Eric, diagnosed with HCM

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EMPOWERING

muscle

EMPOWERING

lives

Forward-Looking Statements

This presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements express or implied related Cytokinetics' research and development and commercial readiness activities, including the initiation, conduct, design, enrollment, progress, continuation, completion, timing and results of clinical trials, projections regarding growing prevalence, low survival rates and market opportunity in heart failure, hypertrophic cardiomyopathy (HCM) or heart failure with preserved ejection fraction (HFpEF); the likelihood and/or timing of regulatory approval for our planned new drug application for *aficamten*, *omecamtiv mecarbil* or any future new drug application for any of our other drug candidates or the anticipated timing of any interactions with FDA, EMA or any other regulatory authorities in connection thereto; the timing of completion of ACACIA-HCM, CEDAR-HCM, or any of our other clinical trials, the efficacy or safety of *aficamten*, *omecamtiv mecarbil,* CK-586 or any of our other drug candidates, our ability to fully enroll or to announce the results of any of our clinical trials by any particular date; the properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, CK-586 or any of Cytokinetics' other drug candidates, our ability to satisfy the conditions for disbursement of additional capital/loans under our agreements with Royalty Pharma, or Royalty Pharma's decision to opt-in to the further development of CK-586 for additional funding. Such statements are based on management's current expectations; but actual results may differ materially due to various risks and uncertainties, including, but not limited to, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, patient enrollment for or conduct of clinical trials may be difficult or delayed, Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy, the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics may incur unanticipated research, development and other costs or be unable to obtain financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. These forward-looking statements speak only as of the date they are made, and Cytokinetics undertakes no obligation to subsequently update any such statement, except as required by law. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission (the "SEC"). This presentation concerns drug candidates that are under clinical investigation, and which have not yet been approved by the U.S. Food and Drug Administration. These are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Disclaimer: The assumptions used in the preparation of this presentation, although considered reasonable by us at the time of preparation, may prove to be incorrect. You are cautioned that the information is based on assumptions as to many factors and that actual results may vary from the results projected and such variations may be material. Accordingly, you should not place undue reliance on any forward-looking statements contained herein or rely on them as predictions of future events.

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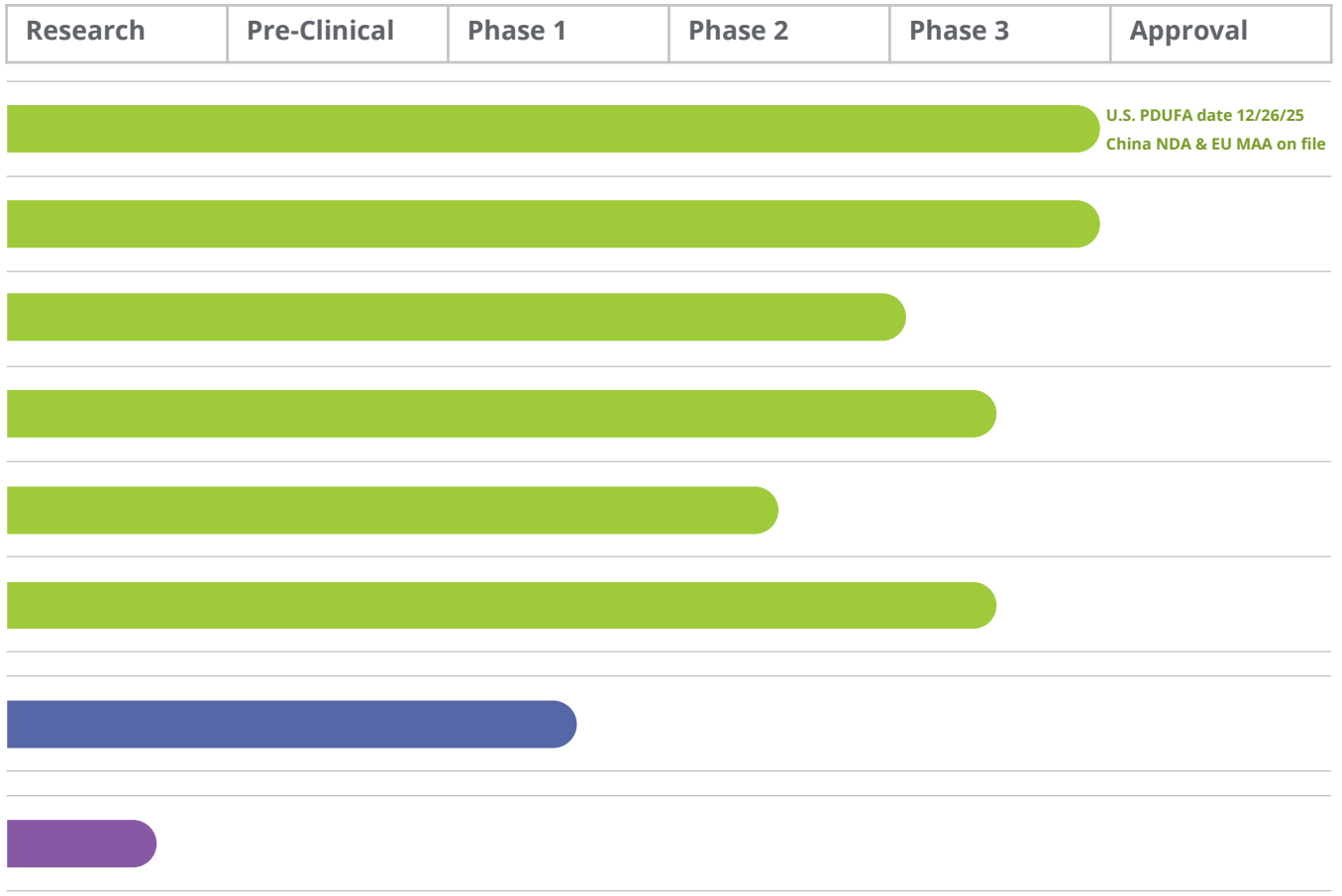
Our Mission

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

A Commitment to Muscle-Directed Cardiac Medicines

Protein Target	Therapeutic Area	Drug Candidate
Myosin	oHCM	*Aficamten*
	oHCM (Monotherapy*)	*Aficamten*
Myosin-Targeted Therapy	Pediatric oHCM	*Aficamten*
	nHCM	*Aficamten*
	HFpEF	*CK-586*
	HFrEF	*Omecamtiv Mecarbil*
Troponin	Troponin-Targeted Therapy	Muscular Dystrophy, other	*CK-089*
Other Biology	Muscle Biology Directed	*Research*



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

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

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Strong Financial Position

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

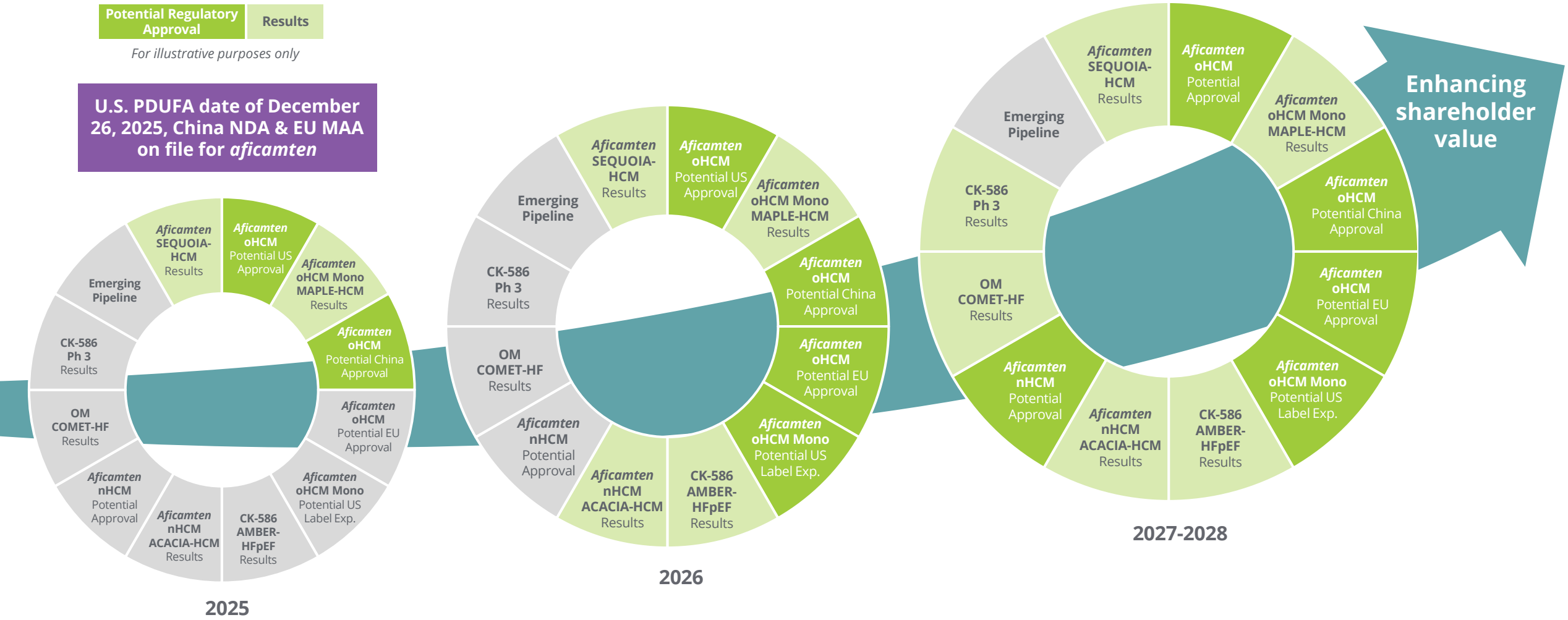
~$1.1B in cash, cash equivalents and investments as of March 31, 2025

Further access to capital through term loans[1] with Royalty Pharma (RP)	Proceeds of $75M from Tranche 4 loan received in April 2025 Eligible to draw up to $100M in 2025[2] Access to additional $175M[3] subject to conditions
Potential further funding through RP opt-in	RP, at its option, can invest up to **$150M** in a Phase 3 trial of CK-586 in exchange for an additional 3.5% revenue participation interest in worldwide net sales of CK-586[4]

Add'l $500M

[1]Term loans are comprised of Tranche 4, 5, and 7 Loans.
[2]Tranche 5: Cytokinetics is eligible to draw up to $100M at any time prior to November 25, 2025.
[3]Tranche 7: Cytokinetics, at its option, is eligible to draw up to $175m subject to conditions related to the approval of the NDA for aficamten in oHCM on or prior to December 31, 2025.
[4]Royalty Pharma currently has a revenue participation interest of 1.0% of worldwide net sales of CK-586.

Myosin Platform Fuels Multiple Milestones and Increased Value



Aficamten, omecamtiv mecarbil and CK-586 are investigational drugs and are not approved by any regulatory agency. Their safety and efficacy have not been established.

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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

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.

Addressing Difficult to Treat Populations Within Heart Failure

Specialty cardiology franchise strategy applies to markets with similar characteristics

HCM

Opportunity for *aficamten* as the anchor

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

HFrEF
Severely reduced EF

Expanding into adjacent population

- ✓ Few available therapies
- ✓ Significant unmet need
- ✓ Tractable customer base
- ✓ Payers manage to label

HFpEF
Supranormal EF

Addressing underserved segment of HF market

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

Aficamten, omecamtiv mecarbil and CK-586 are investigational drugs and are not approved by any regulatory agency. Their safety and efficacy have not been established.

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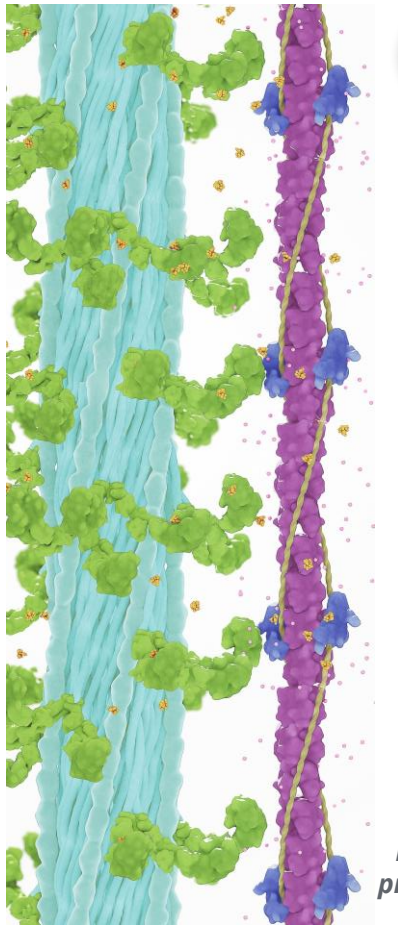
Building a Specialty Cardiology Franchise Anchored by *Aficamten*

Potential patient market for specialty cardiology franchise strategy



Estimated prevalence in US only

Myosin-Targeted Therapies

450-700K[1,2]
oHCM patients in 2025-2026

Aficamten

oHCM
SEQUOIA-HCM
First potential indication

250-400K[1,2]
nHCM patients in 2027

Aficamten

oHCM
MAPLE-HCM
Potential to expand to monotherapy

Aficamten

nHCM
ACACIA-HCM
Potential to expand into nHCM

~840K[3]
HFrEF + EF <30% in 2029

Omecamtiv Mecarbil

HFrEF
Potential in HFrEF

800K[4]
HFpEF + EF ≥ 65% in 2030

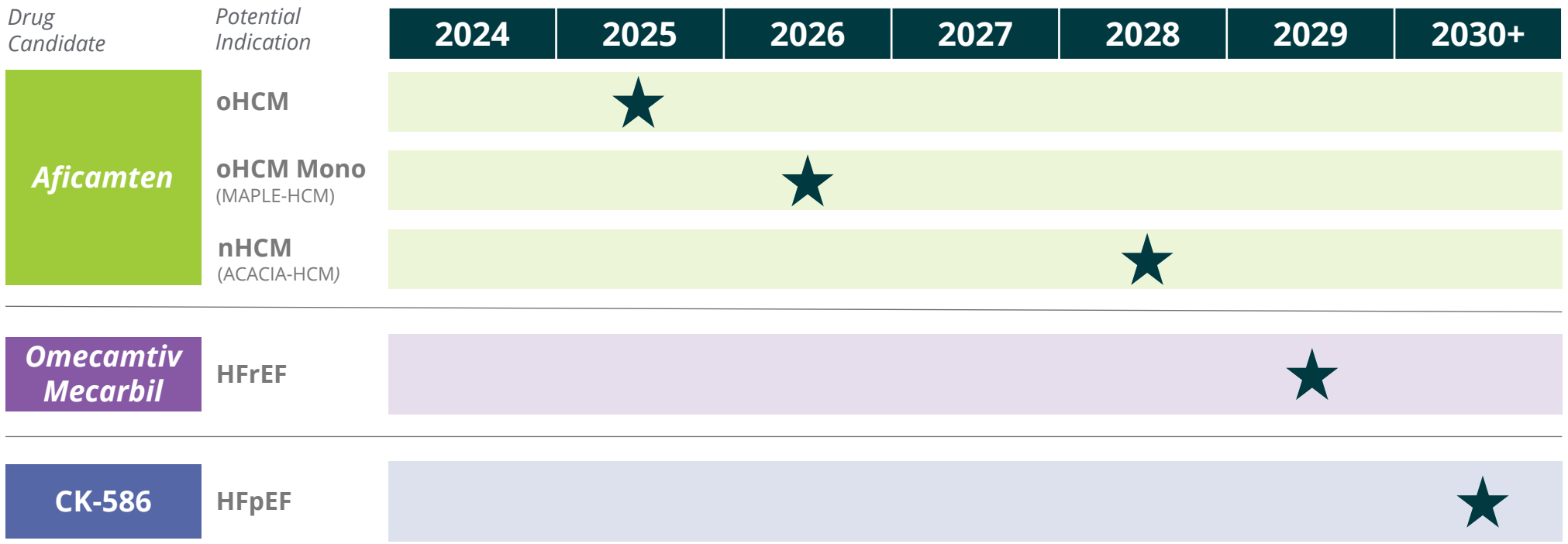
CK-586

HFpEF
With nHCM as a proxy, potential to expand into HFpEF

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

1. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ: et al: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, Circulation 1995;92;785-789; Semsarian C. et al: New Perspectives on the Prevalence of Hypertrophic Cardiomyopathy, J. Am, Coll. Cardiol. 2015; 65: 1249-1254;
2. Lu DY et al: Clinical Outcomes in Patients With Nonobstructive, Labile, and Obstructive Hypertrophic Cardiomyopathy. J. Am. Heart Assoc. 2018;7:1-11
3. Greene et al JACC 2023; 81:413-424
4. Dunlay et al (2012) Circ Heart Fail. 2012 Nov;5(6):720-6. doi: 10.1161/CIRCHEARTFAILURE.111.966366. Epub 2012 Aug 30.

Potential for Multiple Specialty Cardiology Launches



Aficamten, omecamtiv mecarbil and CK-586 are investigational drugs and are not approved by any regulatory agency. Their safety and efficacy have not been established.

