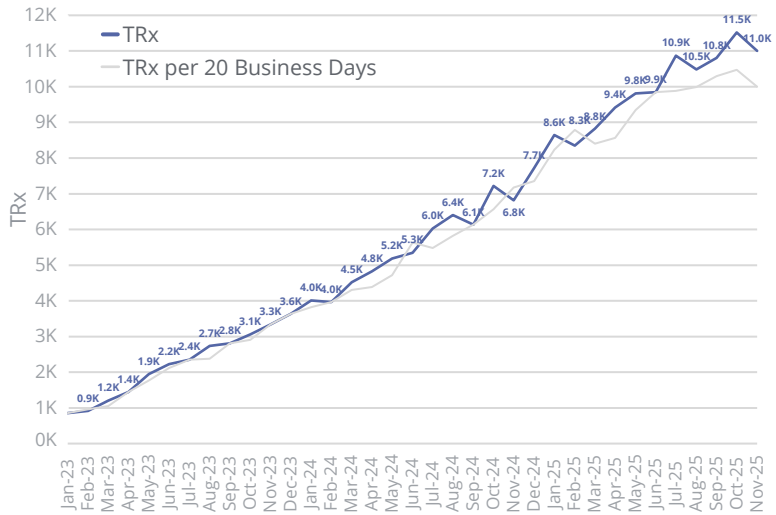
Rx per year (in M)[1]



Rx Per Month (in 000s)[2]



CAMZYOS® National Prescription Monthly Trend



Afib: atrial fibrillation; Rx: Prescription; ATTR: Transthyretin Amyloidosis; TRx: total prescriptions
1. Symphony National Projected Annual TRx data, 2010 – 2022
2. Symphony National Projected Annual TRx data, 2023 – 2025
3. Source: Symphony Metys national projections (TRxs) 2023-2025
Historical prescription trends for other therapeutic classes may not be predictive of future performance of MYQORZO or the CMI class. Differences in clinical profiles, market dynamics, reimbursement environment and competitive landscape may materially affect outcomes.

Cytokinetics®

MYQORZO™: Advancing Global Availability in 2026

United States

Approved by FDA for adults with symptomatic oHCM to improve functional capacity and symptoms

LAUNCHED JAN 2026

Cytokinetics

China

Approved by NMPA for adults with NYHA class II-III oHCM to improve exercise capacity and symptoms

LAUNCHED JAN 2026

Cytokinetics

sanofi

European Union

Approved by the European Commission for symptomatic (NYHA class II-III) oHCM in adult patients

LAUNCH EXPECTED IN GERMANY Q2 2026

Cytokinetics

Canada

New Drug Submission accepted for review by Health Canada

Expect to receive decision in 2H 2026

Cytokinetics

Japan

Phase 3 clinical trials ongoing in oHCM & nHCM

Cytokinetics

BAYER

FDA: U.S. Food & Drug Administration; oHCM: obstructive hypertrophic cardiomyopathy; NMPA: National Medical Products Administration; NYHA: New York Heart Association; MAA: marketing authorization application; EMA: European Medicines Agency; CHMP: Committee for Medicinal Products for Human Use; nHCM: non-obstructive hypertrophic cardiomyopathy.

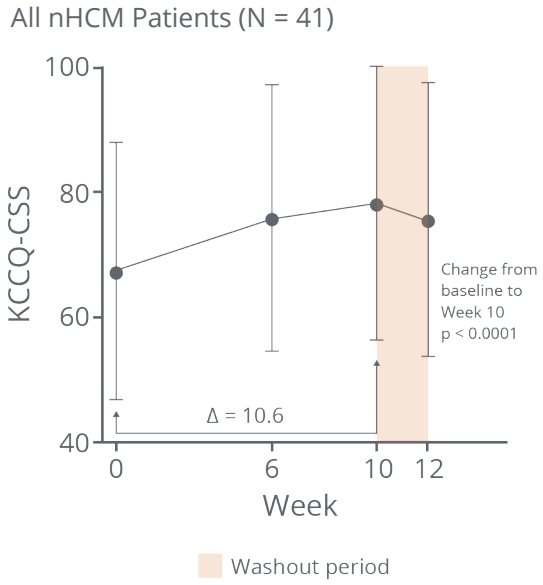
MYQORZO is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

REDWOOD-HCM Cohort 4: Phase 2 Trial in nHCM

Significant Improvements in KCCQ & NYHA Class

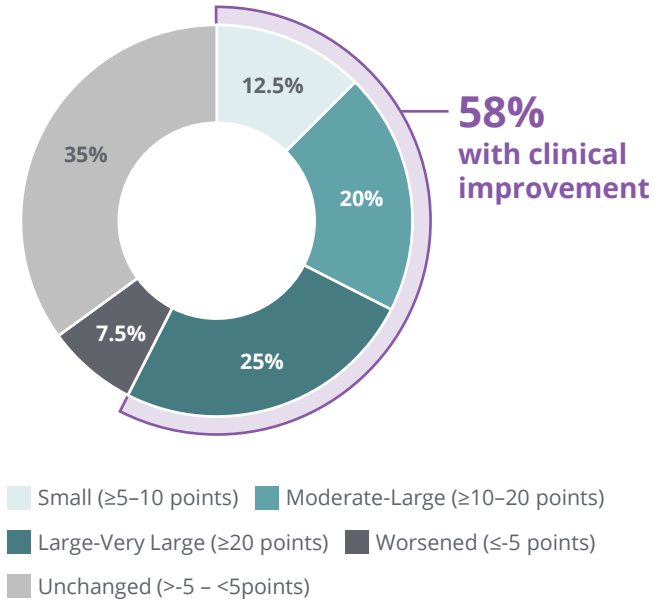
85% of patients achieved 15 mg dose; no discontinuations due to adverse events

Kansas City Cardiomyopathy Questionnaire
Mean improvement in KCCQ of 10.6 points

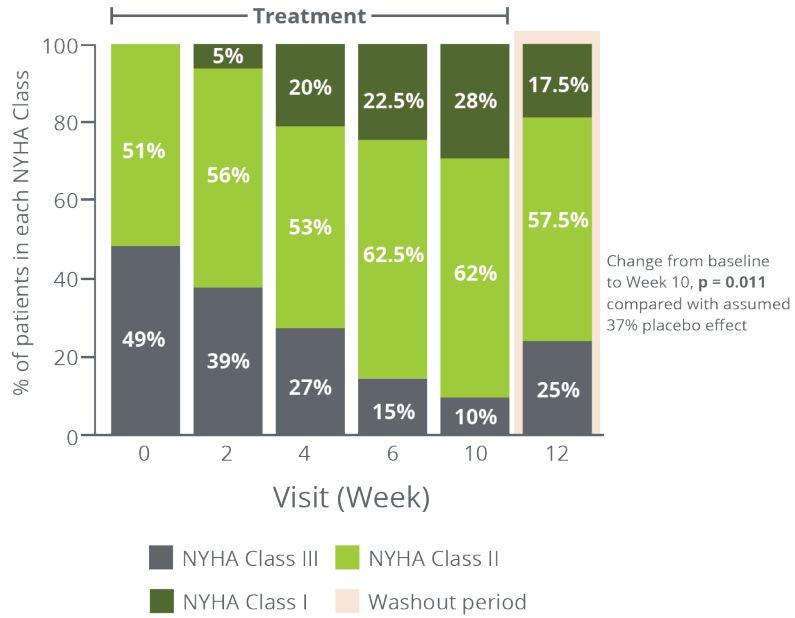


Data presented as mean and standard deviation

Categorical Changes at Week 10 in KCCQ-CSS



NYHA Functional Class
56% of patients improved by ≥1 NYHA class



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

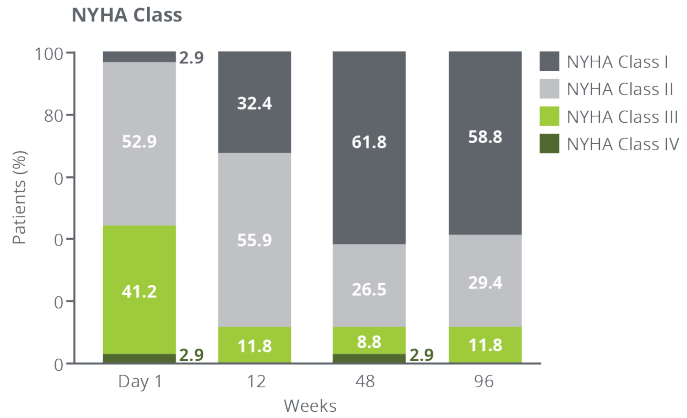
MYQORZO™ (aficamten) is only approved in the U.S., China and EU for the treatment of adults with symptomatic oHCM.