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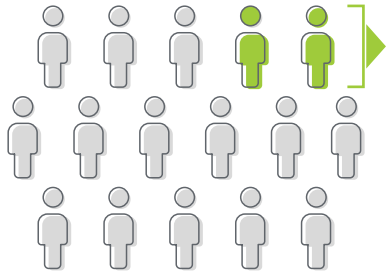
Specialty Cardiology Business Has Potential for High ROI

Concentrated Prescribers

~80K cardiologists/PCPs treat CV diseases

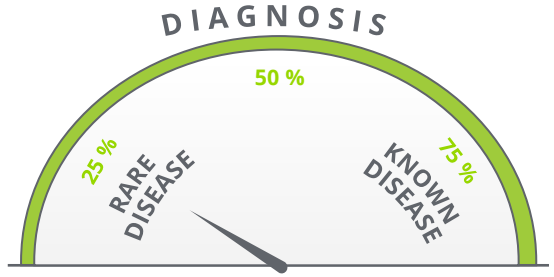


~10K

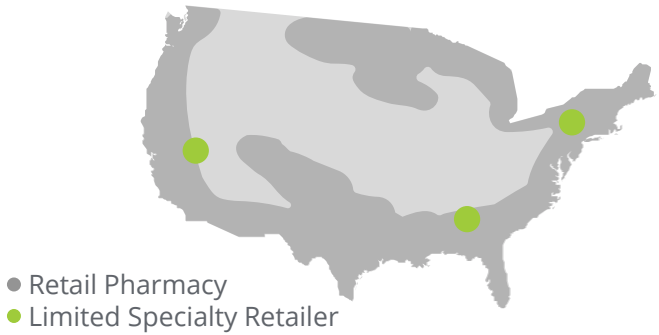
cardiologists treat ~80% HCM

Higher Revenue Per Prescriber

Opportunity To Grow Market Through Diagnosis

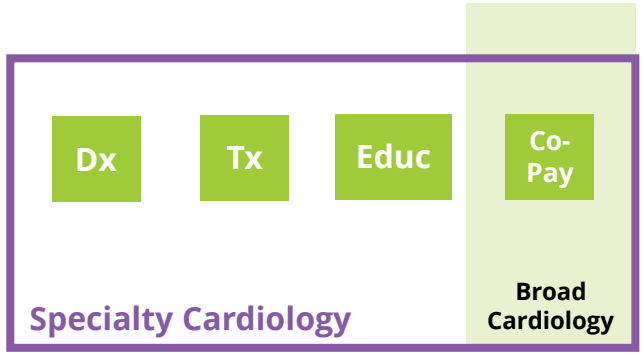


Distribution Limited to Specialty Retailers



- Retail Pharmacy
- Limited Specialty Retailer

Differentiated Patient Experience



Path to Reimbursement

Broad Cardiology

High Rebates

Winners/loser

Specialty Cardiology

Access to Label

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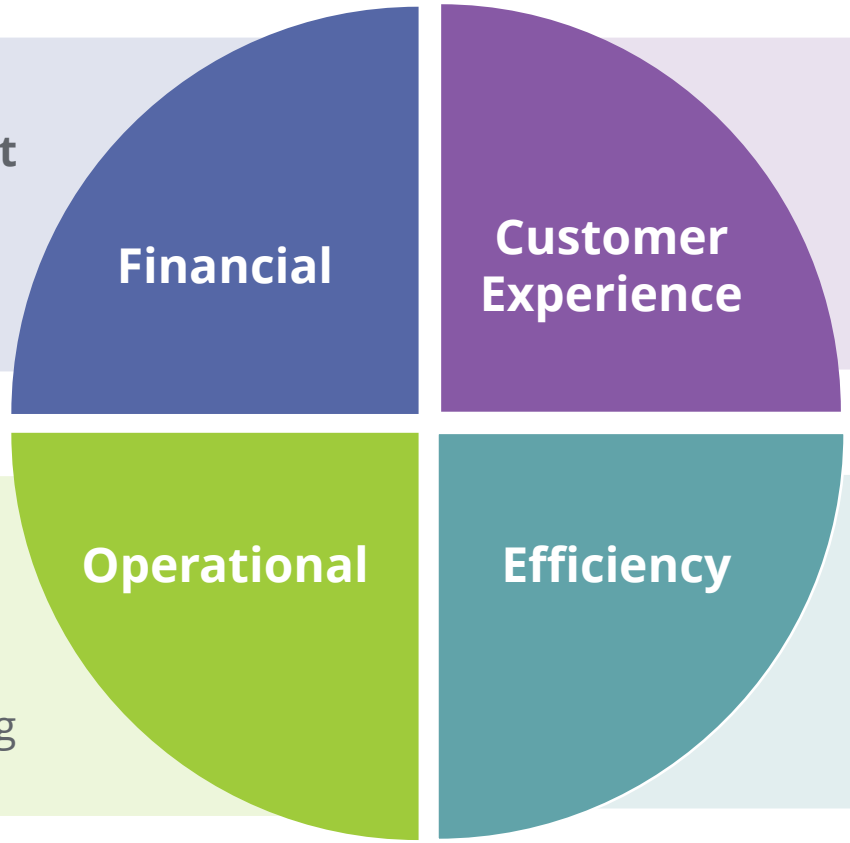
Potential Benefits of a Specialty Cardiology Franchise

- Significant **FTE cost savings**
- **Reduced operational support** teams, IT systems & analytics
- **Efficiency** in sales training, meetings



- **1:1** customer – rep relationship
- **Single point of contact** for HCP & office staff enables **improved access & focus**

- **Flexibility** in team structure based on local market needs
- **No** multiple representative coordination concerns
- **Simplified IC**, CRM & reporting
- Single point of **accountability**

- **Multiple products** can be discussed on every call
- "Low value" targets for one product can be replaced with "high value" targets from other products

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HCP & Patient-Directed HCM Awareness Campaigns Launched

HCP Portal
(Medscape)

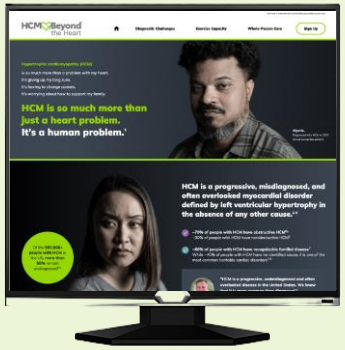
Paid Social
(Facebook)

Paid Search

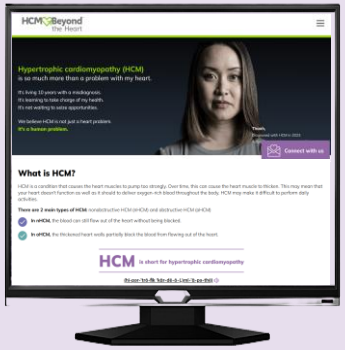
Programmatic/ Digital Journals

Congress
(HFSA, HCM Society, HCM8)

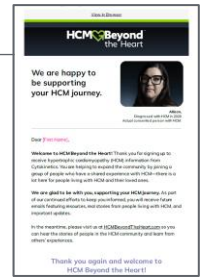
HCP Market Development Website
HCMBeyondTheHeart.com/HCP



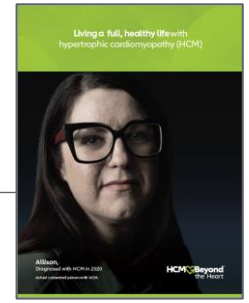
Patient Market Development Website
HCMBeyondTheHeart.com



CRM Registration



Educational Materials



Programmatic/Digital Media
(DeepIntent, MayoClinic, Healthline, Nativo)

Video Content

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Aficamten

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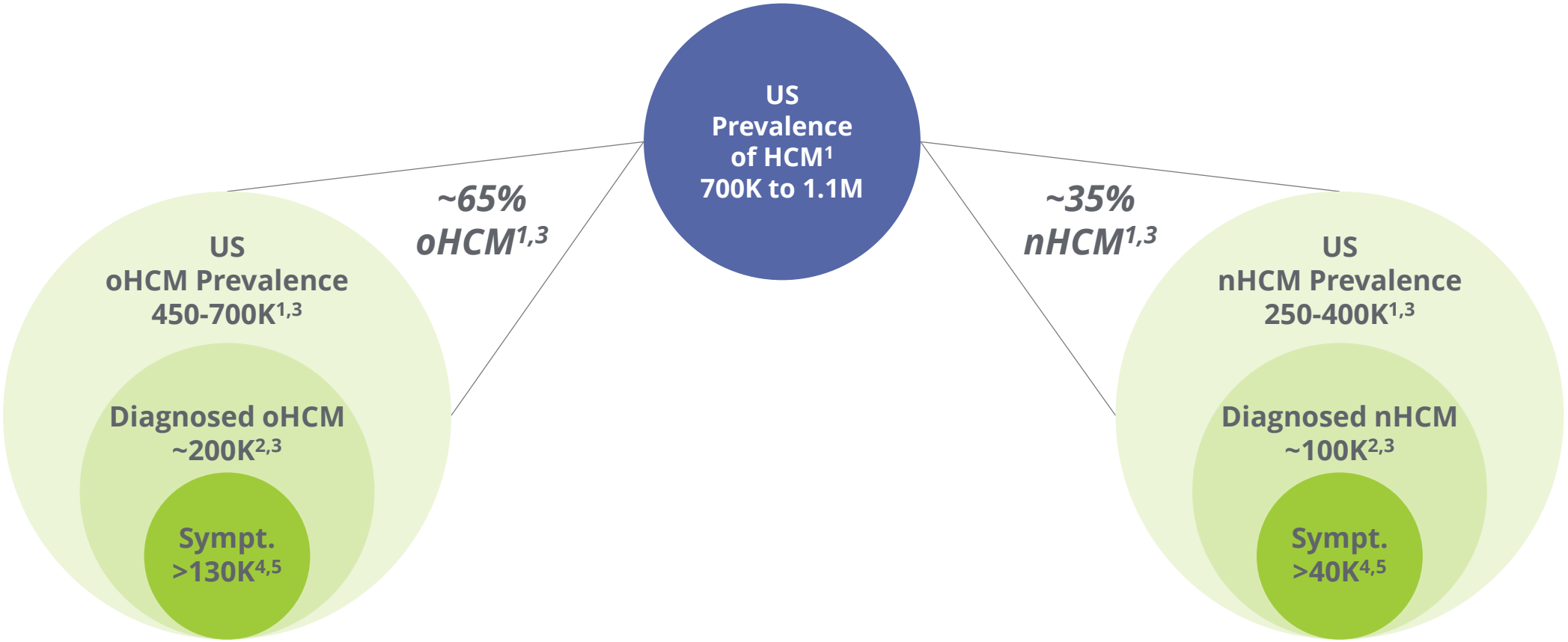
Aficamten is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product have not been established.

Opportunity for CMIs in Diagnosed, Symptomatic HCM Patients



Projections and forecasts for illustration.

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

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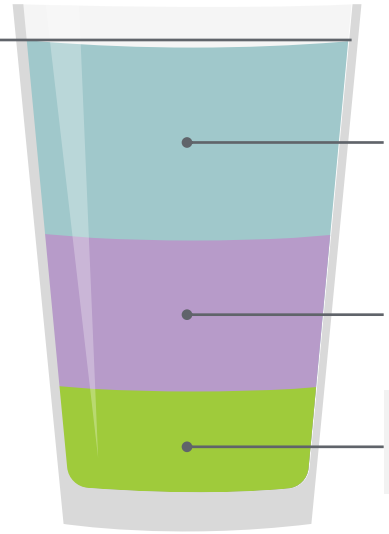
$10B Potential Market of CMI-Eligible Patients

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

US and EU HCM Patients in 2035

Illustrative

880K[1,2]
Expected global population of diagnosed patients with oHCM & nHCM in 2035



Projected Diagnosed HCM Patients
(5x the growth rate of the US population)[3]

Symptomatic o/nHCM Patients
(Considered for CMI)[3]

Potential CMI Use: 30-50%
of diagnosed, symptomatic HCM patients[3]

~$10B Potential US + EU Market in 2035

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

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

- If approved with target profile, *aficamten* **may expand total CMI market** & create opportunity in newly treated CMI patients

Key attributes that may **drive preference** include the potential for:

LVOT gradient reduction

Change in NYHA Functional Class

Pharmacodynamics /LVEF maintenance

Change in KCCQ

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

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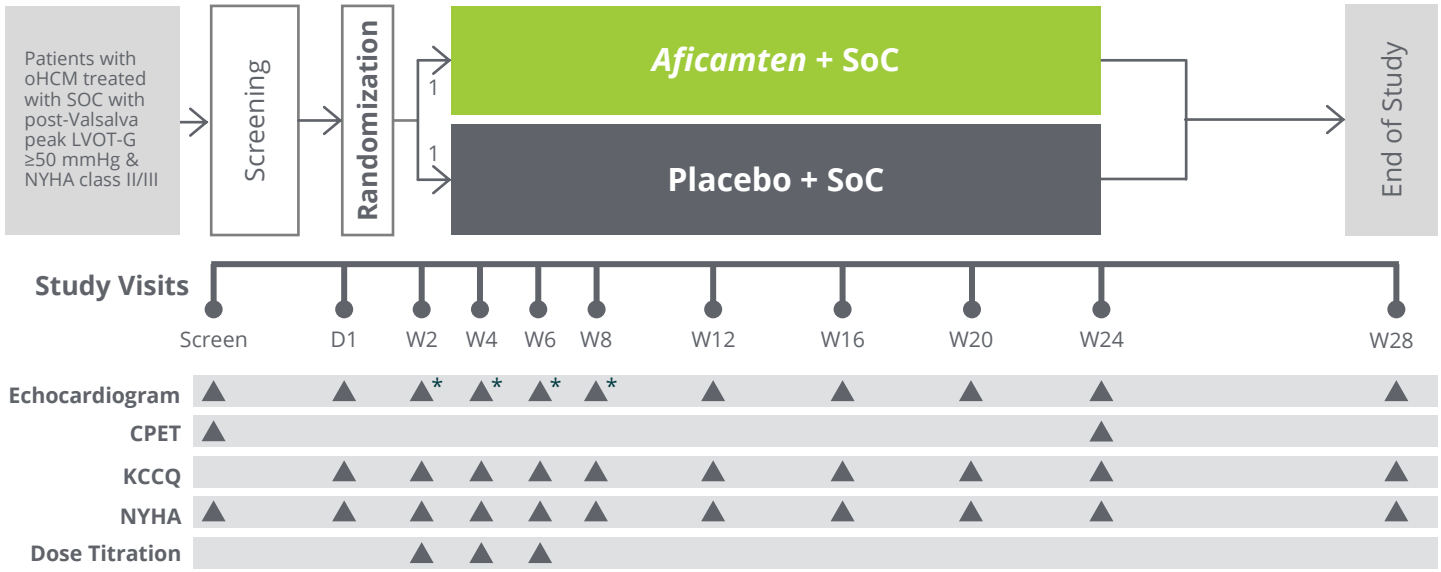
SEQUOIA-HCM: Pivotal Phase 3 Trial

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



SOC: standard of care
** Focused echocardiogram*
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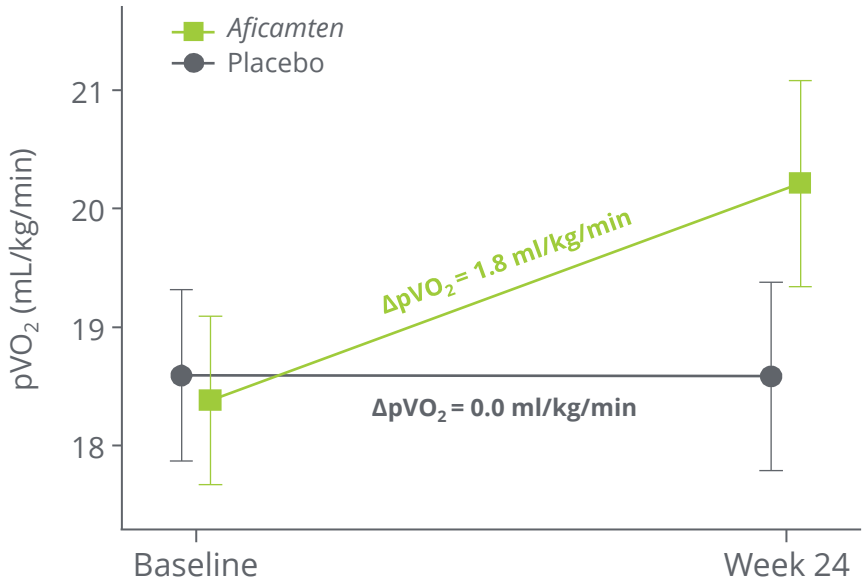
SEQUOIA-HCM: Primary Endpoint

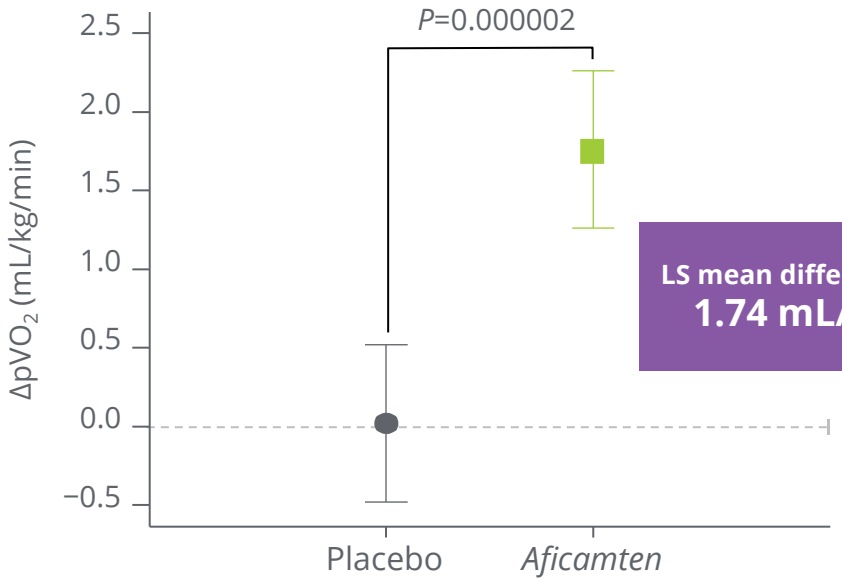
Significant improvement in exercise capacity compared to placebo

Results presented at Heart Failure 2024 and published in *NEJM*

Absolute Change from Baseline to Week 24



LS mean Change from Baseline to Week 24



Data are mean and 95% CI

LS mean difference (SE) vs placebo:
1.74 mL/kg/min (0.36)

Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.