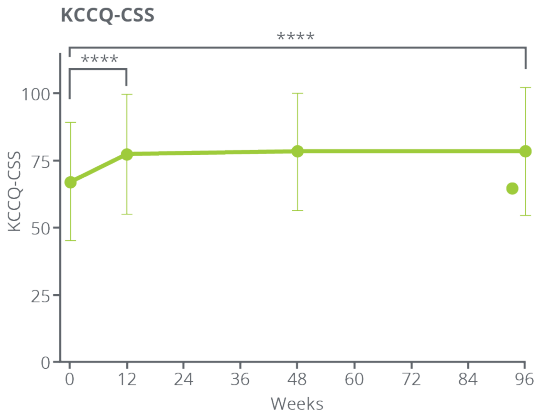
Cytokinetics®

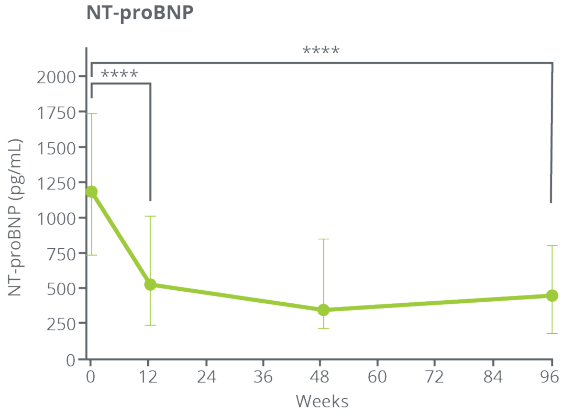
FOREST-HCM: 96-Week Open-Label Data in nHCM

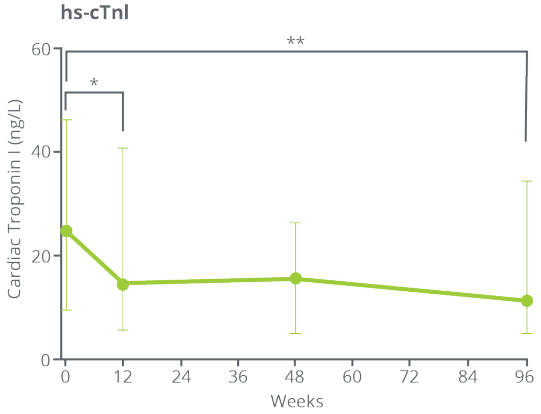
Analysis of 34 patients enrolled in FOREST-HCM after REDWOOD-HCM Cohort 4

- ✓ No early treatment discontinuations, with sustained reductions in symptom burden
- ✓ 79% of patients improved by at least one NYHA Functional Class
- ✓ Mean increase in KCCQ-CSS of 11.2 points
- ✓ Improvements in cardiac biomarkers









****P<0.0001, **P<0.01, *P<0.05

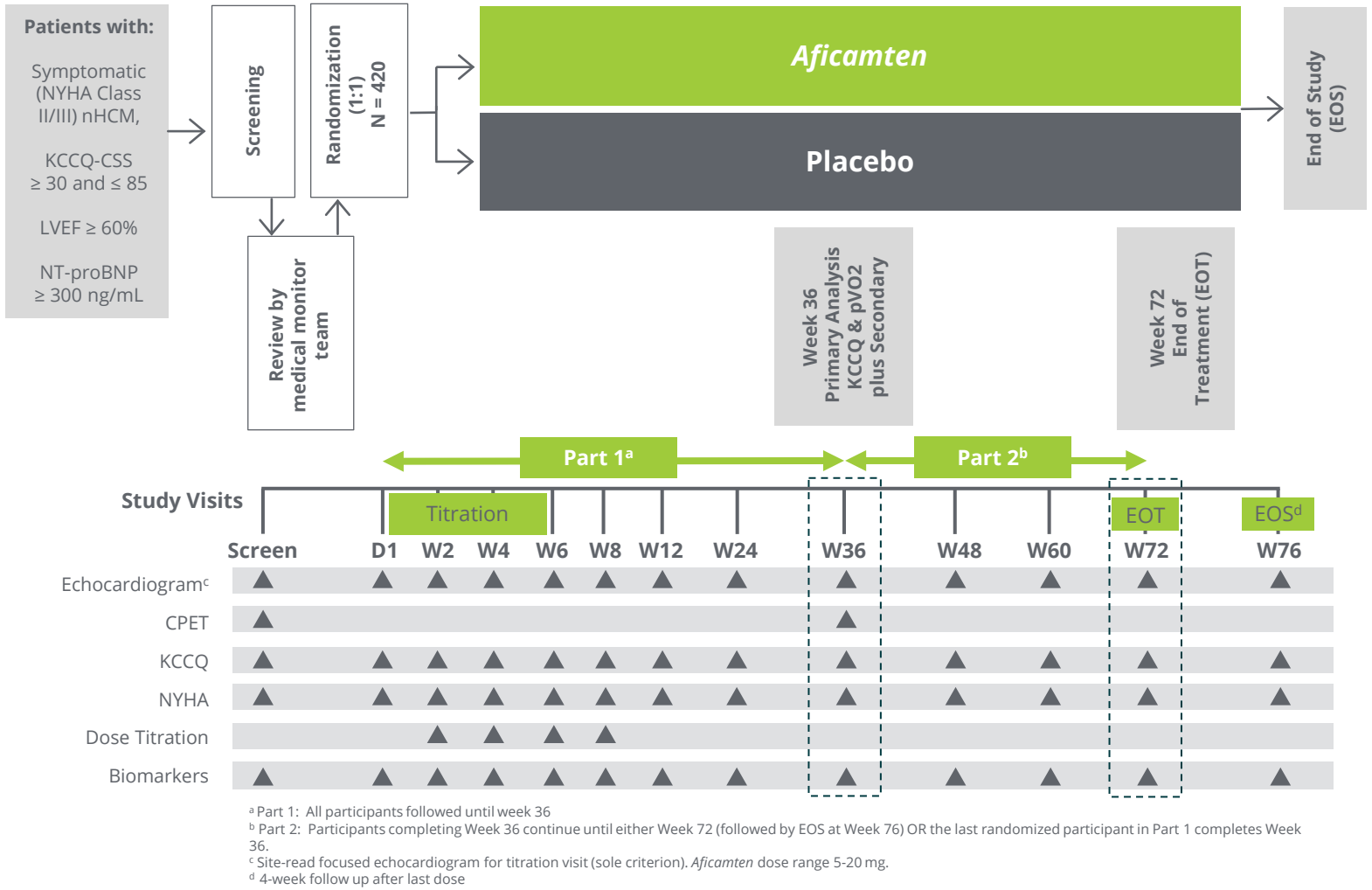
NYHA: New York Heart Association; KCCQ: Kansas City Cardiomyopathy Questionnaire; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; hs-cTnI: high-sensitivity cardiac troponin I
Masri A. et al. "Safety and Efficacy of Aficamten in Patients With Nonobstructive Hypertrophic Cardiomyopathy: A 96-Week Analysis From FOREST-HCM". Journal of Cardiac Failure. 2025.
MYQORZO™ (aficamten) is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

Cytokinetics®

ACACIA-HCM: Pivotal Phase 3 Trial in nHCM

Enrollment complete; topline readout expected in Q2 2026

- Trial enrolled over **516 symptomatic nHCM patients**
- Dual primary endpoint: **change in KCCQ Clinical Summary Score and peak VO2** from baseline to Week 36
- **5-20 mg doses**; 6-week titration period
- Secondary endpoints:
  - Change in 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

MYQORZO™ is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.

Omecamtiv Mecarbil

Cytokinetics®

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

Omecamtiv Mecarbil: Potential for High-Risk Severe HF Patients Despite GDMT

Efficient, pragmatic Phase 3 clinical trial

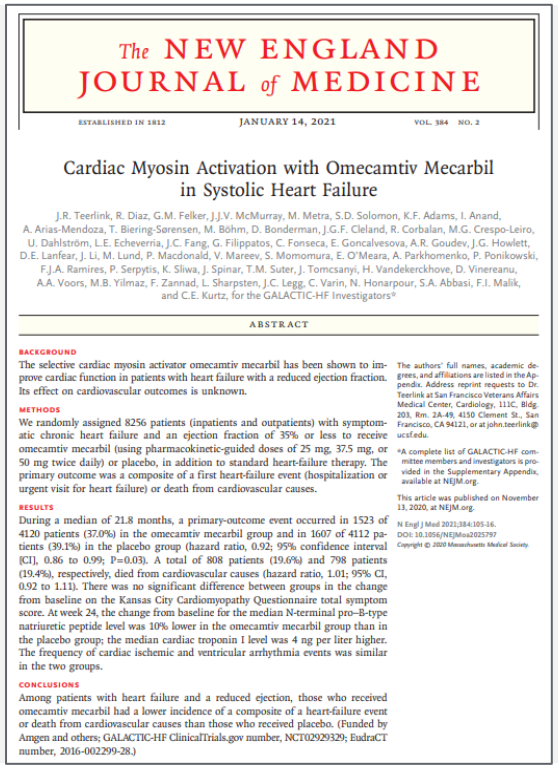
High Unmet Need

The large and growing heart failure population faces frequent hospitalizations, high mortality rates, comorbidities, and challenges staying on GDMT. Despite SGLT2 inhibitors, patients remain at significant risk.

Market Opportunity

18% of 7.1M patients with HFrEF have worsening heart failure (LVEF <30%)

Estimated 8+ years of market exclusivity



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 14, 2021 VOL. 384 NO. 2

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

J.R. Teerlink, R. Diaz, G.M. Felker, J.J.V. McMurray, M. Metra, S.D. Solomon, K.F. Adams, I. Anand, A. Arias-Mendoza, T. Biering-Sørensen, M. Böhm, D. Bonderman, J.G.F. Cleland, R. Corbalan, M.G. Crespo-Leiro, U. Dahlström, L.E. Echeverria, J.C. Fang, G. Filippatos, C. Fonseca, E. Goncalvesova, A.R. Goudev, J.G. Howlett, D.E. Lanfear, J. Li, M. Lund, P. Macdonald, V. Mareev, S. Momomura, E. O'Meara, A. Parkhomenko, P. Ponikowski, F.J.A. Ramires, P. Serpytis, K. Sliwa, J. Spinar, T.M. Suter, J. Tomcsanyi, H. Vandekerckhove, D. Vinereanu, A.A. Voors, M.B. Yilmaz, F. Zannad, L. Sharpsten, J.C. Legg, C. Varin, N. Honarpour, S.A. Abbasi, F.I. Malik, and C.E. Kurtz, for the GALACTIC-HF Investigators*

ABSTRACT

BACKGROUND

The selective cardiac myosin activator omecamtiv mecarbil has been shown to improve cardiac function in patients with heart failure with a reduced ejection fraction. Its effect on cardiovascular outcomes is unknown.

METHODS

We randomly assigned 8256 patients (inpatients and outpatients) with symptomatic chronic heart failure and an ejection fraction of 35% or less to receive omecamtiv mecarbil (using pharmacokinetic-guided doses of 25 mg, 37.5 mg, or 50 mg twice daily) or placebo, in addition to standard heart-failure therapy. The primary outcome was a composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes.

RESULTS

During a median of 21.8 months, a primary-outcome event occurred in 1523 of 4120 patients (37.0%) in the omecamtiv mecarbil group and in 1607 of 4112 patients (39.1%) in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI], 0.86 to 0.99; P=0.03). A total of 808 patients (19.6%) and 798 patients (19.4%), respectively, died from cardiovascular causes (hazard ratio, 1.01; 95% CI, 0.92 to 1.11). There was no significant difference between groups in the change from baseline on the Kansas City Cardiomyopathy Questionnaire total symptom score. At week 24, the change from baseline for the median N-terminal pro–B-type natriuretic peptide level was 10% lower in the omecamtiv mecarbil group than in the placebo group; the median cardiac troponin I level was 4 ng per liter higher. The frequency of cardiac ischemic and ventricular arrhythmia events was similar in the two groups.

CONCLUSIONS

Among patients with heart failure and a reduced ejection, those who received omecamtiv mecarbil had a lower incidence of a composite of a heart-failure event or death from cardiovascular causes than those who received placebo. (Funded by Amgen and others; GALACTIC-HF ClinicalTrials.gov number, NCT02929329; EudraCT number, 2016-002299-28.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Teerlink at San Francisco Veterans Affairs Medical Center, Cardiology, 111C, Bldg. 203, Rm. 2A-49, 4150 Clement St., San Francisco, CA 94121, or at john.teerlink@ucsf.edu.

*A complete list of GALACTIC-HF committee members and investigators is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 13, 2020, at NEJM.org.

N Engl J Med 2021;384:105-16.
DOI: 10.1056/NEJMoa2025797
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Ph 3 clinical trial results in 8,000 patients point to important treatment benefit

Planning confirmatory Ph 3 trial, **n= ~1,800, ~3 years** to completion

Primary endpoint: time to CV death, HF events, transplant/LVAD, or stroke

Larger treatment benefit in patients with lower LVEF and other markers of advanced HF

Pragmatic design elements including EHR screening, limited monitoring visits, remove visits, and limited safety labs & AE reporting

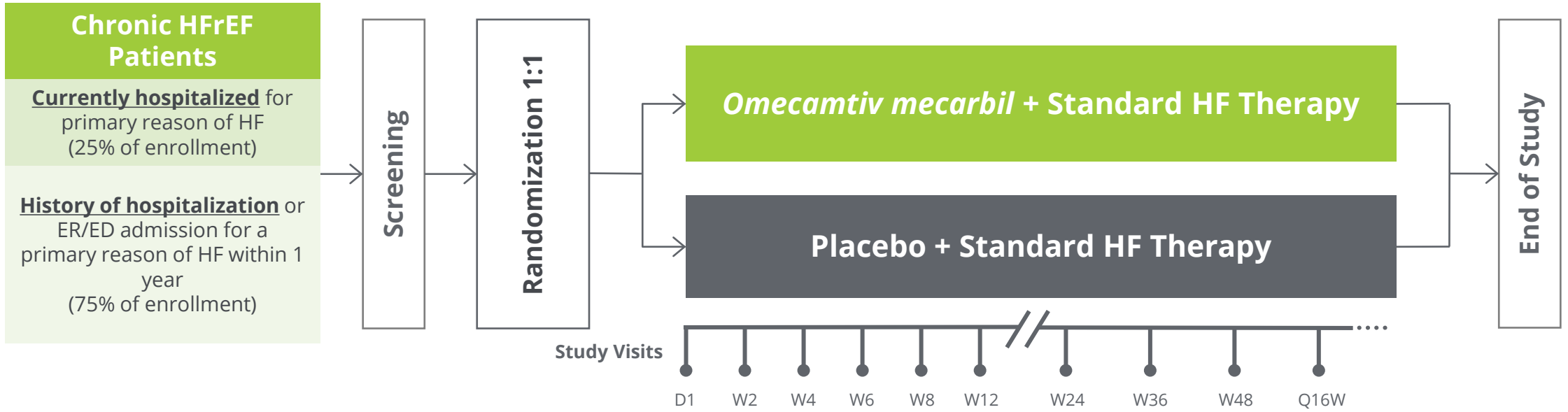
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Cytokinetics®

GALACTIC-HF: Clinical Trial Overview

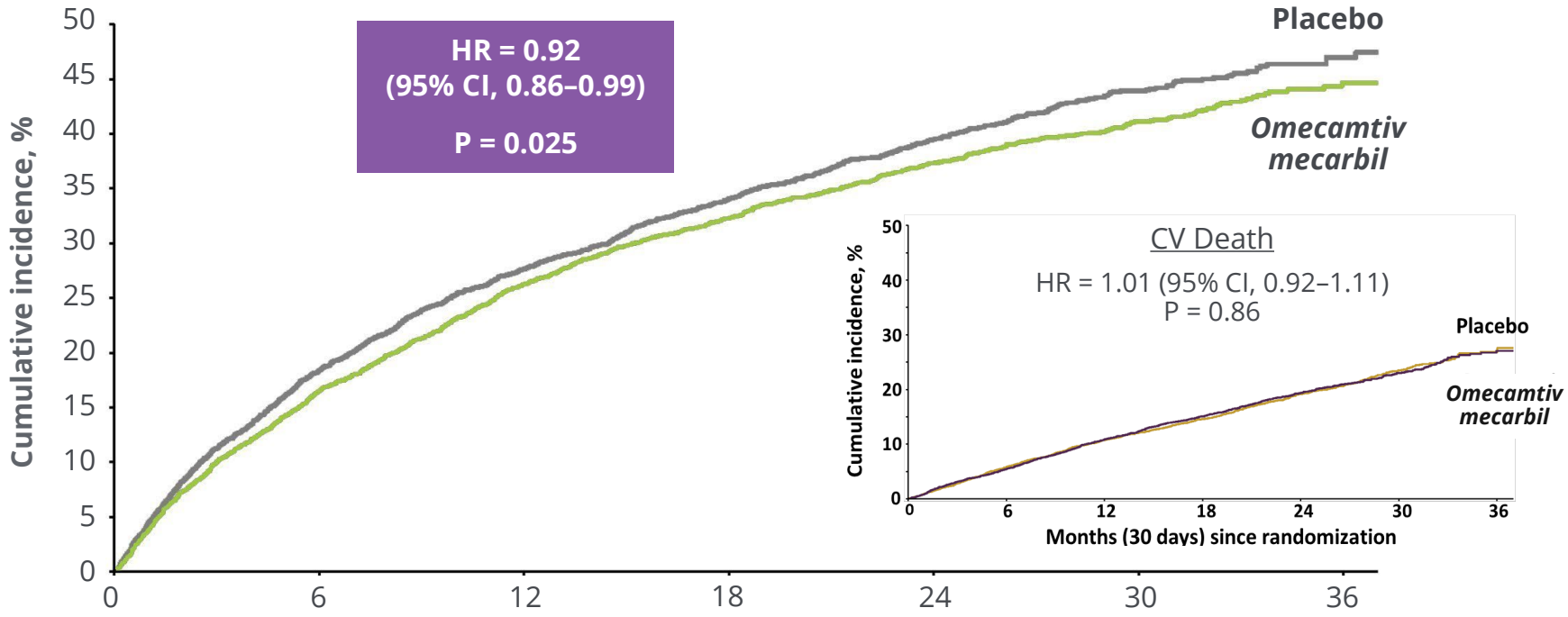
Phase 3 clinical trial

Event-driven clinical trial; 8,256 patients randomized in 35 countries at 944 clinical trial sites