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

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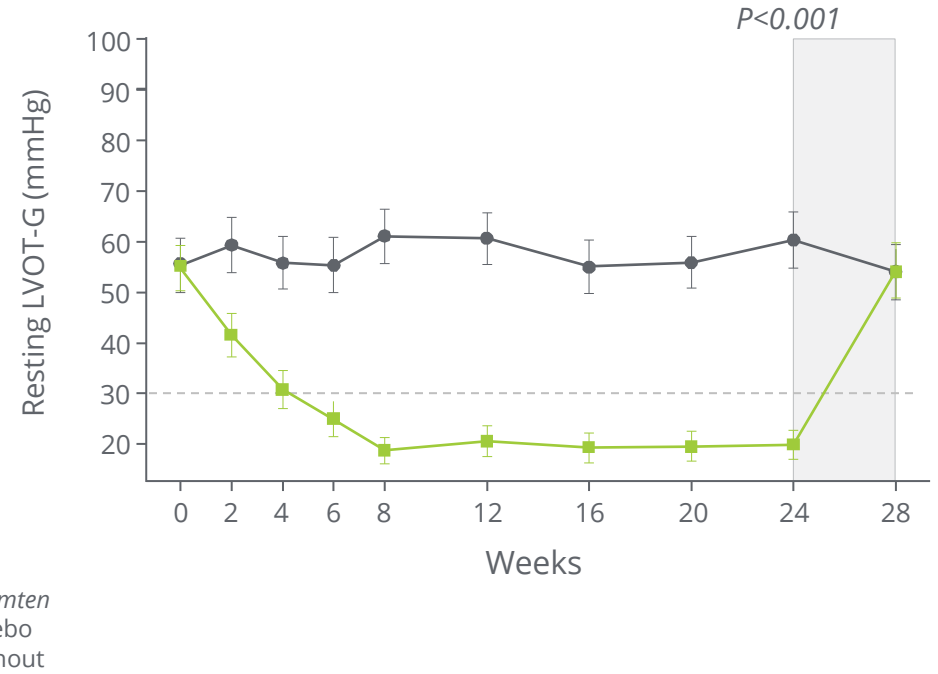
SEQUOIA-HCM: Secondary & Exploratory Endpoints

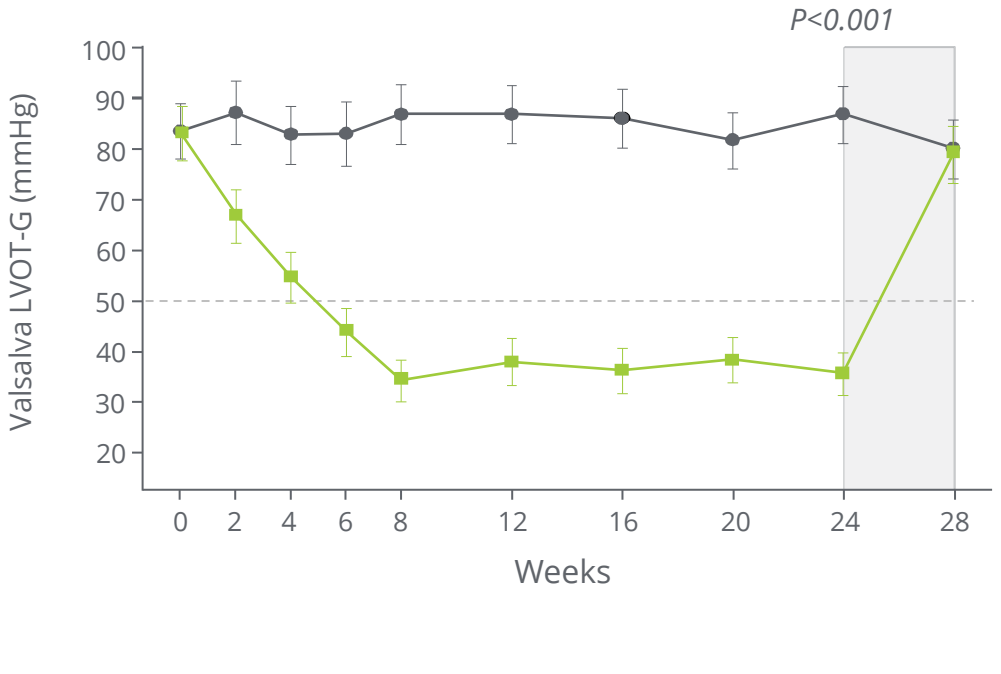
Significant improvement in gradients by ~60% with no significant adverse change in LVEF

LS mean difference: - 50 mmHg

Resting LVOT-G



Valsalva LVOT-G



Aficamten
Placebo
Washout

Error bars are 95% CI

Hegde S, et al. Impact of Aficamten on Echocardiographic Cardiac Structure and Function in Symptomatic Obstructive Hypertrophic Cardiomyopathy. JACC. 2024.

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

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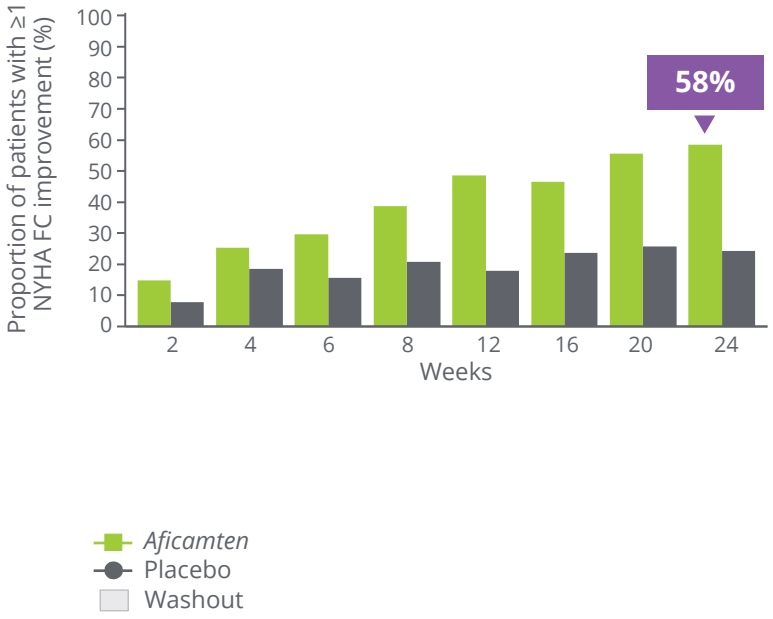
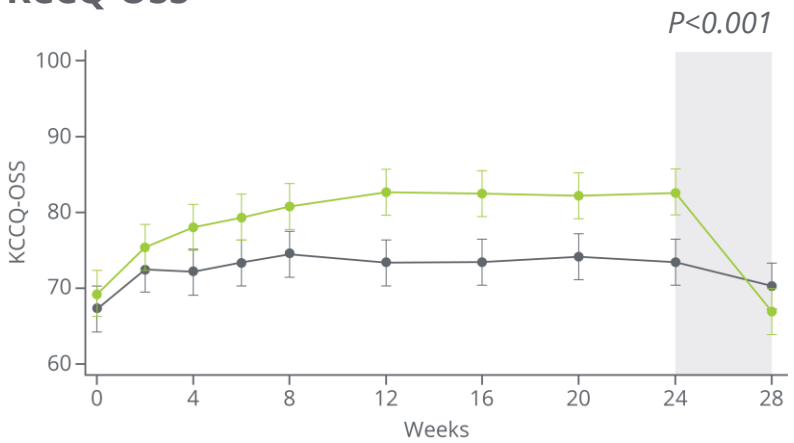
SEQUOIA-HCM: Secondary & Exploratory Endpoints

Significant improvement in patient symptom burden and quality of life

≥1 NYHA FC Improvement[1]



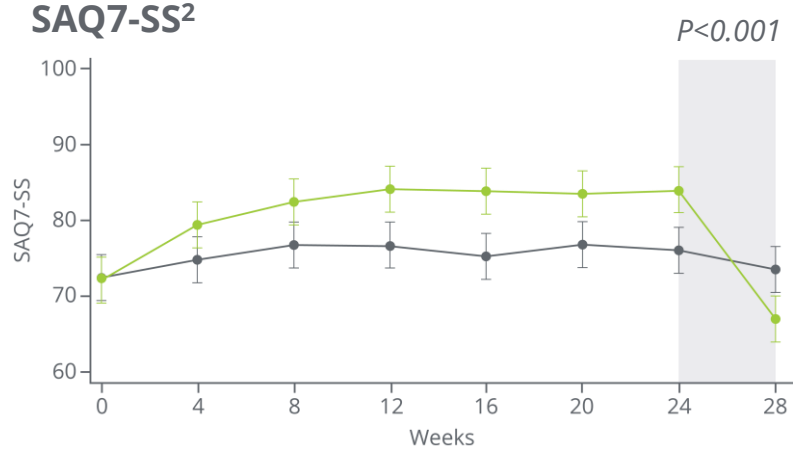
KCCQ-OSS[2]



Mean difference between *aficamten* & placebo = **7.9 points**

30% on *aficamten* vs. 12% on placebo had an improvement of ≥20 points

SAQ7-SS[2]



Mean difference between *aficamten* & placebo = **7.8 points**

31% on *aficamten* vs. 14% on placebo had an improvement of ≥20 points

Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.
Sherrod C, et al. Effect of Aficamten on Health Status Outcomes in Obstructive Hypertrophic Cardiomyopathy: Results from SEQUOIA-HCM. JACC. 2024.

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

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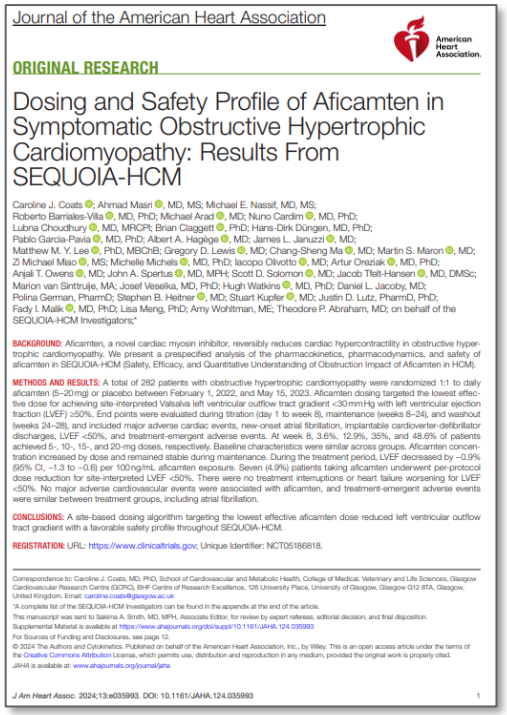
SEQUOIA-HCM: Safety Data

AEs with ≥5% incidence

There were no serious adverse cardiovascular events associated with *aficamten* treatment in SEQUOIA-HCM

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

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



Journal of the American Heart Association

ORIGINAL RESEARCH

Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy: Results From SEQUOIA-HCM

Caroline J. Coats; Ahmad Masri, MD, MS; Michael E. Nassif, MD, MS; Roberto Barriales-Villa, MD, PhD; Michael Arad, MD; Nuno Cardim, MD, PhD; Lubna Choudhury, MD, MRCPI; Brian Claggett, PhD; Hans-Dirk Düngen, MD, PhD; Pablo Garcia-Pavia, MD, PhD; Albert A. Hagège, MD; James L. Januzzi, MD; Matthew M. Y. Lee, PhD, MBChB; Gregory D. Lewis, MD; Chang-Sheng Ma, MD; Martin S. Maron, MD; Zi Michael Miao, MS; Michelle Michels, MD, PhD; Iacopo Olivotto, MD; Artur Oreziak, MD, PhD; Anjali T. Owens, MD; John A. Spertus, MD, MPH; Scott D. Solomon, MD; Jacob Tfelt-Hansen, MD, DMSc; Marion van Sintrujie, MA; Josef Veselka, MD, PhD; Hugh Watkins, MD, PhD; Daniel L. Jacoby, MD; Polina German, PharmD; Stephen B. Heitner, MD; Stuart Kupfer, MD; Justin D. Lutz, PharmD, PhD; Fady I. Malik, MD, PhD; Lisa Meng, PhD; Amy Wohltman, ME; Theodore P. Abraham, MD; on behalf of the SEQUOIA-HCM Investigators;*

BACKGROUND: Aficamten, a novel cardiac myosin inhibitor, reversibly reduces cardiac hypercontractility in obstructive hypertrophic cardiomyopathy. We present a prespecified analysis of the pharmacokinetics, pharmacodynamics, and safety of aficamten in SEQUOIA-HCM (Safety, Efficacy, and Quantitative Understanding of Obstruction Impact of Aficamten in HCM).

METHODS AND RESULTS: A total of 282 patients with obstructive hypertrophic cardiomyopathy were randomized 1:1 to daily aficamten (5–20 mg) or placebo between February 1, 2022, and May 15, 2023. Aficamten dosing targeted the lowest effective dose for achieving site-interpreted Valsalva left ventricular outflow tract gradient <30 mm Hg with left ventricular ejection fraction (LVEF) ≥50%. End points were evaluated during titration (day 1 to week 8), maintenance (weeks 8–24), and washout (weeks 24–28), and included major adverse cardiac events, new-onset atrial fibrillation, implantable cardioverter-defibrillator discharges, LVEF <50%, and treatment-emergent adverse events. At week 8, 3.6%, 12.9%, 35%, and 48.6% of patients achieved 5-, 10-, 15-, and 20-mg doses, respectively. Baseline characteristics were similar across groups. Aficamten concentration increased by dose and remained stable during maintenance. During the treatment period, LVEF decreased by −0.9% (95% CI, −1.3 to −0.6) per 100 ng/mL aficamten exposure. Seven (4.9%) patients taking aficamten underwent per-protocol dose reduction for site-interpreted LVEF <50%. There were no treatment interruptions or heart failure worsening for LVEF <50%. No major adverse cardiovascular events were associated with aficamten, and treatment-emergent adverse events were similar between treatment groups, including atrial fibrillation.

CONCLUSIONS: A site-based dosing algorithm targeting the lowest effective aficamten dose reduced left ventricular outflow tract gradient with a favorable safety profile throughout SEQUOIA-HCM.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique Identifier: NCT05186818.

Correspondence to: Caroline J. Coats, MD, PhD, School of Cardiovascular and Metabolic Health, College of Medical, Veterinary and Life Sciences, Glasgow Cardiovascular Research Centre (GCRC), BHF Centre of Research Excellence, 126 University Place, University of Glasgow, Glasgow G12 8TA, Glasgow, United Kingdom. Email: caroline.coats@glasgow.ac.uk

*A complete list of the SEQUOIA-HCM Investigators can be found in the appendix at the end of the article.

This manuscript was sent to Sakima A. Smith, MD, MPH, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.035993

For Sources of Funding and Disclosures, see page 12.