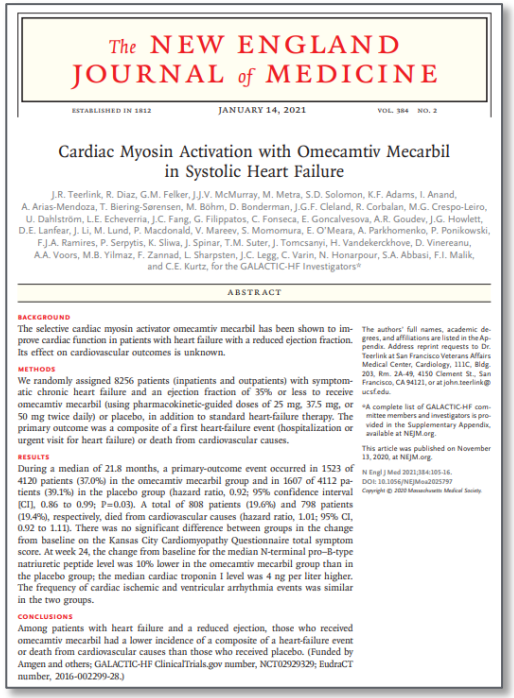


Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Primary Composite Endpoint



Patients at risk, n							
Placebo	4112	3310	2889	2102	1349	647	141
OM	4120	3391	2953	2158	1430	700	164


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 14, 2021 VOL. 384 NO. 2

Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

J.R. Teerlink, R. Diaz, G.M. Felker, J.J.V. McMurray, M. Metra, S.D. Solomon, K.F. Adams, I. Anand, A. Arias-Mendoza, T. Biering-Sørensen, M. Böhm, D. Bonderman, J.G.F. Cleland, R. Corbalan, M.G. Crespo-Leiro, U. Dahlström, L.E. Echeverria, J.C. Fang, G. Filippatos, C. Fonseca, E. Goncalvesova, A.R. Goudev, J.G. Howlett, D.E. Lanfear, J. Li, M. Lund, P. Macdonald, V. Mareev, S. Momomura, E. O'Meara, A. Parkhomenko, P. Ponikowski, F.J.A. Ramires, P. Serpytis, K. Sliwa, J. Spinar, T.M. Suter, J. Tomcsanyi, H. Vandekerckhove, D. Vinereanu, A.A. Voors, M.B. Yilmaz, F. Zannad, L. Sharpsten, J.C. Legg, C. Varin, N. Honarpour, S.A. Abbasi, F.I. Malik, and C.E. Kurtz, for the GALACTIC-HF Investigators*

ABSTRACT

BACKGROUND

The selective cardiac myosin activator omecamtiv mecarbil has been shown to improve cardiac function in patients with heart failure with a reduced ejection fraction. Its effect on cardiovascular outcomes is unknown.

METHODS

We randomly assigned 8256 patients (inpatients and outpatients) with symptomatic chronic heart failure and an ejection fraction of 35% or less to receive omecamtiv mecarbil (using pharmacokinetic-guided doses of 25 mg, 37.5 mg, or 50 mg twice daily) or placebo, in addition to standard heart-failure therapy. The primary outcome was a composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes.

RESULTS

During a median of 21.8 months, a primary-outcome event occurred in 1523 of 4120 patients (37.0%) in the omecamtiv mecarbil group and in 1607 of 4112 patients (39.1%) in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI], 0.86 to 0.99; P=0.03). A total of 808 patients (19.6%) and 798 patients (19.4%), respectively, died from cardiovascular causes (hazard ratio, 1.01; 95% CI, 0.92 to 1.11). There was no significant difference between groups in the change from baseline on the Kansas City Cardiomyopathy Questionnaire total symptom score. At week 24, the change from baseline for the median N-terminal pro–B-type natriuretic peptide level was 10% lower in the omecamtiv mecarbil group than in the placebo group; the median cardiac troponin I level was 4 ng per liter higher. The frequency of cardiac ischemic and ventricular arrhythmia events was similar in the two groups.

CONCLUSIONS

Among patients with heart failure and a reduced ejection, those who received omecamtiv mecarbil had a lower incidence of a composite of a heart-failure event or death from cardiovascular causes than those who received placebo. (Funded by Amgen and others; GALACTIC-HF ClinicalTrials.gov number, NCT02929329; EudraCT number, 2016-002299-28.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Teerlink at San Francisco Veterans Affairs Medical Center, Cardiology, 111C, Bldg. 203, Rm. 2A-49, 4150 Clement St., San Francisco, CA 94121, or at john.teerlink@ucsf.edu.

*A complete list of GALACTIC-HF committee members and investigators is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 13, 2020, at NEJM.org.

N Engl J Med 2021;384:105-16.
DOI: 10.1056/NEJMoa2025797
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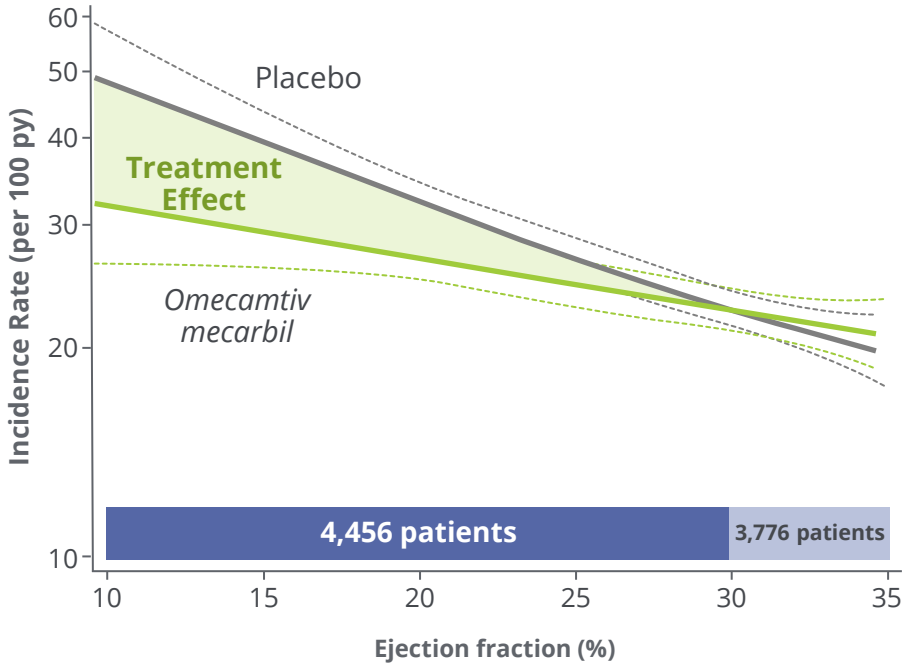
Time to first HF event or CV death

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

Benefit Observed to Increase as Baseline LVEF Decreased

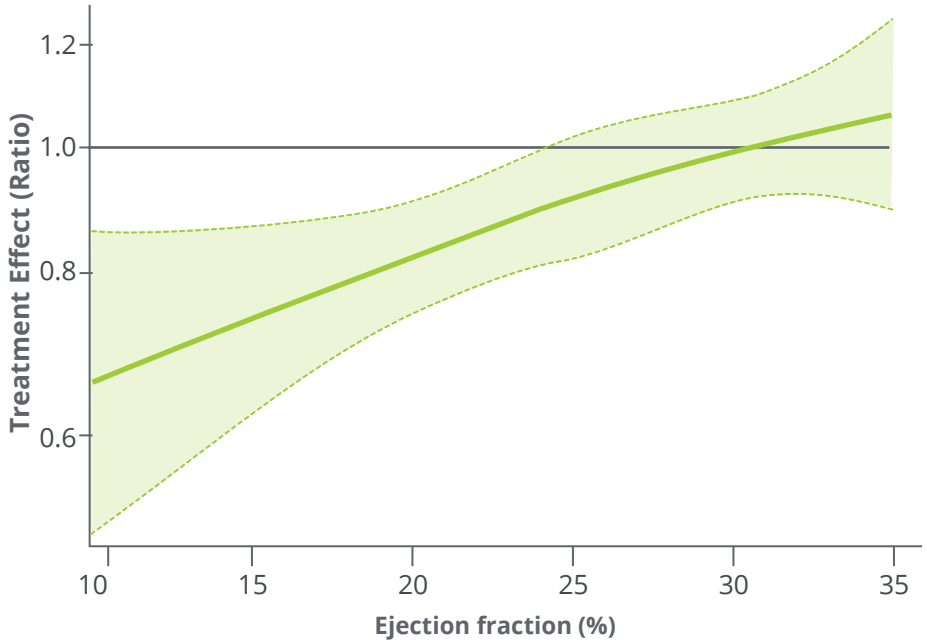
GALACTIC-HF

Incidence of Primary Composite Endpoint



Pre-specified Subgroup	Baseline LVEF	≤ median (28%)	0.84 (0.77, 0.92)
		> median (28%)	1.04 (0.94, 1.16)
	Interaction P-value = 0.004		

Relative Treatment Effect on Primary Endpoint



JACC

ORIGINAL INVESTIGATIONS

Effect of Ejection Fraction on Clinical Outcomes in Patients Treated With Omecamtiv Mecarbil in GALACTIC-HF