JAHA is available at: www.ahajournals.org/journal/jaha

J Am Heart Assoc. 2024;13:e035993. DOI: 10.1161/JAHA.124.035993

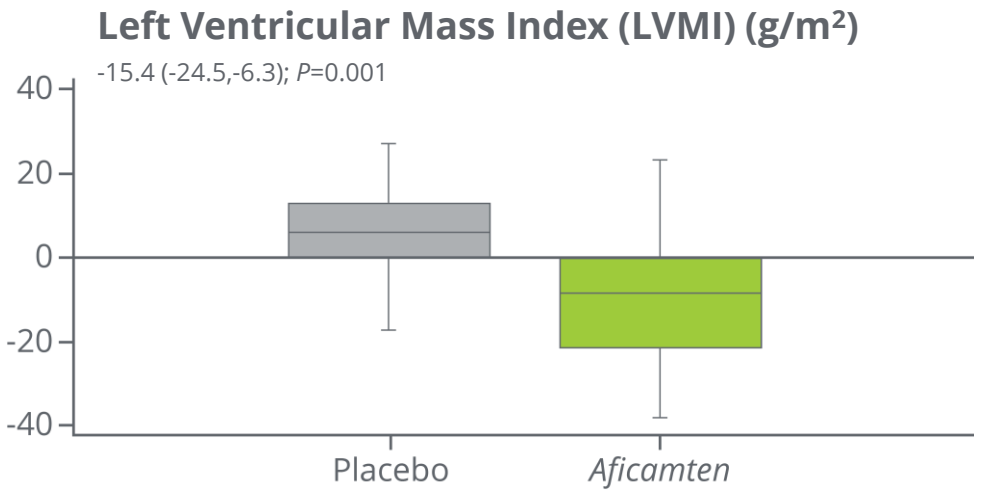
AE, adverse event; SAE, serious adverse event.
Coats CJ. Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: CMR Sub-Study

Aficamten associated with favorable cardiac remodeling

Among 50 of the 284 eligible patients who opted to complete the CMR sub-study there was:

- **Significant improvement in LVMI**
- **Favorable cardiac remodeling** as demonstrated by reductions in:
  - **Left ventricular maximal wall thickness**
  - **Left atrial volume index (LAVI)**
  - **Extracellular volume mass index (ECVi)**



Masri A, et al. Effect of Aficamten on Cardiac Structure and Function in Obstructive Hypertrophic Cardiomyopathy: SEQUOIA-HCM CMR Substudy. JACC. 2024.
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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Integrated Safety Analysis

Analysis represents 206 patient-years* of exposure to *aficamten*

- **<4% of patients** experienced LVEF <50%
- **0 dose terminations** due to LVEF <40%
- **<1% of echocardiograms performed** led to a reduction in dose
- **No difference in atrial fibrillation** between placebo and *aficamten*

	Cumulative[a] *aficamten*-treated pool	Placebo-controlled pool[b]	
	Aficamten	***Aficamten***	**Placebo**
Number of participants	283	170	153
LVEF <50%[c], n (%)	11 (3.9)	9 (5.3)	1 (0.7)
LVEF <50% with clinical HF	0	0	1 (0.7)
Atrial fibrillation	12 (4.2)	4 (2.4)	5 (3.3)
New onset	5 (1.8)	1 (0.6)	3 (2.0)
Recurrent	7 (2.5)	3 (1.8)	2 (1.3)

[a] Parent and extension studies. [b] Placebo-controlled pool of REDWOOD-HCM and SEQUOIA-HCM. [c] Site read.

*Median exposure: 6-months, range of exposure: 0-32 months

Integrated Safety Analysis to reflect real world clinical application.

Masri A. Aficamten in Patients with Obstructive Hypertrophic Cardiomyopathy: An Integrated Safety Analysis. ESC 2024.

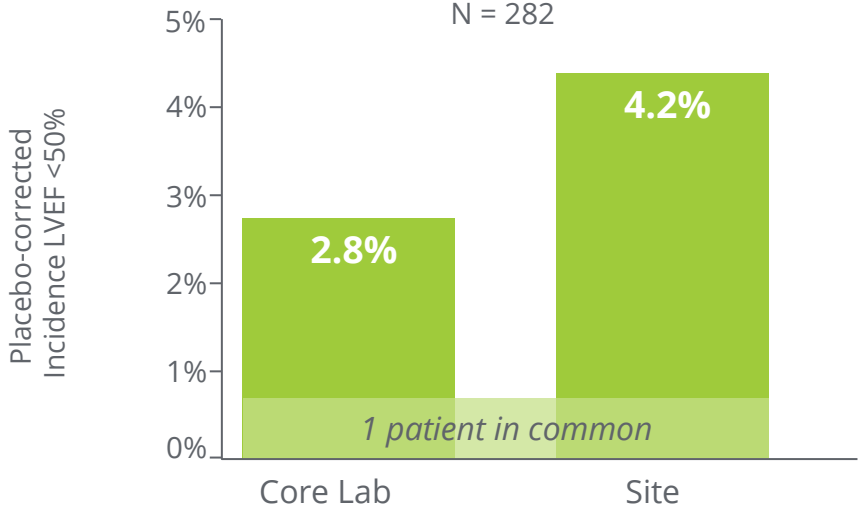
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Implementation of Dosing in Real-World Setting (FOREST-HCM)

Low incidence of LVEF <50% in patients with oHCM treated with *aficamten*

SEQUOIA HCM

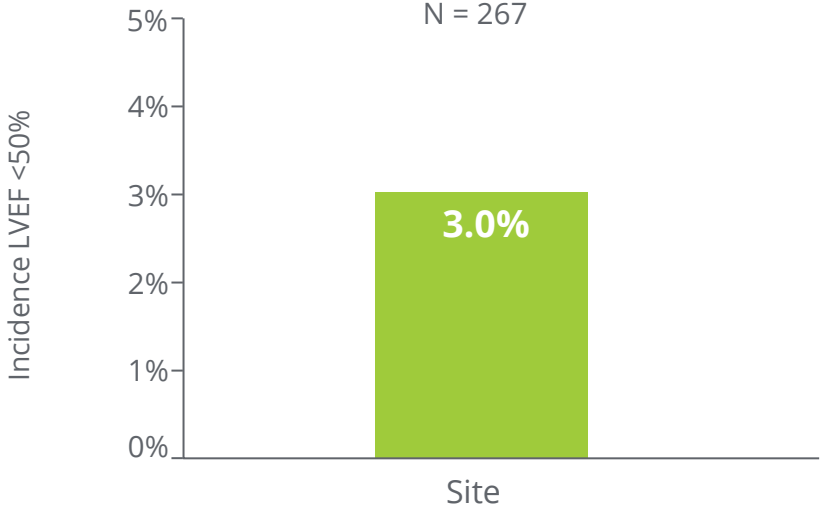
N = 282



- ✓ No treatment interruptions
- ✓ No heart failure events
- ✓ All reversible
- ✓ Great majority of patients on highest doses

FOREST HCM

N = 267



- ✓ No treatment interruptions
- ✓ No heart failure events
- ✓ All reversible
- ✓ Great majority of patients on highest doses

SEQUOIA-HCM Source: Coats CJ. Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.
FOREST-HCM Source: Data on file – data cut 15 Apr 24.
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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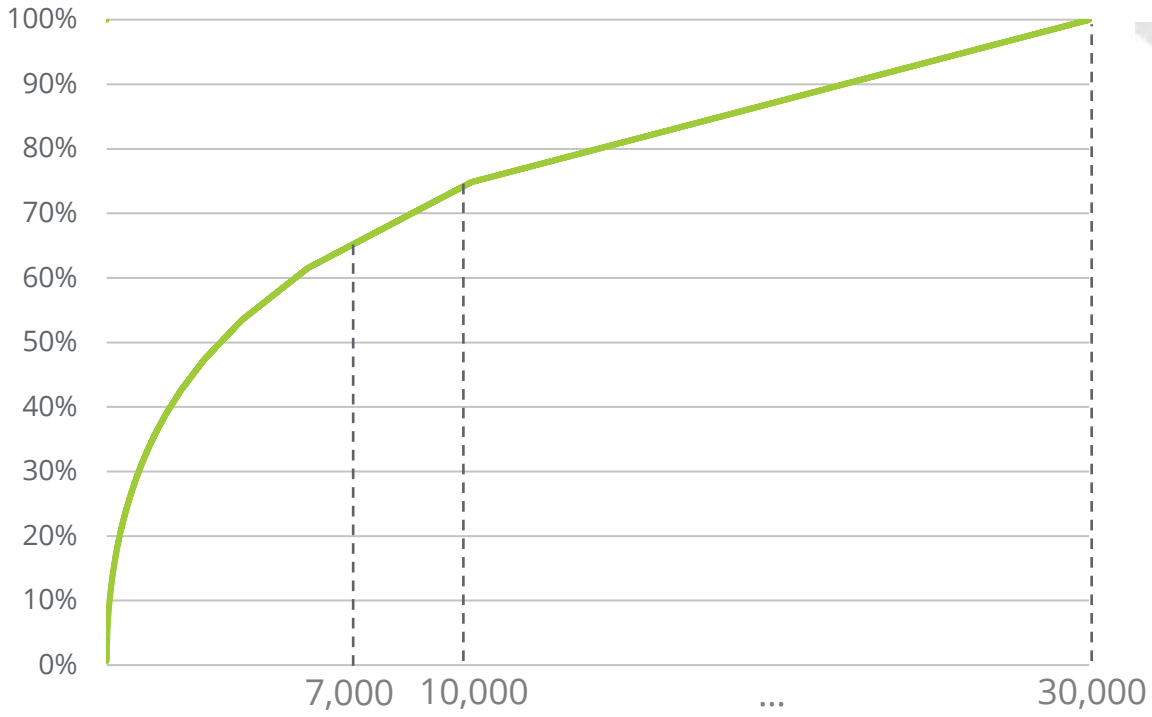
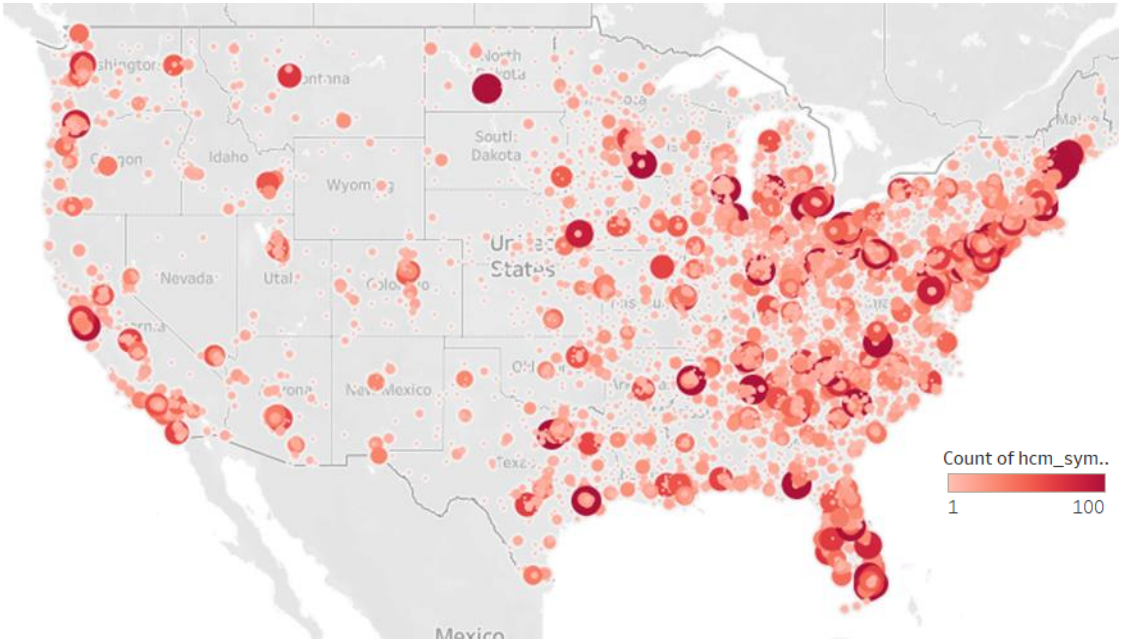
Cardiologists Located in Concentrated Geographic Clusters Across the US

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

HCM Patient Concentration by Cardiologist



Geographic Distribution of HCM Patients



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

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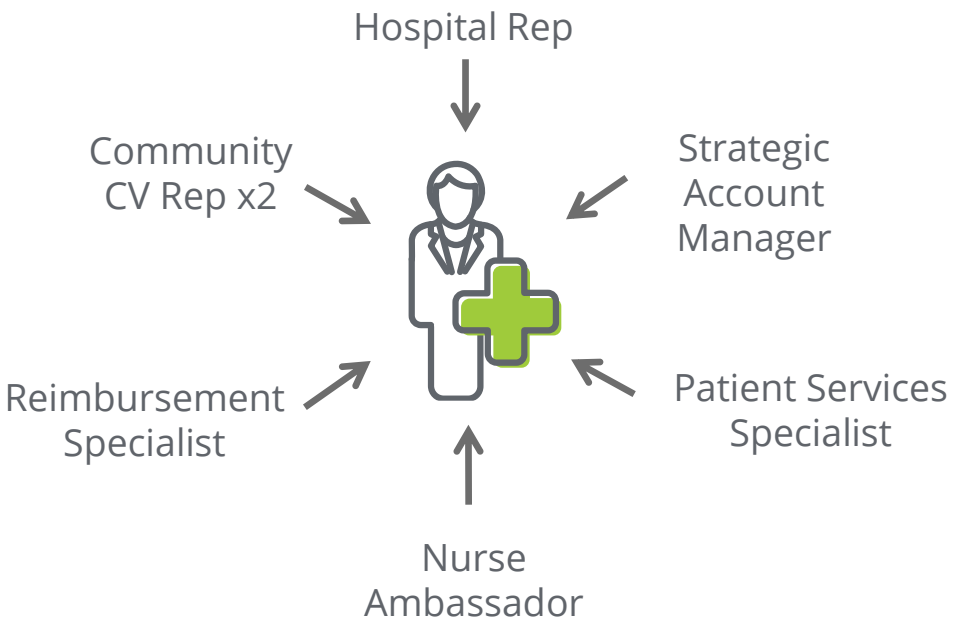
U.S. Sales Team Designed Based on Efficiency & Customer Feedback

Traditional Models

Several functions with very focused roles

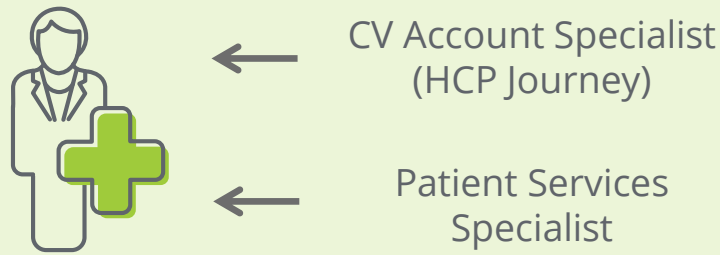
Overwhelmed customers, "It's too much"



Our Design Principles

Simple model creating quality experience

Hire team with deep experience in specialty



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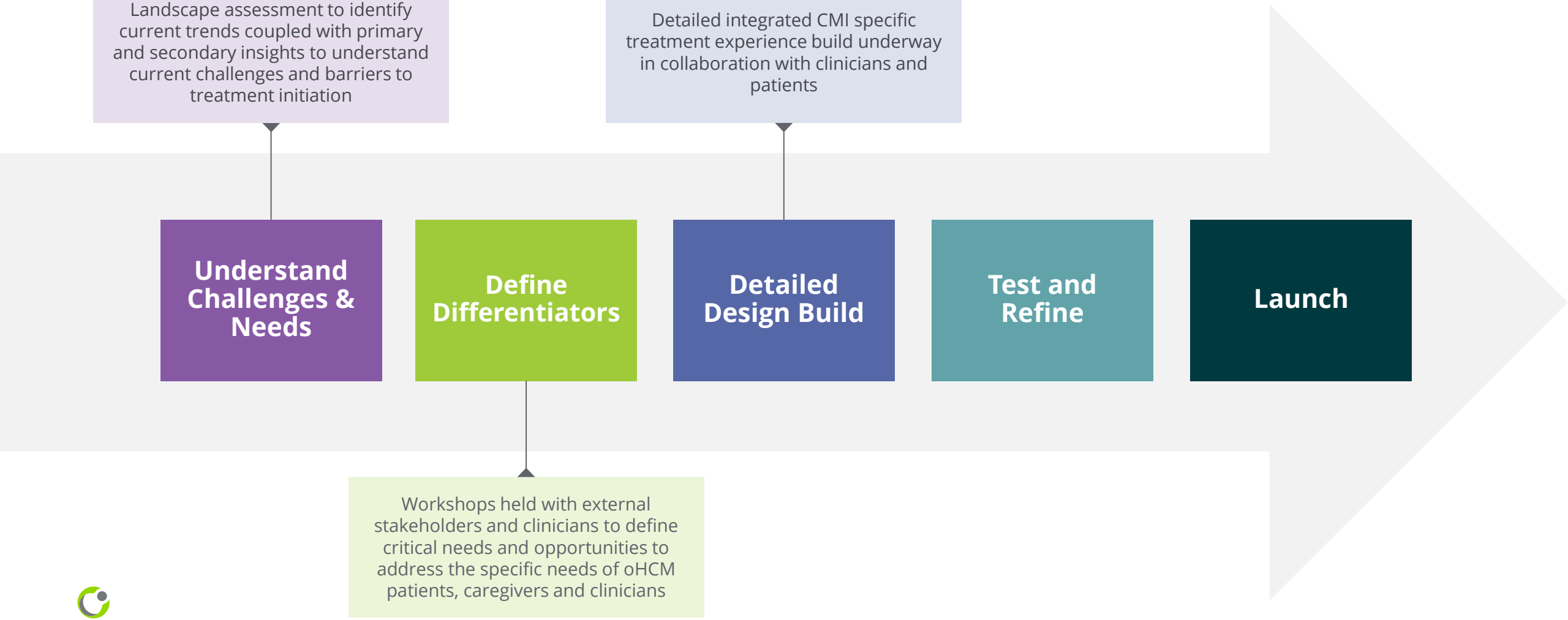
Building a Patient-Centric Treatment Experience