ABSTRACT

ARR = Absolute Risk Reduction. RRR = Relative Risk Reduction.
Teerlink JR., Diaz R., Felker GM., et al. Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF. JACC. 2021
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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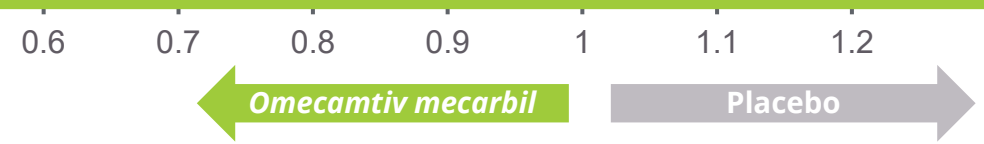
Large Treatment Effect in Easily Defined HF Population

GALACTIC-HF

	N	Hazard Ratio (95% CI)	Nom p-value	ARR
All Patients	8232		0.025	2.1
LVEF <30%	4704		<0.001	4.9
+ Hosp <3 mos	2836		<0.001	6.2
+ SBP <110	1881		0.004	7.2
+ Class III/IV	2249		<0.001	8.9
+ NT-proBNP ≥1000 pg/mL	2852		<0.001	8.8



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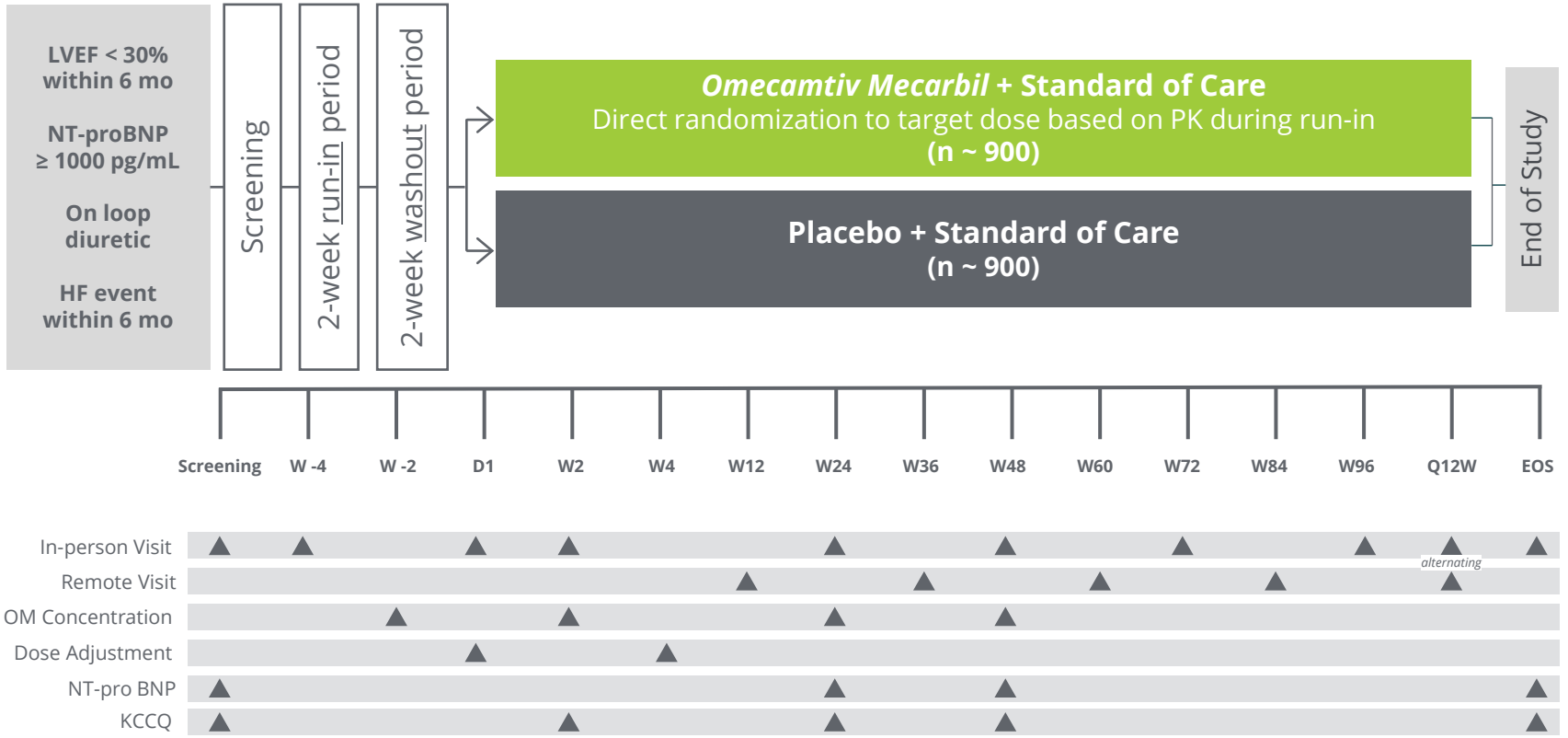
Phase 3 Confirmatory Clinical Trial Design

Currently enrolling

COMET-HF

COMET-HF: Confirmation of *Omecamtiv Mecarbil* Efficacy Trial in Heart Failure

- Primary endpoint: **time to CV death, HF events, transplant/LVAD, or stroke**
- **Enriching population for adherence** with OM run-in period
- **Pragmatic design elements:**
  - Remote clinic visits
  - Limited safety labs & ECGs
  - Streamlined eligibility and study conduct
  - Streamlined AE reporting



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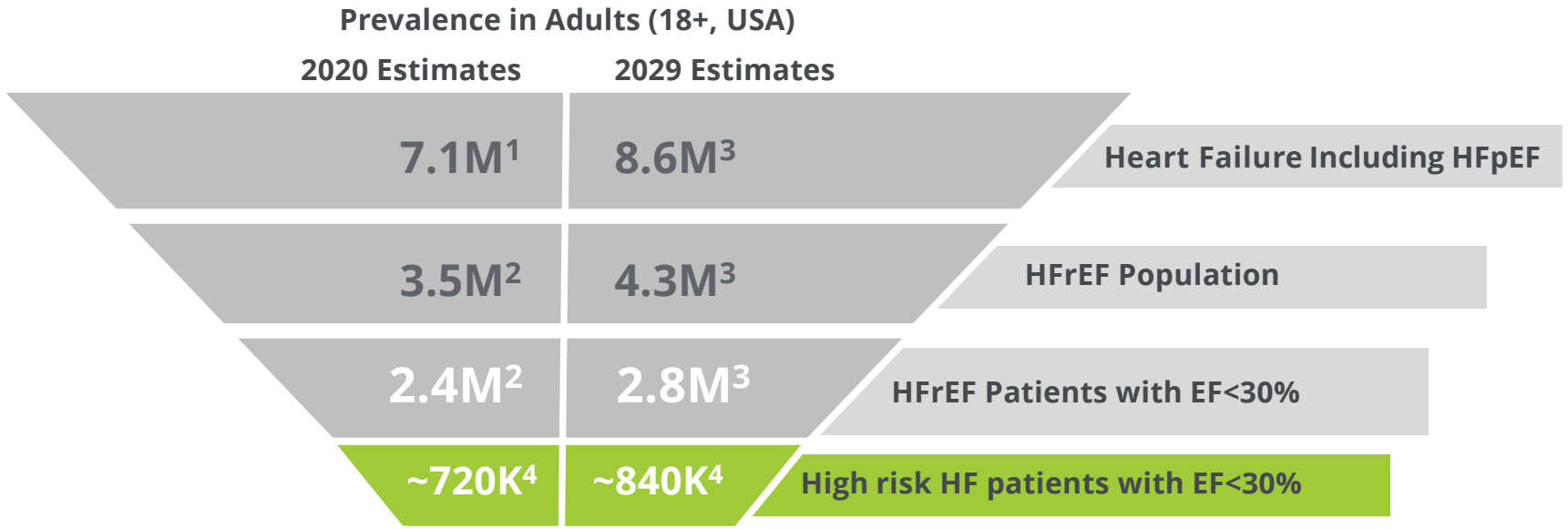
Large and Growing Target Patient Population in US



Proposed
Omecamtiv Mecarbil
Target Patient

Patients treated with GDMT and still experiencing severely reduced EF and symptoms of heart failure

Cardiac Function

LVEF < 30%

+

Markers of High-Risk HFrEF

- **HF Event* within the last 12 months**
- **Elevated NT-pro BNP**
- **Contraindications limiting GDMT, e.g. hypotension, renal dysfunction or hyperkalemia**

1. Tsao 2023, AHA. Racine 2022 CVrg. Bionest 2021.
2. 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.
3. 2.1% annual growth rate:1.9% annual growth rate of patient population 65+ (UN World Populations Prospects Nov 2019) and a 0.2% mortality impact of HF treatment (doi: 10.1136/bmj.l223 | BMJ 2019;364:l223)
4. Greene et al JACC 2023; 81:413-424
** HF Event: Urgent, unscheduled outpatient visit or hospitalization*
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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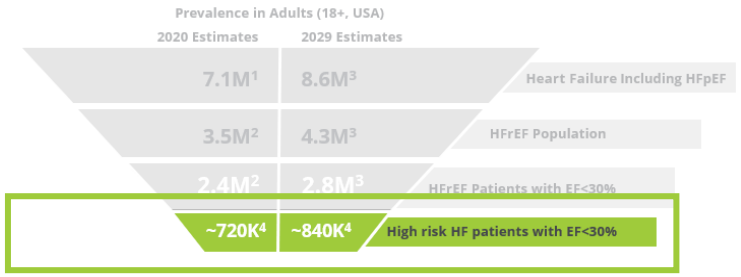
Higher Event Rate & Costs in Patients with Severely Reduced EF