Landscape assessment to identify current trends coupled with primary and secondary insights to understand current challenges and barriers to treatment initiation

Detailed integrated CMI specific treatment experience build underway in collaboration with clinicians and patients



Workshops held with external stakeholders and clinicians to define critical needs and opportunities to address the specific needs of oHCM patients, caregivers and clinicians

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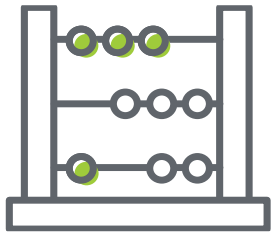
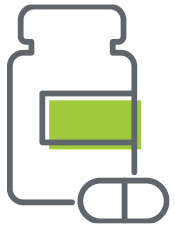
Strategy in Place to Support Market Access at Launch



Payer value proposition strengthened with clinical & HEOR evidence

PIE engagements with key payer accounts



Channel & dispensing strategy designed to enhance patient experience

Patient support services will provide robust prior-authorization & medical exception support

PIE: Pre-Approval Information Exchange
HEOR: Health Economics & Outcomes Research

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Advancing EU Launch Readiness Activities

Key Hires in Europe

- Highly experienced hires in Zug, Switzerland in Regulatory, Medical Affairs, Commercial, Market Access
- Highly experienced leadership hires in Germany, France and the UK
- Multiple product launches in cardiology & oncology both orphan & non-orphan indications
- Proven track record of successfully navigating pricing, reimbursement & market access in Europe

Key Activities to Support Launch

- Design the EU distribution model & select EU 3PL
- Support the MIA (Manufacturing & Importation Authorization)
- Develop regulatory & labeling strategy
- Start implementing all needed processes to support German launch:
  - Market understanding (prescribers concentration curves, patient journey…)
  - HTA Dossier writing for P&R process

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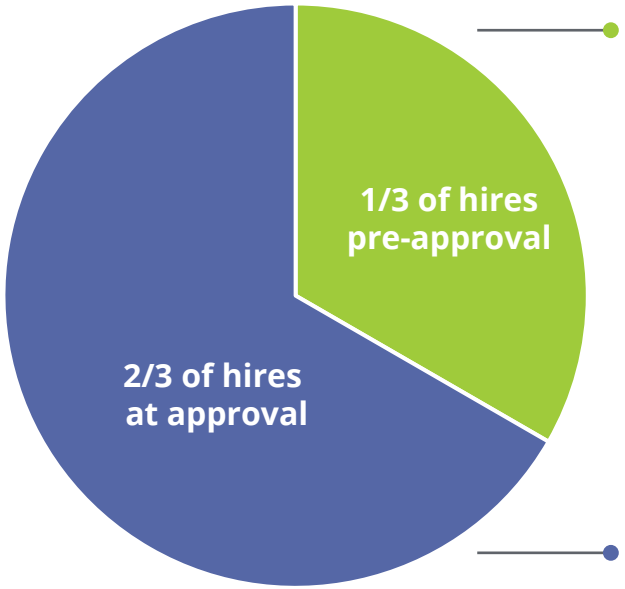
Gated Build of Commercial Infrastructure

Sales representative hiring to occur in proximity to approval

2/3 of hiring to occur at-approval



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

Sales representatives

Activities initiated upon key de-risking events

Underway before SEQUOIA-HCM readout
Market access strategy
Pricing strategy
Distribution approach
Payer engagement
Brand strategy
Customer account identification

Initiated after SEQUOIA-HCM readout
Launch campaign
Commercial training
Payer Pre-approval Information Exchange
Sales force planning
Technology build
Omnichannel execution
Market development

Initiated upon or in Proximity to FDA approval
Media purchases
Patient support programs

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Global Presence of *Aficamten* & Progress of Marketing Applications

2025

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U.S. PDUFA date 12/26/25

2026

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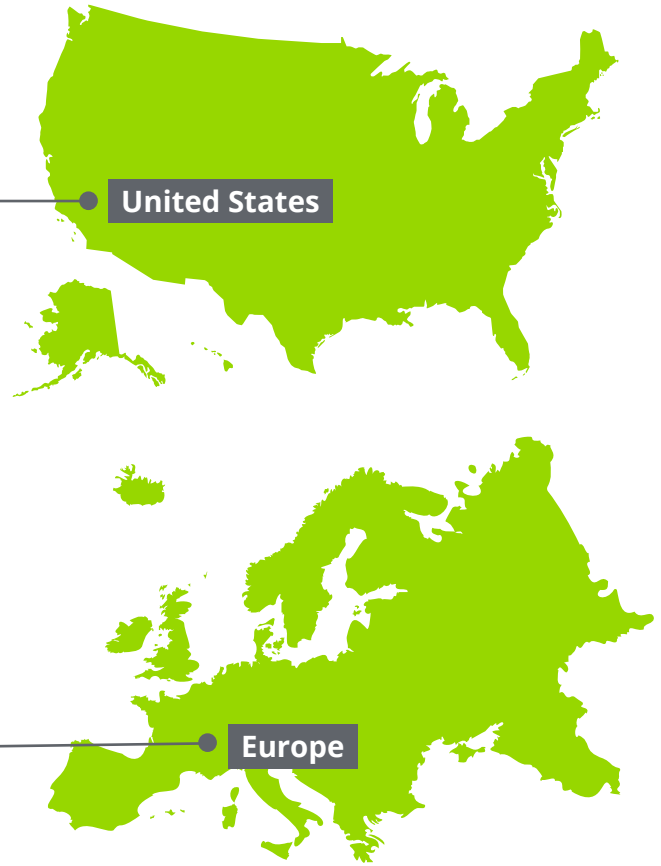
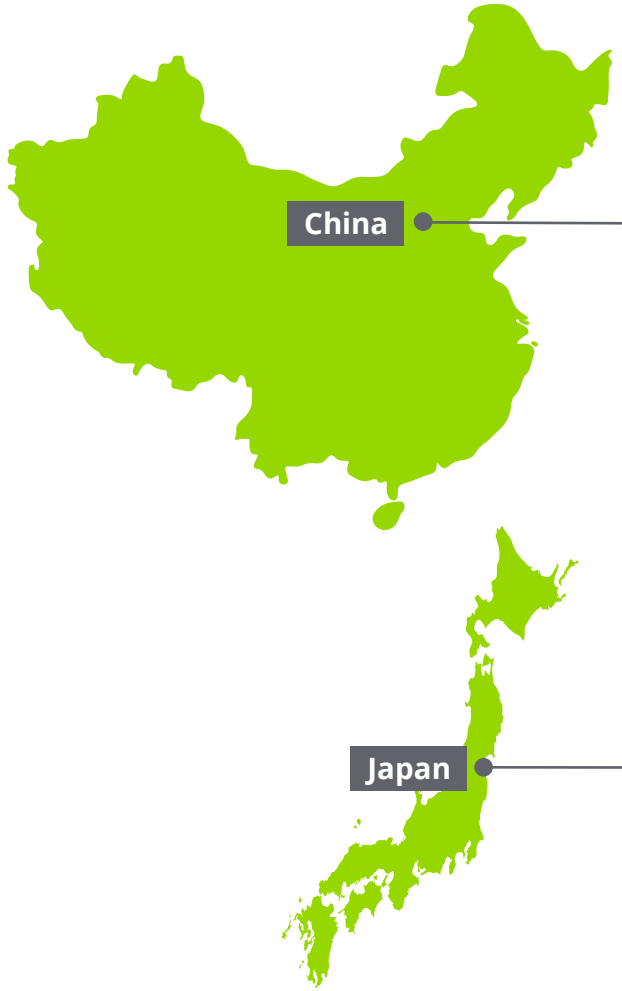
MAA on file in Europe





2025

sanofi

Partnered with Sanofi in China; NDA on file with priority review

BAYER

Partnered with Bayer in Japan

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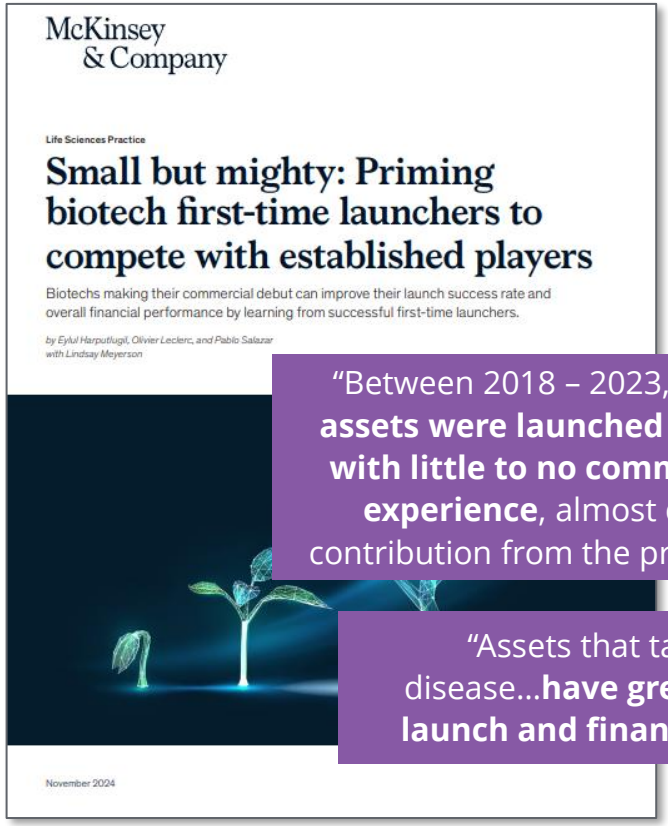
Strategies for Success: First-Time Biotech Launches

Cytokinetics' commercial strategy validated by industry findings

First-time launchers are more likely to succeed if they:

- Develop a **multi-asset portfolio**
- **Invest in SG&A at launch year** & continue over subsequent years
- Leverage **precision-based marketing techniques**
- **Onboard access team early**
- **Support HCP offices with education** on key processes like prior authorization & appeals
- **Engage HCPs early** on access, rapid volume build, and an impactful evidence strategy
- Use a **fit-for-purpose customized distribution strategy**



"Between 2018 – 2023, **~40% of new assets were launched by companies with little to no commercialization experience**, almost double their contribution from the previous 5 years."

"Assets that target rare disease…**have greater odds of launch and financial success**."

Harputlugil, E., Leclerc, O., Salazar, P., & Meyerson, L. (2024, November 25). Small but mighty: Priming biotech first-time launchers to compete with established players. McKinsey & Company. https://www.mckinsey.com/industries/life-sciences/our-insights/small-but-mighty-priming-biotech-first-time-launchers-to-compete-with-established-players

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Positive Topline Results from MAPLE-HCM

- **Positive topline results** from MAPLE-HCM demonstrating **superiority of *aficamten*** to *metoprolol* in patients with obstructive HCM
- Expect to share full results at an upcoming major medical meeting

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

Ongoing Clinical Trials of *Aficamten*

Pivotal Phase 3 clinical trial in nHCM

Enrollment complete; data expected in 1H 2026

Clinical trial in a pediatric population with oHCM

Expect to complete enrollment of adolescent cohort in 2H 2025

Open-label extension clinical study in HCM

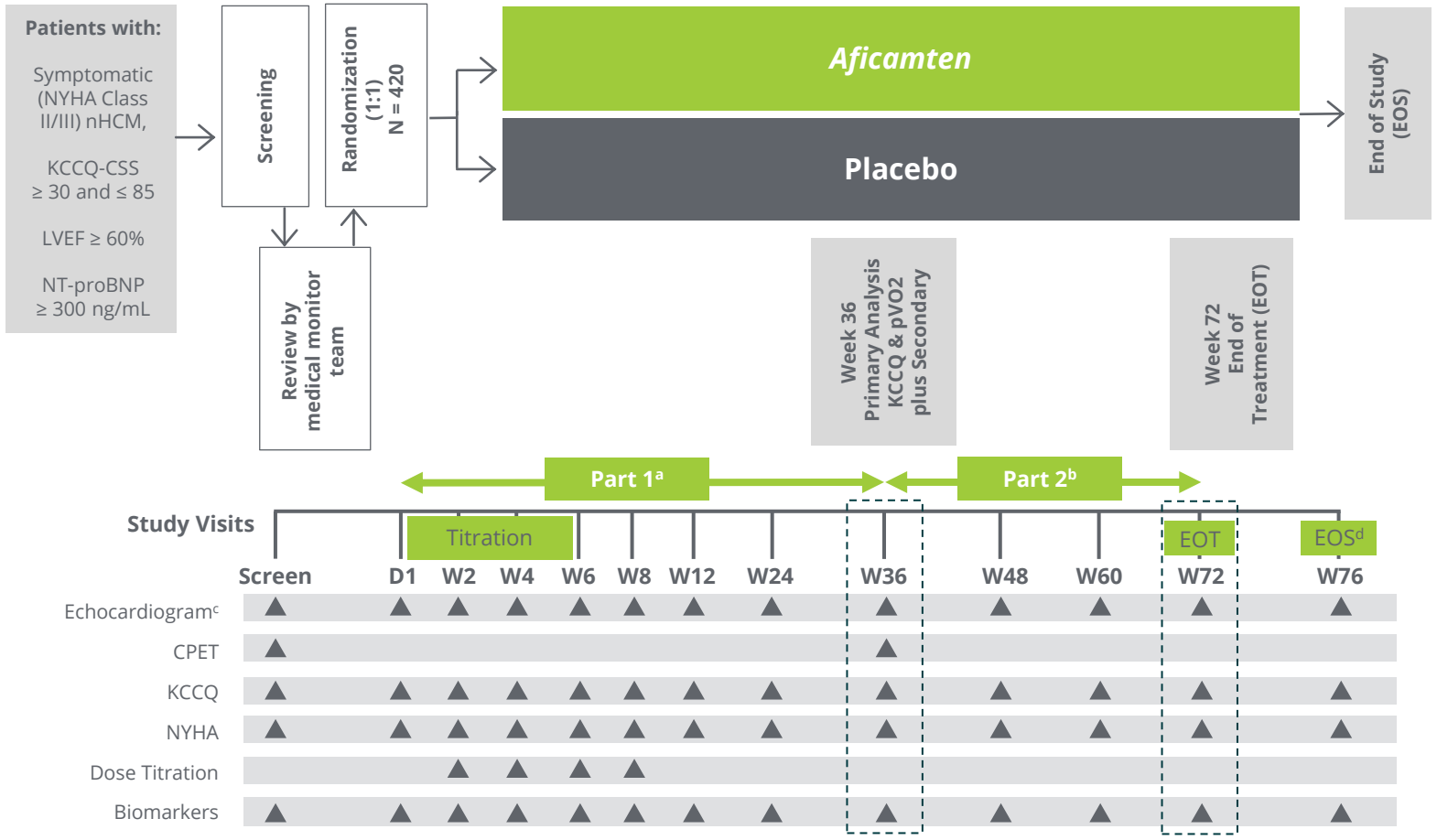
Ongoing

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

ACACIA-HCM: Pivotal Phase 3 Trial in nHCM

Enrollment complete; results expected 1H 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

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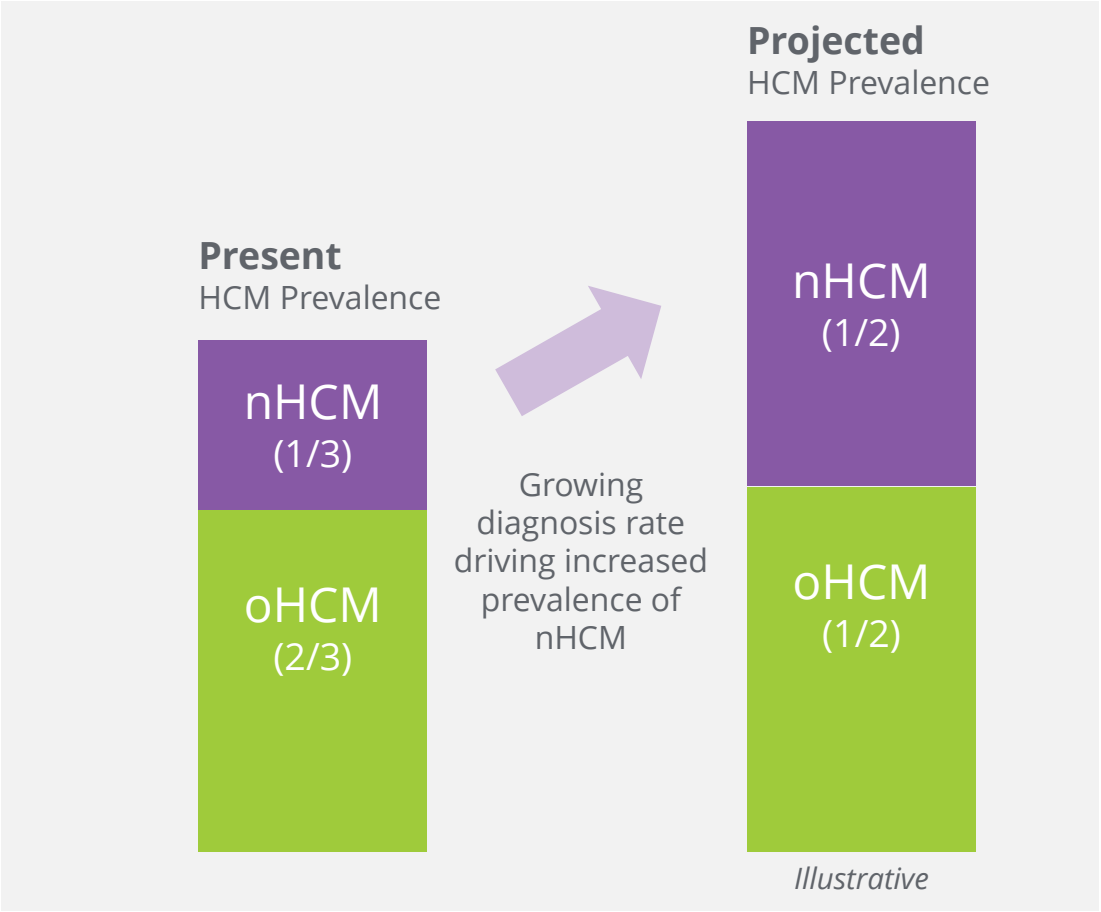
Non-Obstructive HCM: A Growing and Underserved Population

- **Significant underserved segment** of the HCM population
- **No effective medical or surgical treatment** options
- Diagnosis trends indicate that **nHCM is growing at a faster rate** than oHCM
- nHCM could account for up to **half of the total** HCM market



Source: Data on file

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Omecamtiv Mecarbil

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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

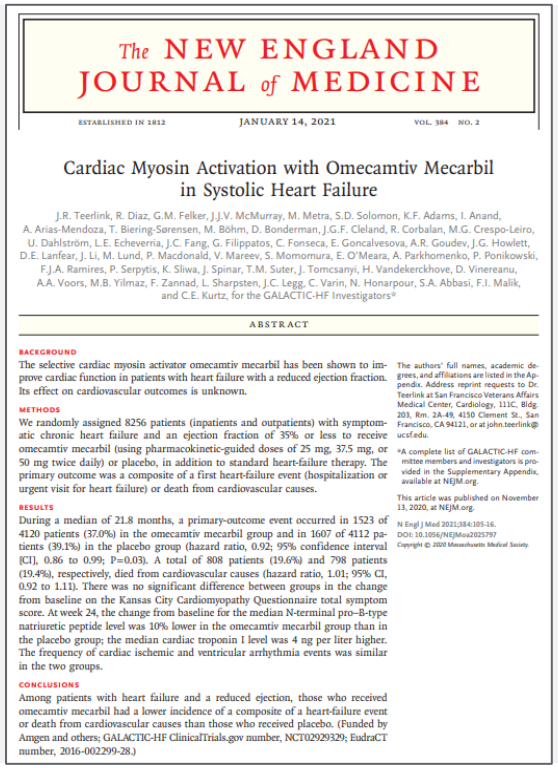
High Unmet Need

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.

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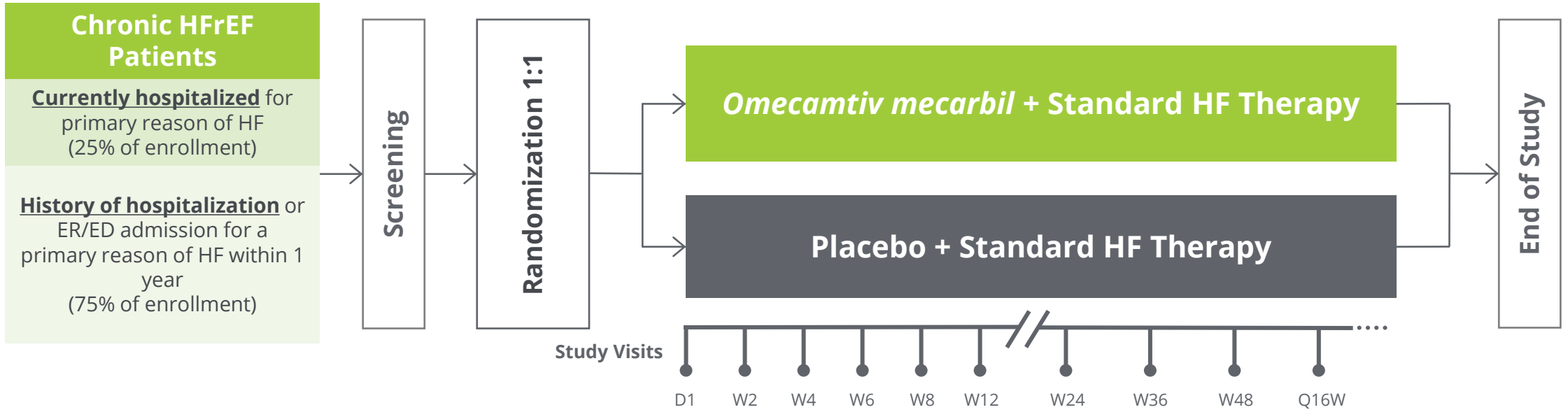
GALACTIC-HF: Clinical Trial Overview

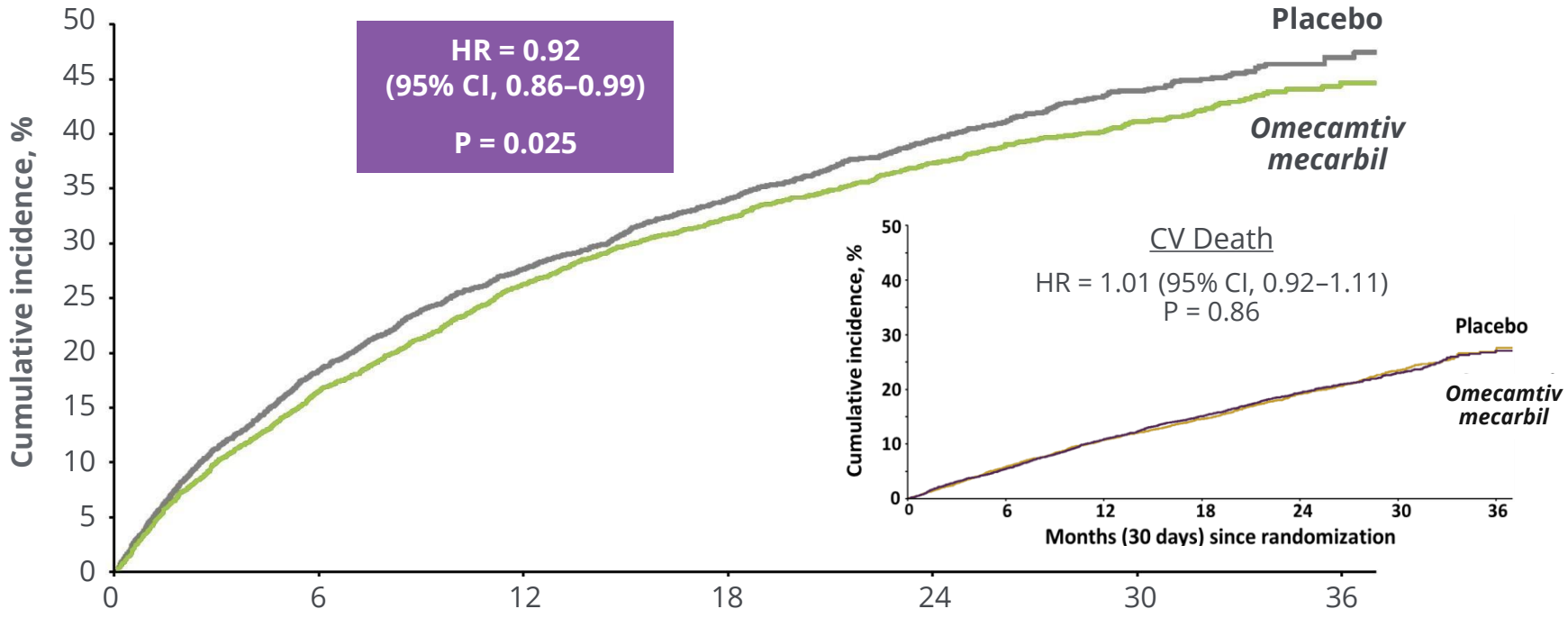
Phase 3 clinical trial

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

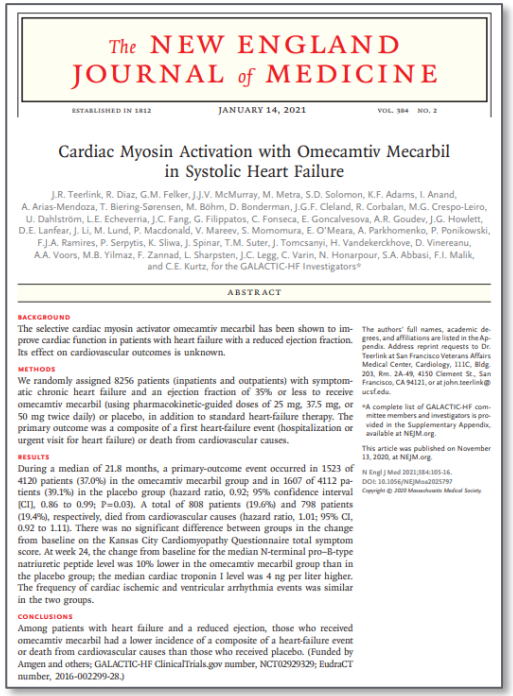


Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Primary Composite Endpoint



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



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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.

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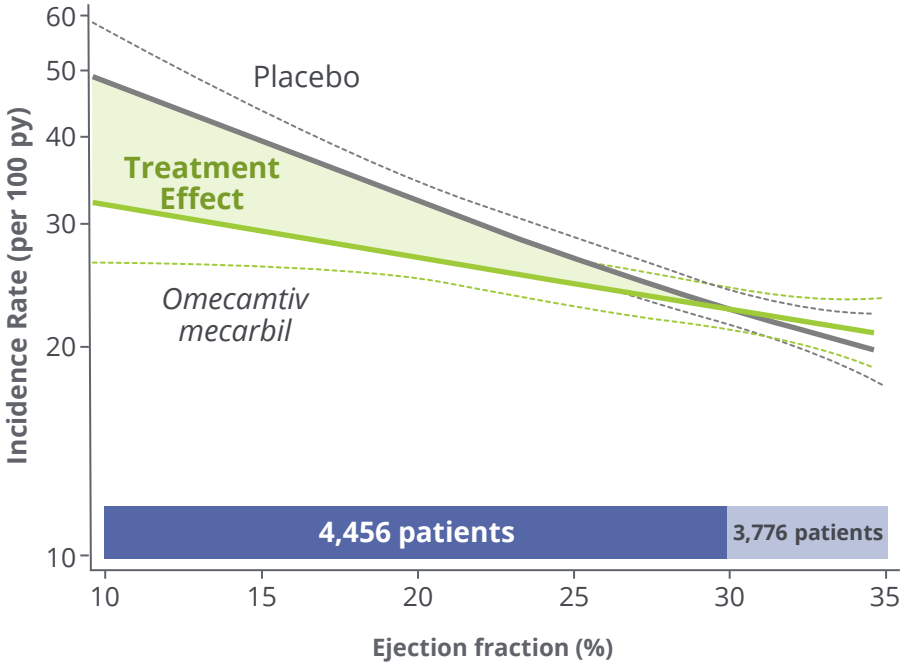
Time to first HF event or CV death

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

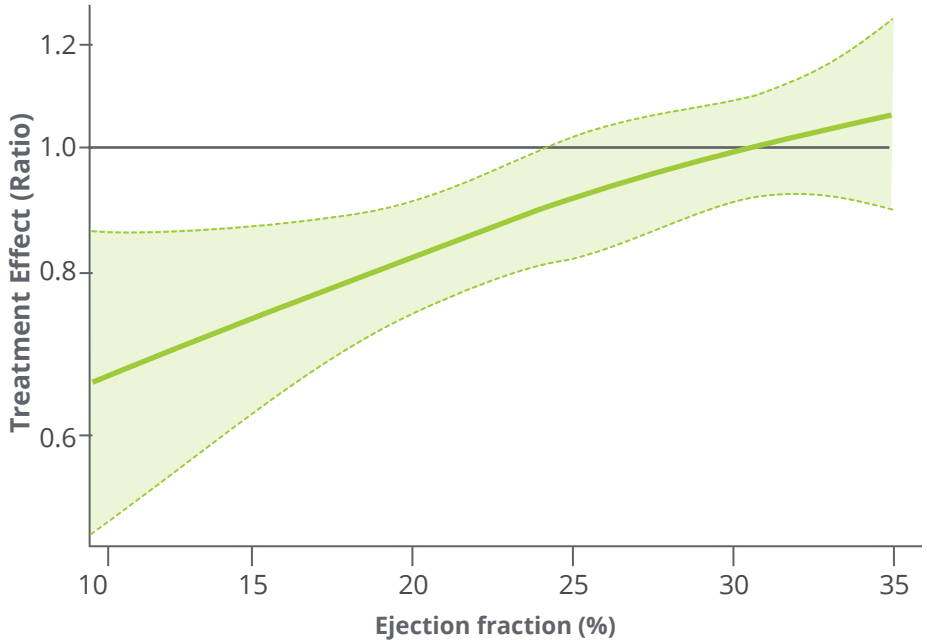
Benefit Observed to Increase as Baseline LVEF Decreased

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

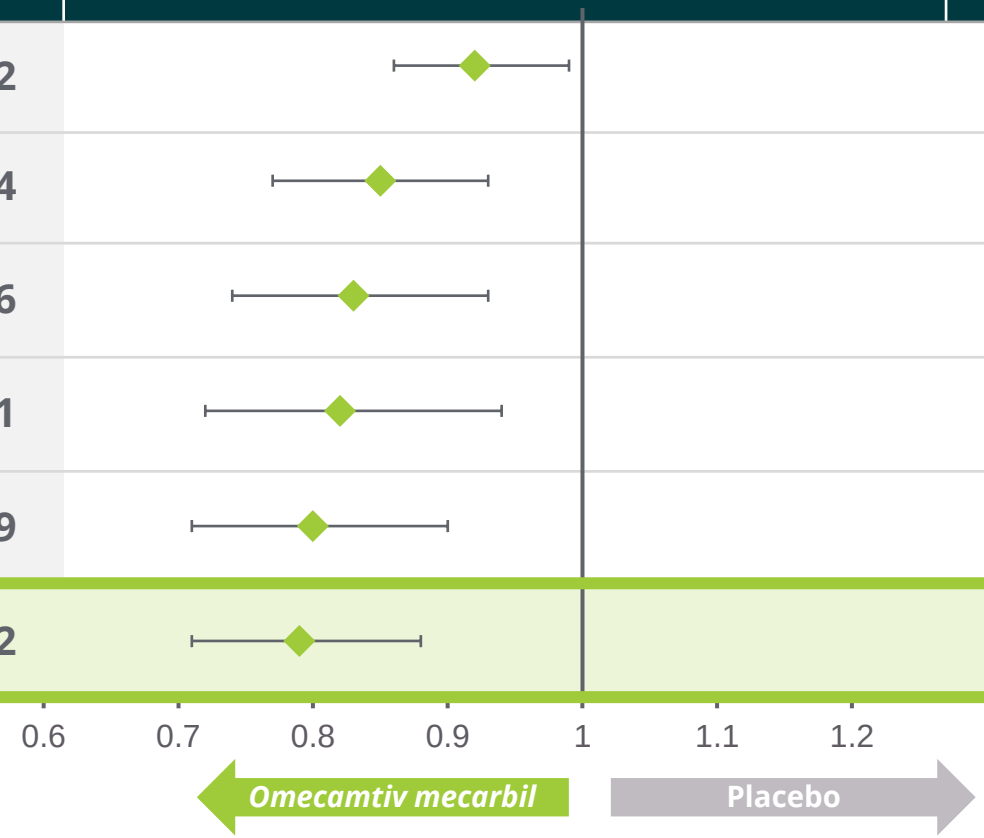
ARR = Absolute Risk Reduction. RRR = Relative Risk Reduction.
Teerlink JR., Diaz R., Felker GM., et al. Effect of Ejection Fraction on Clinical Outcomes in Patients treated with Omecamtiv Mecarbil in GALACTIC-HF. JACC. 2021
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory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