Accounts for **~60% of HFrEF hospitalizations**[5]

35% of patients with severely reduced EF **re-hospitalized within 1 year**[6]

$15,493 per HF re-hospitalization[7]

Direct costs from HF re-hospitalizations projected to increase from **$3.9 billion** in 2020 to **$4.6 billion** by 2029**

1. Tsao 2023, AHA. Racine 2022 CVrg. Bionest 2021.
** HF Event: Urgent, unscheduled outpatient visit or hospitalization **in terms of 2024 dollars*
2. 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.
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4. Greene et al JACC 2023; 81:413-424
5. Extrapolated from Desai NR, Butler J, Binder G, Greene SJ. Prevalence and Excess Risk of Hospitalization in Heart Failure with Reduced Ejection Fraction. Poster presented at: Heart Failure Society of America (HFSA) Annual Scientific Meeting; 2022 Sep 30-Oct 3; Washington, DC.
6. Carnicelli AP, Clare RM, Hofmann P, Chiswell K, DeVore AD, Vemulapalli S, Felker GM, Kelsey AM, DeWald TA, Sarocco P, Mentz RJ. Clinical trajectory of patients with a worsening heart failure event and reduced ventricular ejection fraction. Am Heart J. 2022 Mar;245:110-116. doi: 10.1016/j.ahj.2021.12.003. Epub 2021 Dec 18. PMID: 34932997.
7. Urbich M, Globe G, Pantiri K, Heisen M, Bennison C, Wirtz HS, Di Tanna GL. A Systematic Review of Medical Costs Associated with Heart Failure in the USA (2014-2020). Pharmacoeconomics. 2020 Nov;38(11):1219-1236. doi: 10.1007/s40273-020-00952-0. PMID: 32812149; PMCID: PMC7546989.

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Ulacamten (CK-586)

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Ulacamten 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 have not been established.

Heart Failure with Preserved Ejection Fraction (HFpEF)

Despite broad use of standard treatments & advances in care, the prognosis for patients with HF is poor[1]

~75%

HFpEF patients will die within five years of initial hospitalization[2]

~84%

HFpEF patients will be rehospitalized[2]

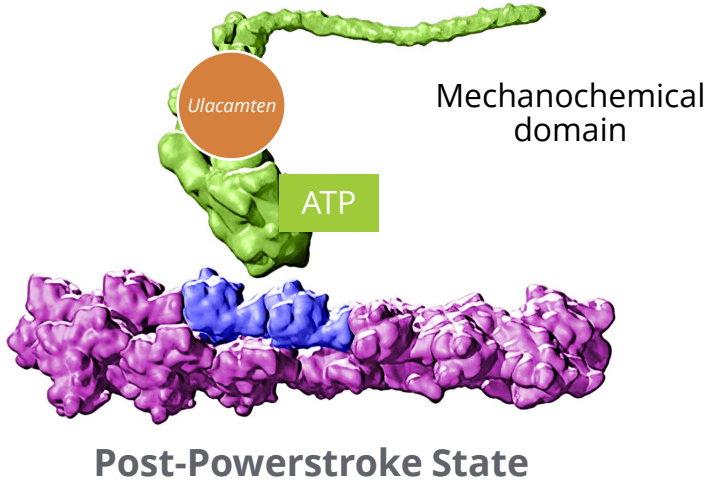
Subset of HFpEF patients with hypercontractility, ventricular hypertrophy, elevated biomarkers & HF symptoms **may benefit from a cardiac sarcomere inhibitor**

Significant increase in hospitalizations due to HFpEF, from 189,260 in 2008 to 495,095 in 2018 [6]

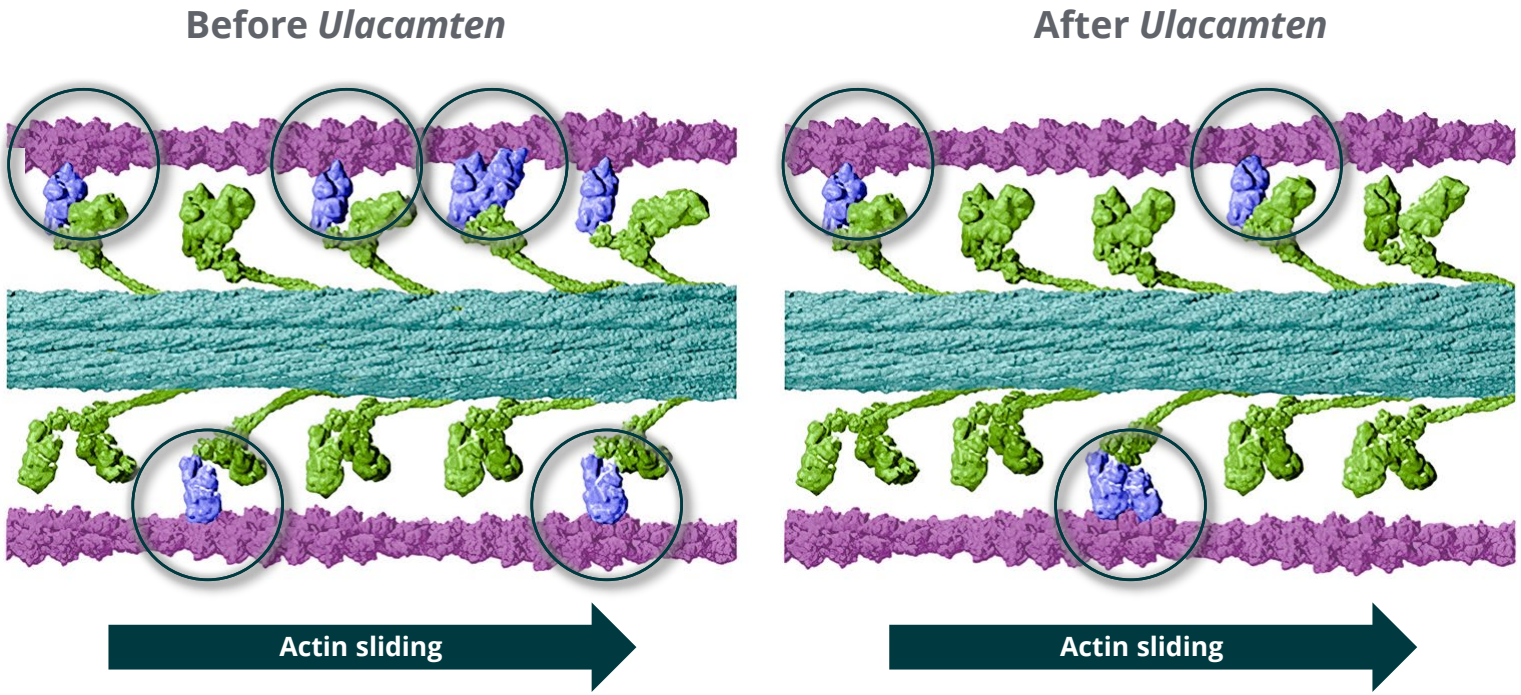
Lifetime healthcare costs for HFpEF are ~ $126,819 per patient[5], per-patient monthly cost for healthcare is $7,482, primarily, driven by **high rates of inpatient & outpatient visits**

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, Hsich 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.
5. Kapelios, Cardiac Failure Review 2023
6. Clark KAA, Reinhardt SW, Chouairi F et al (2022) Trends in heart failure hospitalizations in the US from 2008 to 2018. J Card Fail 28(2):171–180.
7. Lam CSP, Wood R, Vaduganathan M et al (2021) Contemporary economic burden in a real-world heart failure population with Commercial and Medicare supplemental plans. Clin Cardiol 44(5):646–655.