Cytokinetics®

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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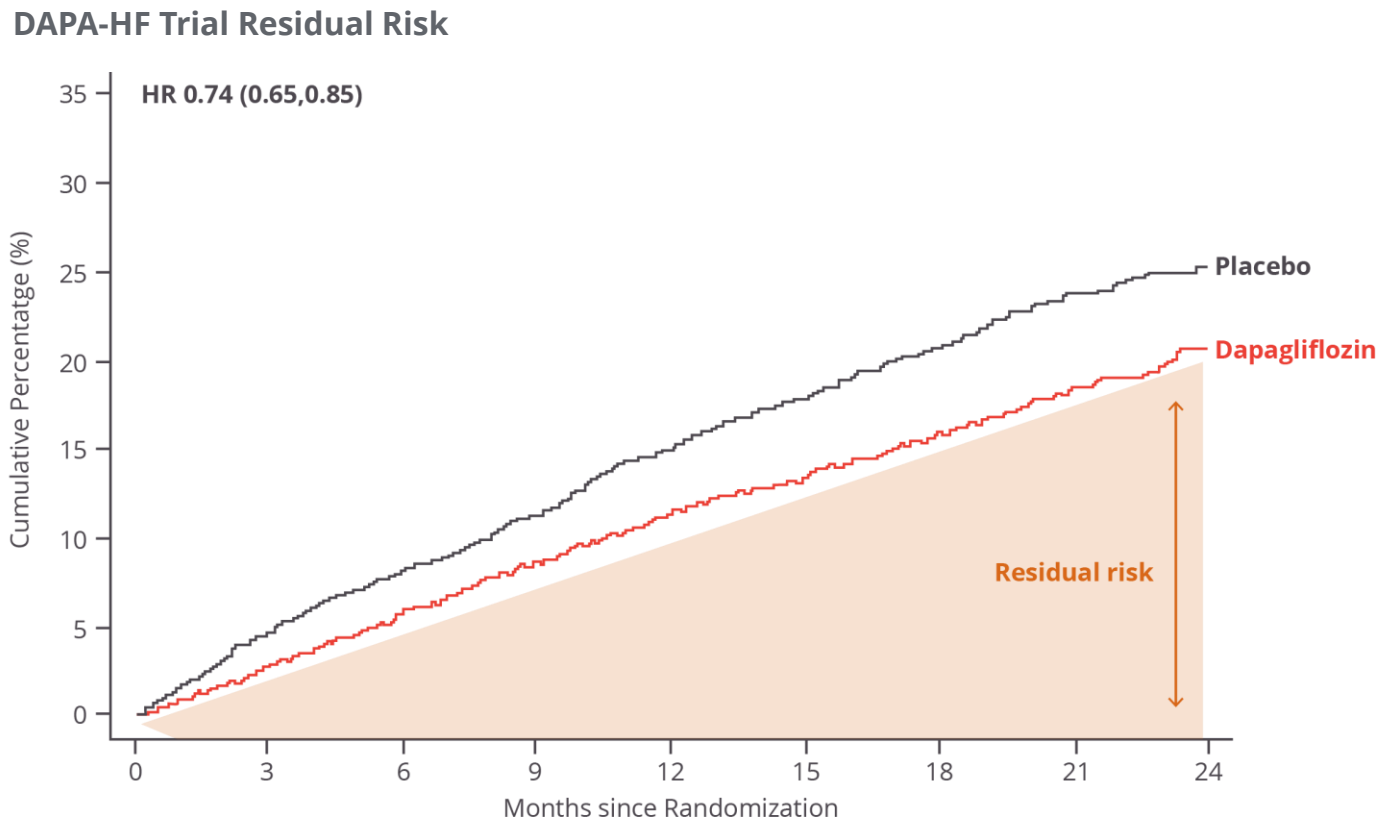
Residual Risk is High Despite Best Therapy

DAPA-HF Trial: Patients on GDMT including SGLT2-i

DAPA-HF trial
(dapagliflozin group)

- **Primary endpoint: CV Death/HF hospitalization/urgent HF visit**
- **4744 patients**
- Renin-angiotensin system blocker **94%**
- Dapagliflozin **96%**
- Mineralocorticoid receptor (aldosterone) antagonist **71%**



McMurray J et al, N Engl J Med. 2019;381:1995-2008

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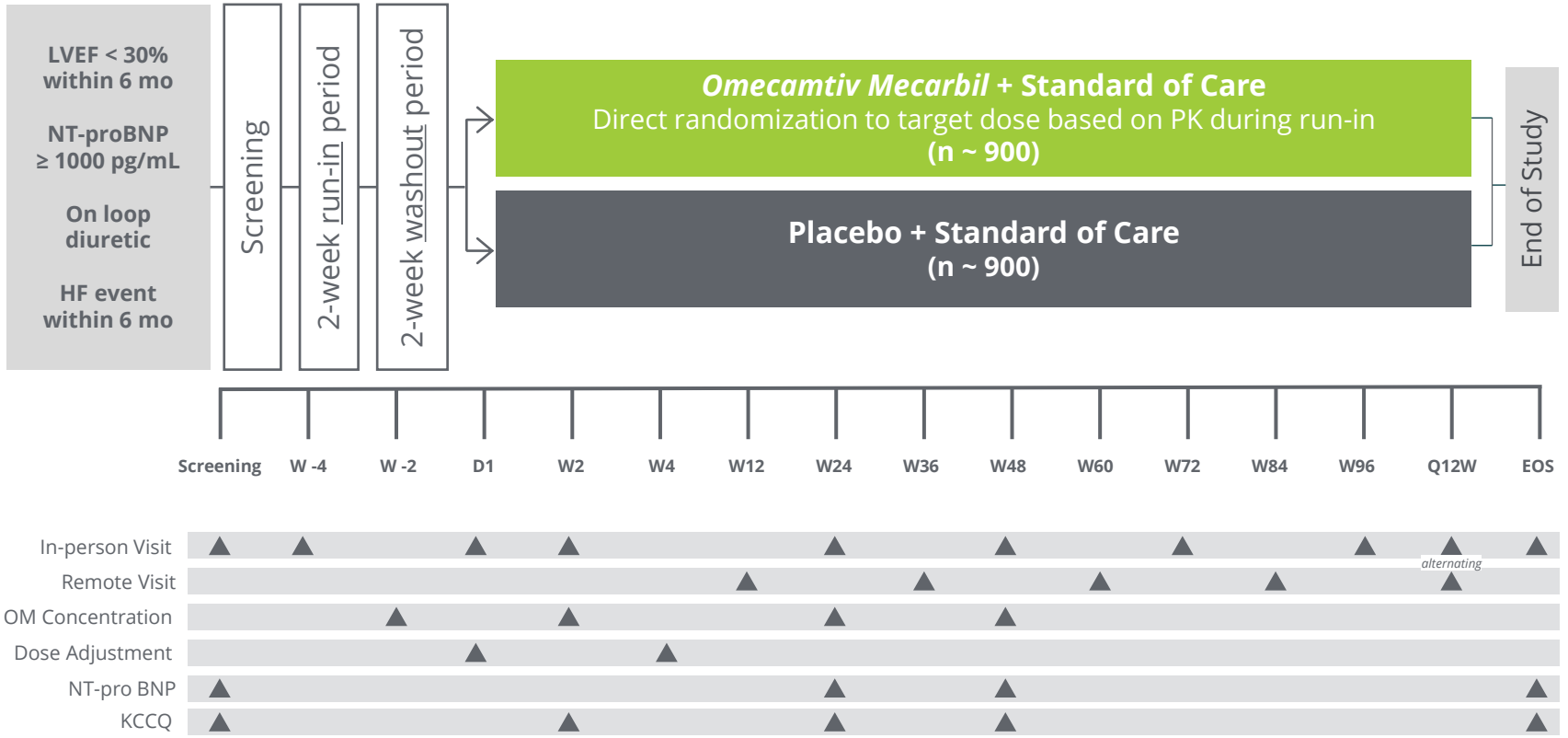
Phase 3 Confirmatory Clinical Trial Design

Currently enrolling

COMET-HF: Confirmation of ***O**mecamtiv **M**ecarbil* **E**fficacy **T**rial in **H**eart **F**ailure

- 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



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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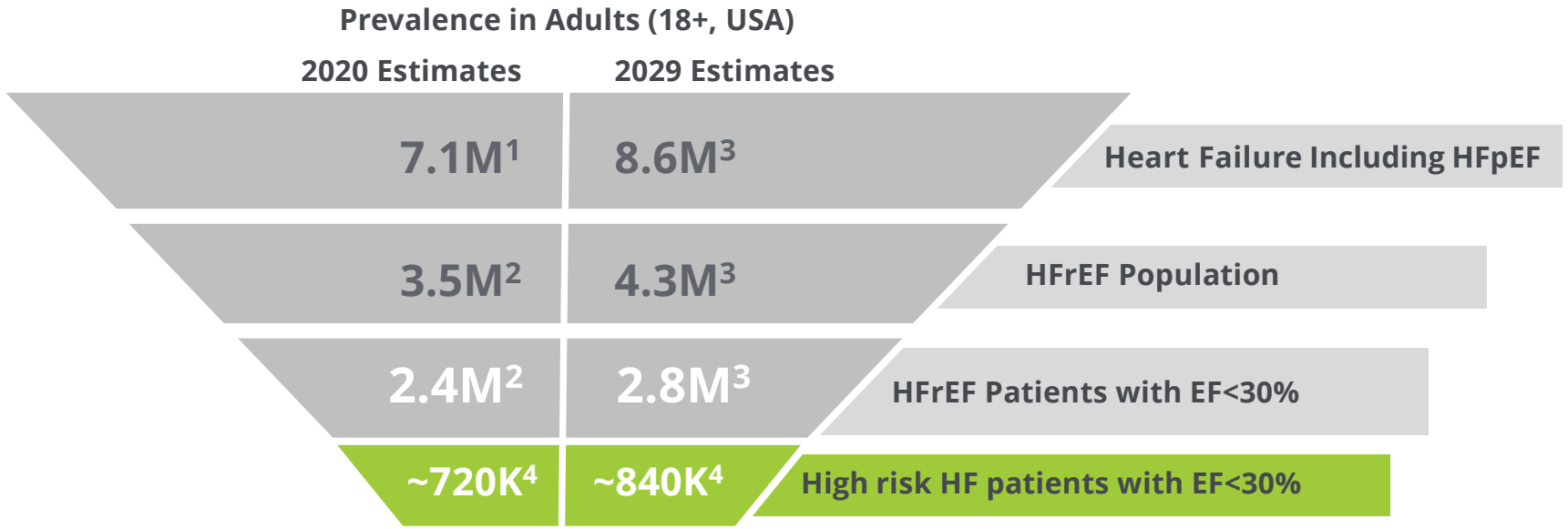
Large and Growing Target Patient Population in US



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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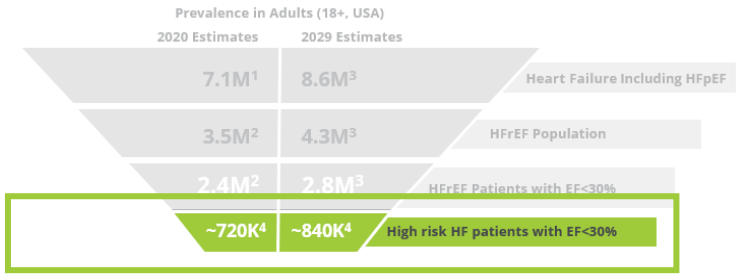
Higher Event Rate & Costs in Patients with Severely Reduced EF



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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The Business Case for *Omecamtiv Mecarbil*

Significant clinical need, lack of treatments drives higher price potential in HF with severely reduced EF

		"Severely Reduced EF"
US Price Potential		Premium to market
Market Insights	**Disease Severity**	**Severely Reduced EF** LVEF <30
	Payer Positioning	**~1M patients** Post tolerated GDMT
	Therapeutic Choices	**Limited to no treatment options**, +50% patients share vs. ≤30 EF
Financials	**Improved Margin[1]**	+20% incremental improvement in brand margin*
	Cost Savings[1]	+70% cost avoidance driven by portfolio synergies*

**Based on internal analysis*
Financials compared to launching OM alone vs launching as second product following aficamten
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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CK-586

Cytokinetics®

CK-586 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]

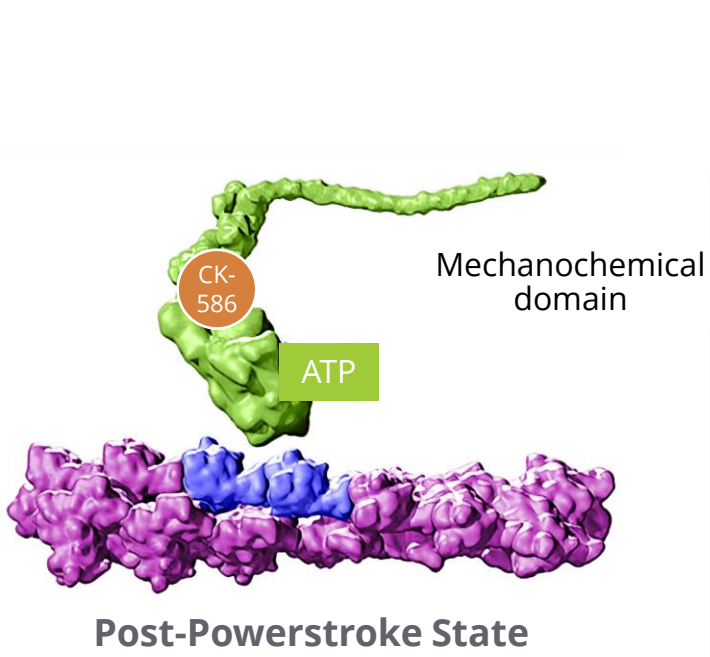
Subset of HFpEF patients with hypercontractility, ventricular hypertrophy, elevated biomarkers & HF symptoms **may benefit from a cardiac sarcomere inhibitor**

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

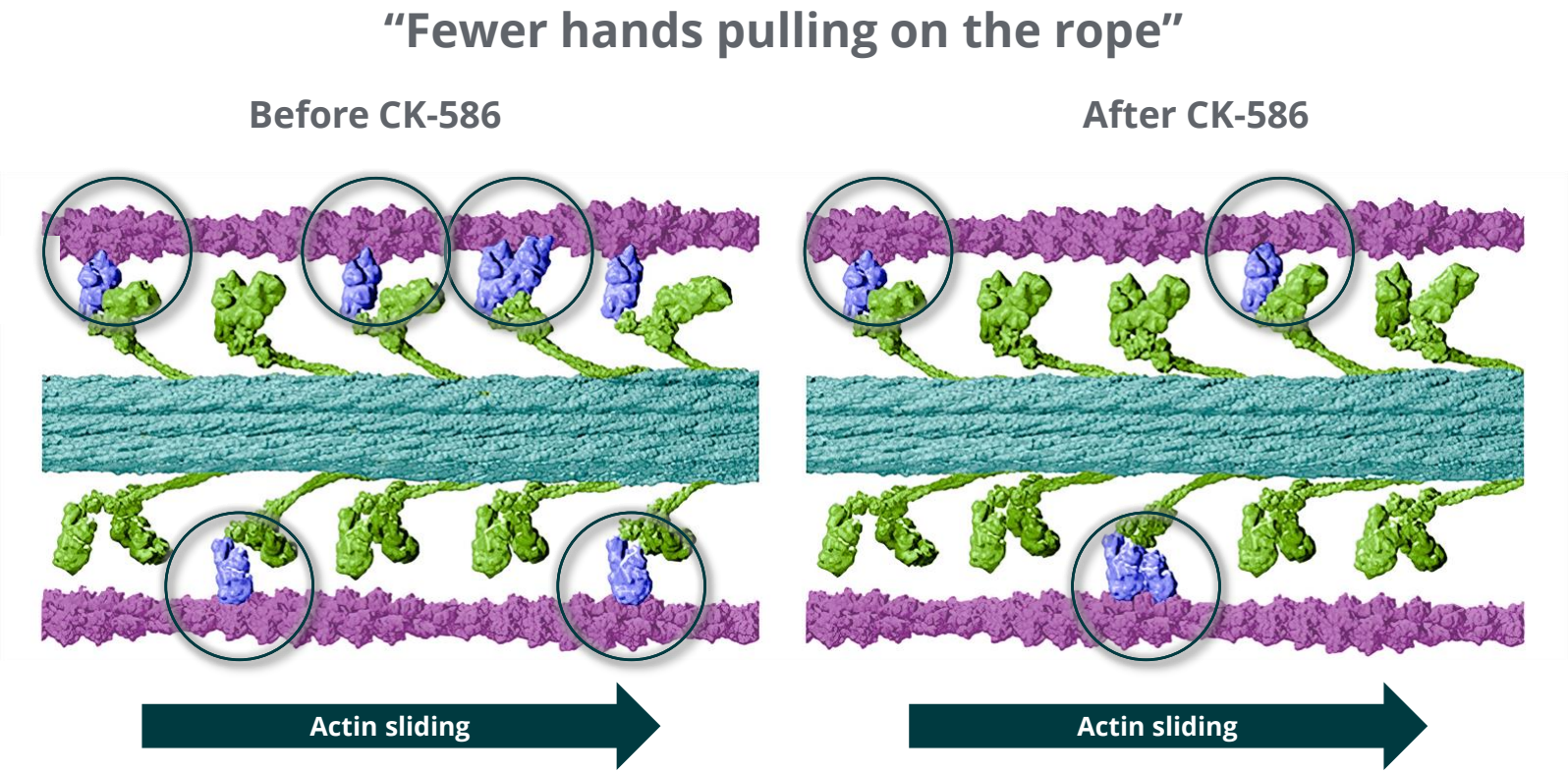
Lifetime healthcare costs for HFpEF are ~ $126,819 per patient[5], per-patient monthly cost for healthcare is $7,482, primarily, driven by **high rates of inpatient & outpatient visits**

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.