Ulacamten: Distinct Mechanism of Action from *Aficamten*



"Fewer hands pulling on the rope"



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

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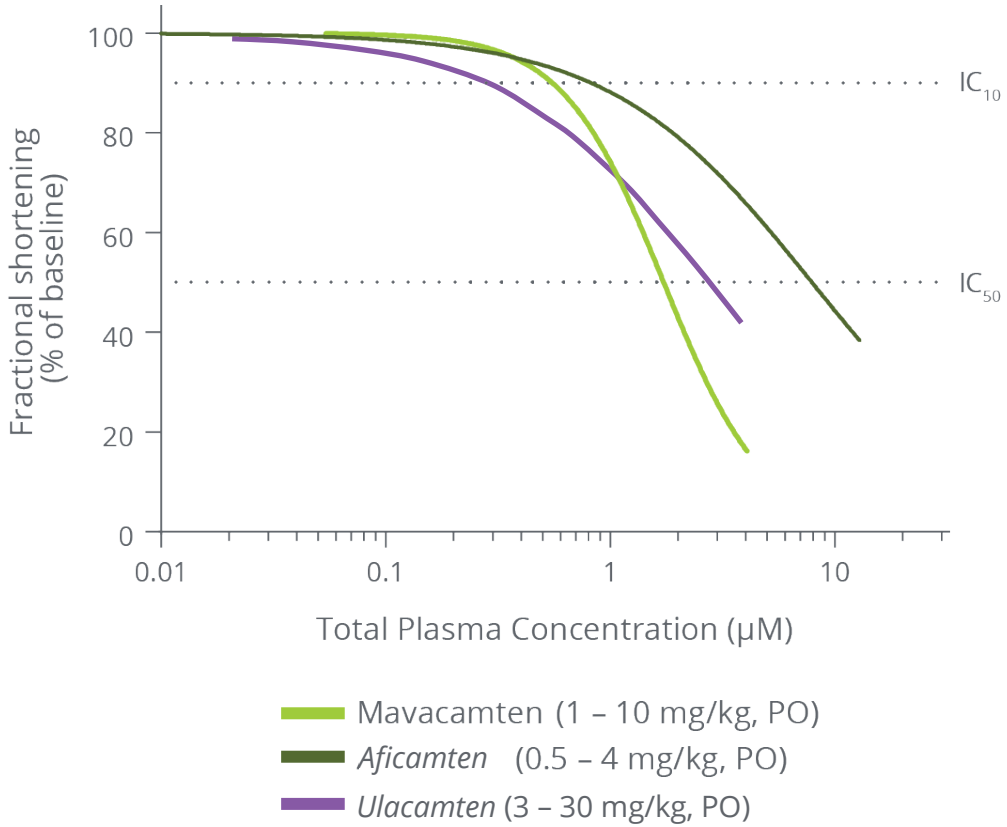
Ulacamten: Shallow *In Vivo* Concentration-Response

Ulacamten has a shorter half-life than *aficamten*



Pharmacodynamic window Fractional shortening IC_{50} /IC_{10} ratio	
mavacamten	2.8x
aficamten	9.9x
ulacamten	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
ulacamten	~15 hours	15 hours

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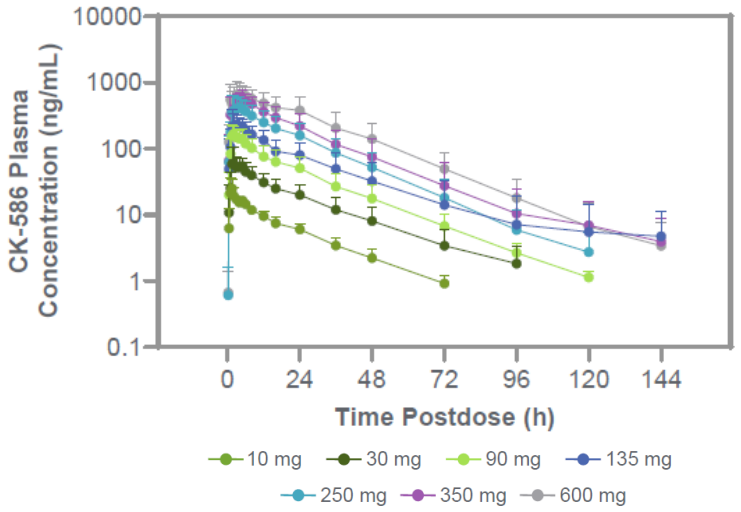
Phase 1 Data Support Advancement to Phase 2 Clinical Trial

Phase 1 study design: 7 SAD cohorts (10 mg to 600 mg) & 2 MAD cohorts (100 & 200 mg once daily), 10 participants each

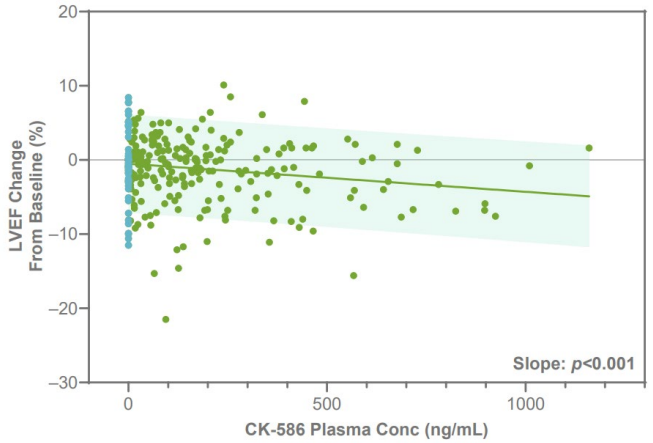
- **Less than 24-hour** half-life
- **Shallow and predictable** PK/PD relationship based on LVEF and LVFS
- **Well-tolerated** across all cohorts
- **No serious adverse events** were observed
- **Stopping criteria were not met**

Plasma Concentration

(mean [SD]) over time after single ascending doses of ulacamten



Change in LVEF vs. *Ulacamten* Plasma Concentration



PK/PD: pharmacokinetic/pharmacodynamic
LVEF: left ventricular ejection fraction
LVFS: left ventricular fractional shortening
Lutz JD., Simpkins T., Cheplo K., et al. A First-in-Human, Single and Multiple Ascending Dose Study of CK-4021586, a Novel Cardiac Myosin. Poster, American College of Clinical Pharmacology 2024.
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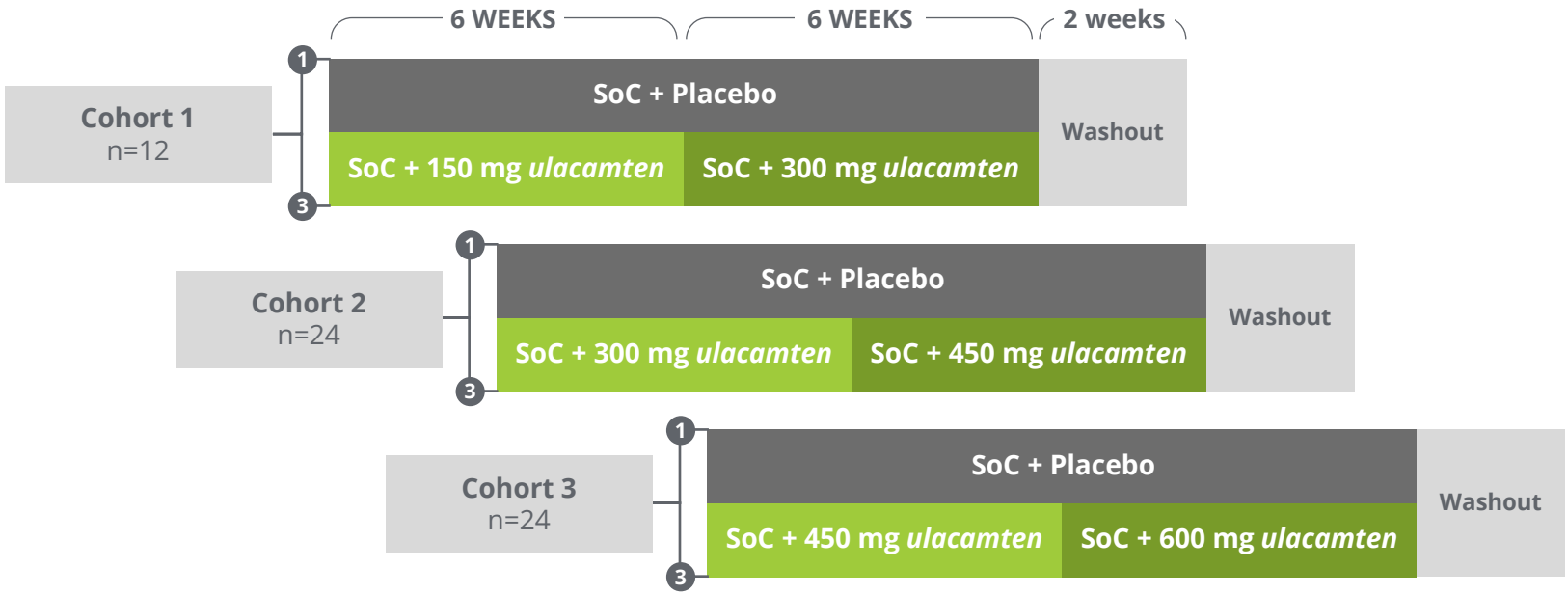
Phase 2 Study Schema

Currently enrolling

AMBER-HFpEF: Assessment of CK-586 in a **M**ulti-Center, **B**linded **E**valuation of Safety and Tolerability **R**esults in **HFpEF**

Enrolling HFpEF patients with:

- LVEF ≥ 60%
- Structural abnormality
- BMI < 40
- NYHA FC II or III
- NT-proBNP ≥ 300 (or ≥ 900 in AF)



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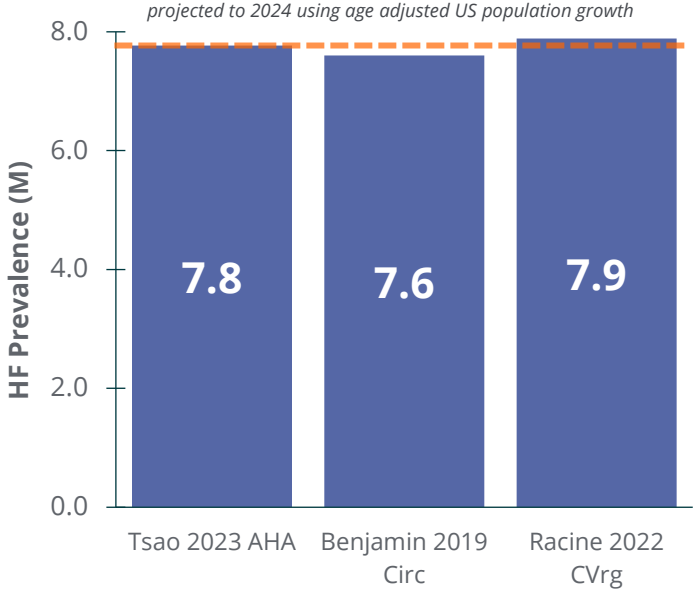
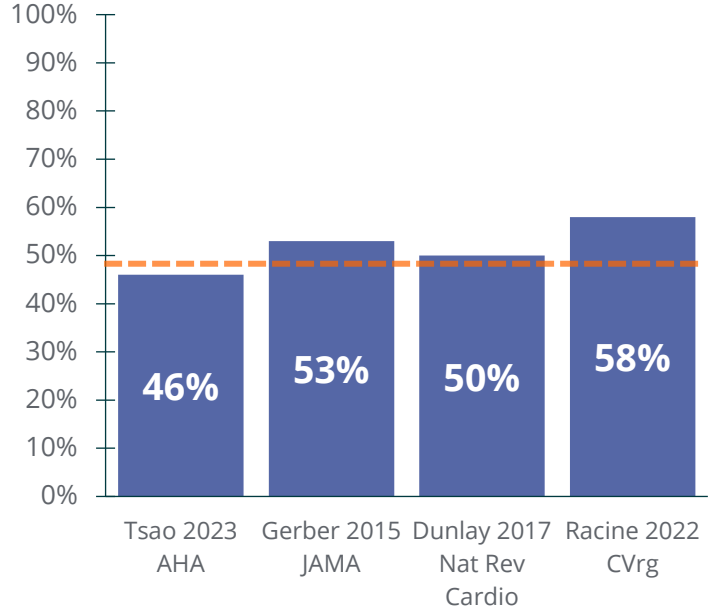
Ulacamten: Focusing on Patients with HFpEF and EF ≥ 60

7.9M
Heart Failure Prevalence in 2024, US

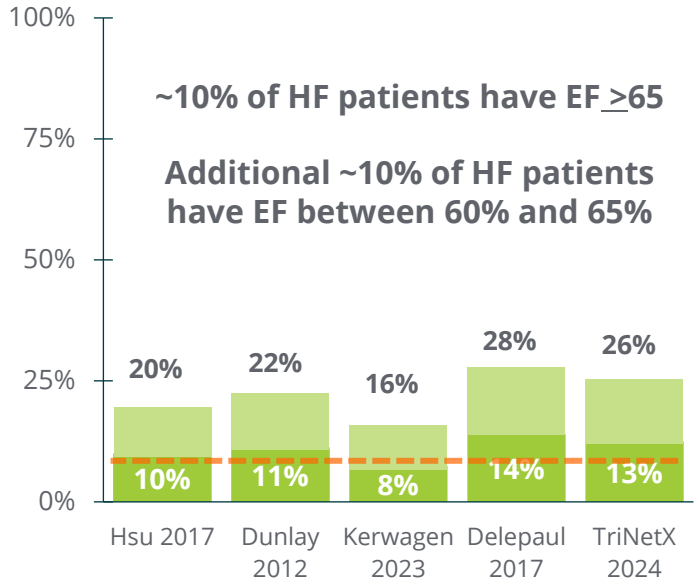
2024 prevalence calculated using published, historic estimate and projected to 2024 using age adjusted US population growth



4.0M (2024)
50% of HF with HFpEF (EF ≥ 50%)



1.0M (EF≥65) to 2.0M (EF ≥ 60)
~20% of HF with EF ≥ 60%



Source: Racine et al Heart Failure 2020-2029, CVrg March 2020 p 26; includes patients in long term care settings, which NHANES epi does not incorporate; Benjamin, E. et al. Heart Disease and Stroke Statistics—2019 Update: A Report From the AHA Circulation Vol 139, Issue 10, 5 March 2019; Pages e56-e528 historic growth rate of HF 2009-2012 vs. 2013-2016: 2.1%; the population of 65+ year old is expected to grow at 1.9% according to the UN – mortality improvement of 0.2% per year.; Heidenreich P. at al: Forecasting the Impact of Heart Failure in the United States Circulation: Heart Failure Volume 6, Issue 3 May 2013; Tsao C., et al Heart Disease and Stroke Statistics—2023 Update: A Report From the American Heart Association, Circulation Volume 139, Issue 10 Mar 2019; UN Population Report Nov 2020; 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, Gerber 2015 JAMA, Hsu JJ, Ziaeian B, Fonarow GC. Heart Failure With Mid-Range (Borderline) Ejection Fraction: Clinical Implications and Future Directions. JACC Heart Fail. 2017 Nov;5(11):763-771. doi: 10.1016/j.jchf.2017.06.013. Epub 2017 Oct 11. PMID: 29032140; PMCID: PMC6668914. Kerwagen F, Koehler K, Vettorazzi E, Stangl V, Koehler M, Halle M, Koehler F, Störk S. Remote patient management of heart failure across the ejection fraction spectrum: A pre-specified analysis of the TIM-HF2 trial. Eur J Heart Fail. 2023 Sep;25(9):1671-1681. doi: 10.1002/ejhf.2948. Epub 2023 Jul 31. PMID: 37368507. Delepaul B, Robin G, Delmas C, Moine T, Blanc A, Fournier P, Roger-Rollé A, Domain G, Delon C, Uzan C, Boudjellil R, Carrié D, Roncalli J, Galinier M, Lairez O. Who are patients classified within the new terminology of heart failure from the 2016 ESC guidelines? ESC Heart Fail. 2017 May;4(2):99-104. doi: 10.1002/ehf2.12131. Epub 2017 Jan 31. PMID: 28451445; PMCID: PMC5396039.

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Ulacamten May Address Unmet Needs of HFpEF Patients

Proposed Mechanistic Benefits

- *Ulacamten* may benefit cardiac relaxation during diastole
- *Ulacamten* may reduce symptoms and improve functional capacity

Target Product Profile

- Statistically significant reduction in composite of mortality and hospitalization outcomes
- Oral QD tablet
- Minimal drug interactions
- Simple dose titration with biomarker monitoring

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

Financials & Milestones

Strong Financial Position

Well-capitalized to execute launch & advance R&D pipeline

~$1.2B in cash, cash equivalents and investments as of December 31, 2025

Further access to capital through term loans with Royalty Pharma (RP)	Proceeds of $100M from Tranche 5 loan received in October 2025 Eligible to draw up to $175M from Tranche 7 loan
Potential further funding through RP opt-in	RP, at its option, can invest up to **$150M** in a Phase 3 trial of *ulacamten* in exchange for an additional 3.5% revenue participation interest in worldwide net sales of *ulacamten**

Add'l $325M

**Royalty Pharma currently has a revenue participation interest of 1.0% of worldwide net sales of ulacamten.*

2026 Financial Guidance

	Guidance Issued on Feb. 24, 2026
GAAP Combined R&D and SG&A Expense	**$830M to $870M**
Non-cash stock-based compensation expense included in GAAP Combined R&D and SG&A Expense	**$130M to $120M**

The financial guidance does not include: 1) collaboration expenses which can include reimbursed expenses and cost of inventory sales of *aficamten* to partners, 2) potential costs related to commercialization of *aficamten* in nHCM, and 3) the effect of GAAP adjustments as may be caused by events that occur subsequent to publication of this guidance including, but not limited to, Business Development activities.

2026 Expected Milestones

MYQORZO™ (aficamten) 5·10·15·20mg tablets	*Omecamtiv Mecarbil*	*Ulacamten*
Launch MYQORZO in Germany in Q2 2026 Report topline results from **ACACIA-HCM** in Q2 2026 Potential FDA decision on the sNDA for **MAPLE-HCM** in Q4 2026 Complete enrollment in the adolescent cohort of **CEDAR-HCM** in Q4 2026 Potential **Health Canada** decision on New Drug Submission in 2H 2026	Continue enrollment in **COMET-HF** through 2026	Complete enrollment in Cohort 1 of **AMBER-HFpEF** in Q1 2026 Complete enrollment in Cohort 2 of **AMBER-HFpEF** by the end of 2026

oHCM: obstructive hypertrophic cardiomyopathy; sNDA: Supplemental New Drug Application
MYQORZO is only approved in the U.S., China and the EU for the treatment of adults with symptomatic oHCM.
Ulacamten, omecamtiv mecarbil and CK-089 are investigational agents and have not been approved for use by any regulatory agency. Their safety and efficacy has not been established.
Timing of regulatory approvals is subject to regulatory review and may differ materially.

THANK YOU

Vi, diagnosed with HCM

Cytokinetics®

Actual patient who consented to use of their name, image, and condition.