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



"Fewer hands pulling on the rope"



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

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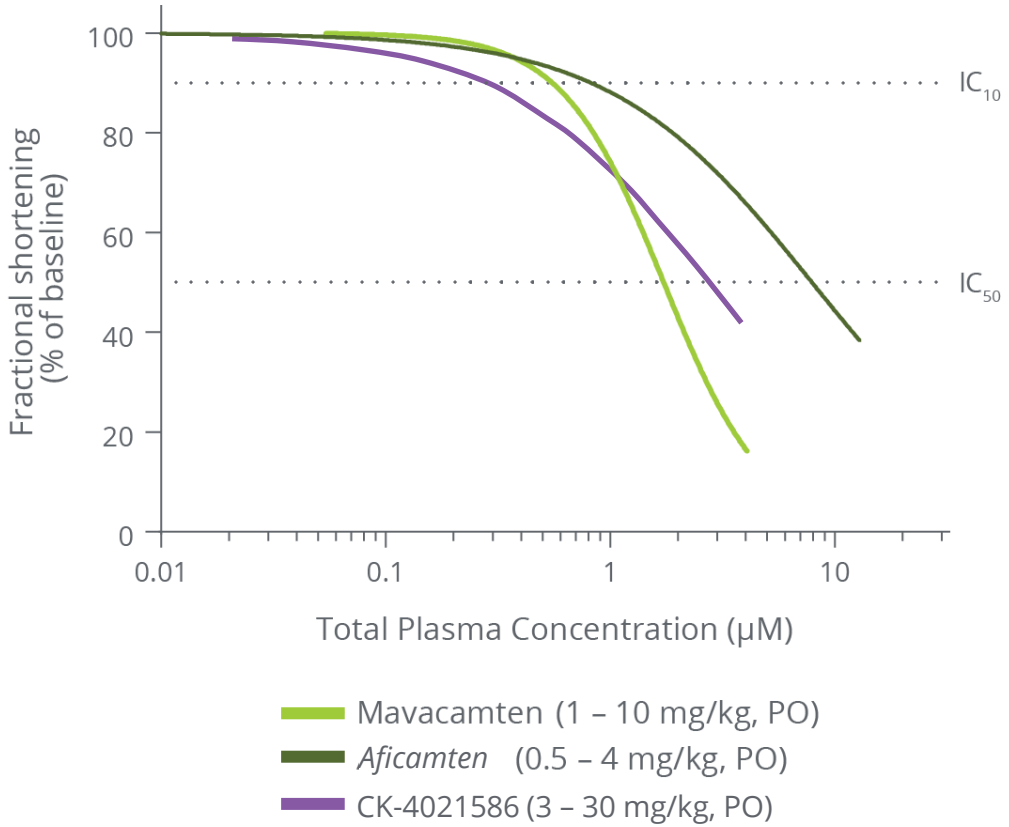
CK-586: Shallow *In Vivo* Concentration-Response

CK-586 has a shorter half-life than *aficamten*



Pharmacodynamic window Fractional shortening IC_{50} /IC_{10} ratio	
mavacamten	2.8x
aficamten	9.9x
CK-586	9.3x

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

Compound half-life in humans	Actual	Predicted
aficamten	~3 days	2.8 days
CK-586	~15 hours	15 hours

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

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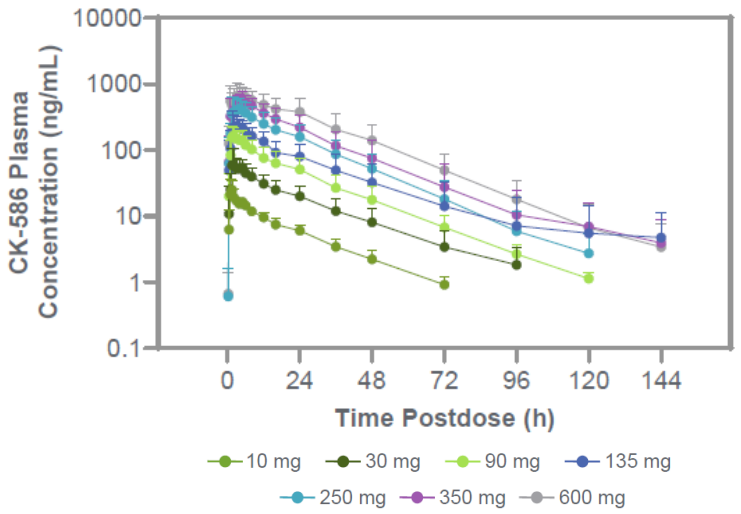
Phase 1 Data Support Advancement to Phase 2 Clinical Trial

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

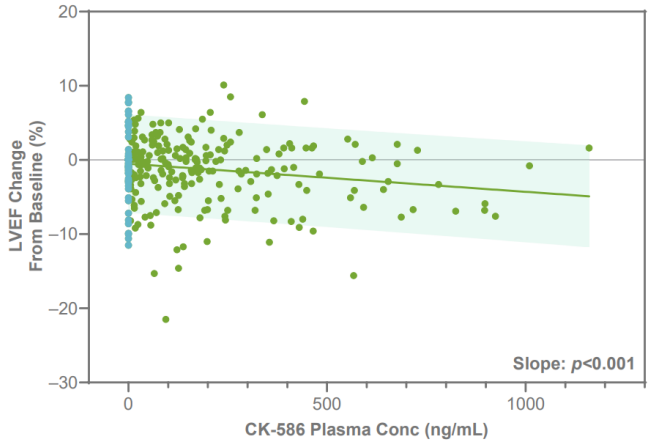
- **Less than 24-hour** half-life
- **Shallow and predictable** PK/PD relationship based on LVEF and LVFS
- **Well-tolerated** across all cohorts
- **No serious adverse events** were observed
- **Stopping criteria were not met**

Plasma Concentration

(mean [SD]) over time after single ascending doses of CK-586



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

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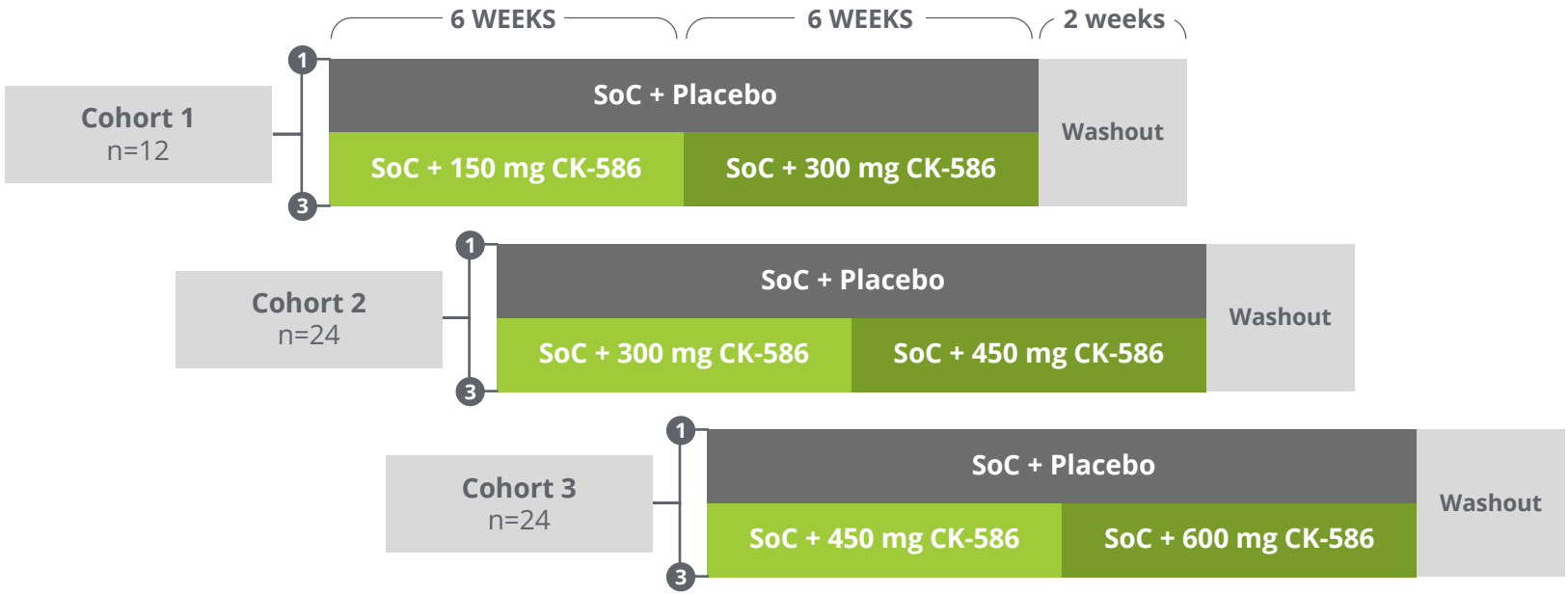
Phase 2 Study Schema

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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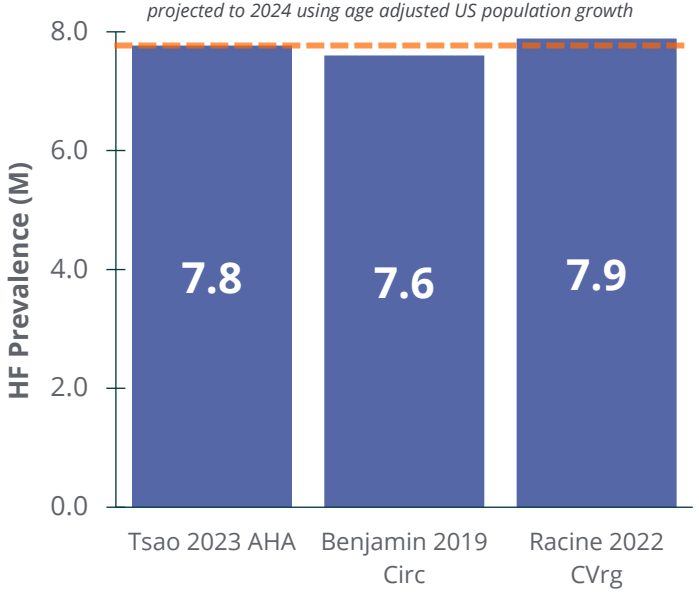
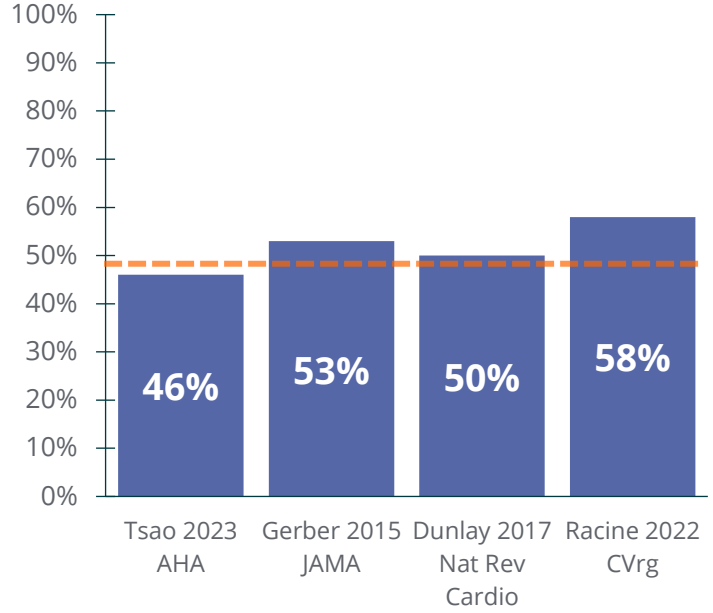
CK-586: Focusing on Patients with HFpEF and EF ≥ 60

7.9M
Heart Failure Prevalence in 2024, US

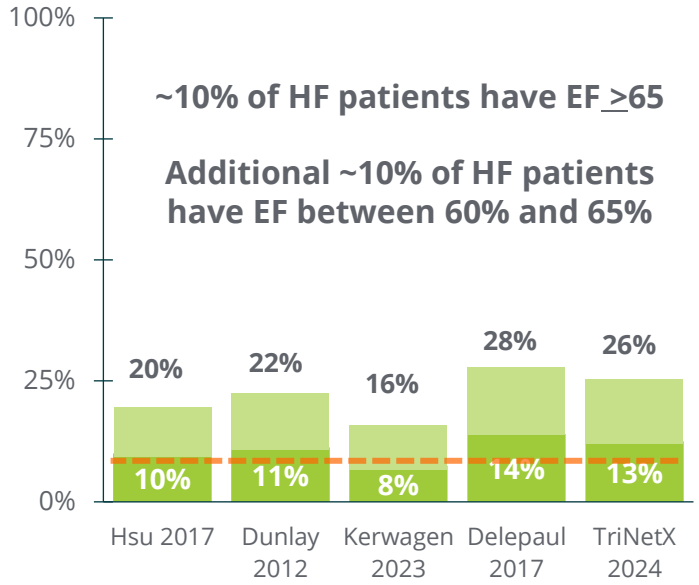
2024 prevalence calculated using published, historic estimate and projected to 2024 using age adjusted US population growth



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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CK-586 May Address Unmet Needs of HFpEF Patients

Proposed Mechanistic Benefits

- CK-586 may benefit cardiac relaxation during diastole
- CK-586 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

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

Financials & Milestones

Cytokinetics®

Strong Financial Position

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

~$1.1B in cash, cash equivalents and investments as of March 31, 2025

Further access to capital through term loans[1] with Royalty Pharma (RP)	Proceeds of $75M from Tranche 4 loan received in April 2025 Eligible to draw up to $100M in 2025[2] Access to additional $175M[3] subject to conditions
Potential further funding through RP opt-in	RP, at its option, can invest up to **$150M** in a Phase 3 trial of CK-586 in exchange for an additional 3.5% revenue participation interest in worldwide net sales of CK-586[4]

Add'l $500M

[1]Term loans are comprised of Tranche 4, 5, and 7 Loans.
[2]Tranche 5: Cytokinetics is eligible to draw up to $100M at any time prior to November 25, 2025.
[3]Tranche 7: Cytokinetics, at its option, is eligible to draw up to $175m subject to conditions related to the approval of the NDA for aficamten in oHCM on or prior to December 31, 2025.
[4]Royalty Pharma currently has a revenue participation interest of 1.0% of worldwide net sales of CK-586.

2025 Financial Guidance

	Guidance Issued on Feb. 27, 2025
GAAP Operating Expense[1]	$670M to $710M
Stock-based Compensation included in GAAP Operating Expense	$120M to $110M

The financial guidance does not include 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.

Anticipated year-over-year increase in GAAP operating expense includes investments toward commercial readiness for the potential approval and launch of *aficamten* for patients with oHCM.

[1]GAAP operating expense comprised of R&D and G&A expenses.

Robust Pipeline, Upcoming Commercial Launch & Solid Financial Position

Commercial

U.S. PDUFA date of December 26, 2025 for *aficamten*
U.S go-to-market strategies anchored in optimized market access & patient experience

China NDA and EU MAA on file
European commercial readiness activities underway

Pipeline

Aficamten
SEQUOIA-HCM: Positive Phase 3 results
Label-expanding opportunities including:
MAPLE-HCM: Positive Phase 3 results show superiority of *aficamten* to *metoprolol*
ACACIA-HCM: Phase 3 nHCM
CEDAR-HCM: Phase 2-3 pediatric oHCM
FOREST-HCM: OLE in oHCM & nHCM

Omecamtiv mecarbil
Phase 3 confirmatory clinical trial **COMET-HF** ongoing

CK-586
Phase 2 **AMBER-HFpEF** clinical trial ongoing

CK-089
Phase 1 study ongoing in healthy participants

Ongoing R&D
Additional research in muscle biology, energetics & metabolism

Foundation

R&D platform rooted in **myosin modulation**

Pioneers in muscle biology

$1.1B cash & investments* with further access to capital, up to $425M**

**As of March 31, 2025*
**$425M comprised of up to $275M in term loan facilities with Royalty Pharma, and up to $150M investment by Royalty Pharma, at its option, in a Phase 3 clinical trial of CK-586 in exchange for an additional 3.5% revenue participation interest in worldwide net sales of CK-586.
Aficamten, omecamtiv mecarbil, CK-586 and CK-089 are investigational drugs and are not approved by any regulatory agency. Their safety and efficacy have not been established.

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Expected 2025 Milestones

Aficamten

- ○ Continue advancing **go-to-market strategies & prepare to launch *aficamten* in the U.S.** in 2H 2025
- ✓ **Report topline results from MAPLE-HCM** in May 2025
- ✓ **Complete patient enrollment in ACACIA-HCM** in 2H 2025
- ○ **Complete patient enrollment of adolescent cohort of CEDAR-HCM** in 2H 2025

Omecamtiv Mecarbil

- ○ **Continue patient enrollment in COMET-HF** through 2025 with objective to **complete enrollment** in 2026

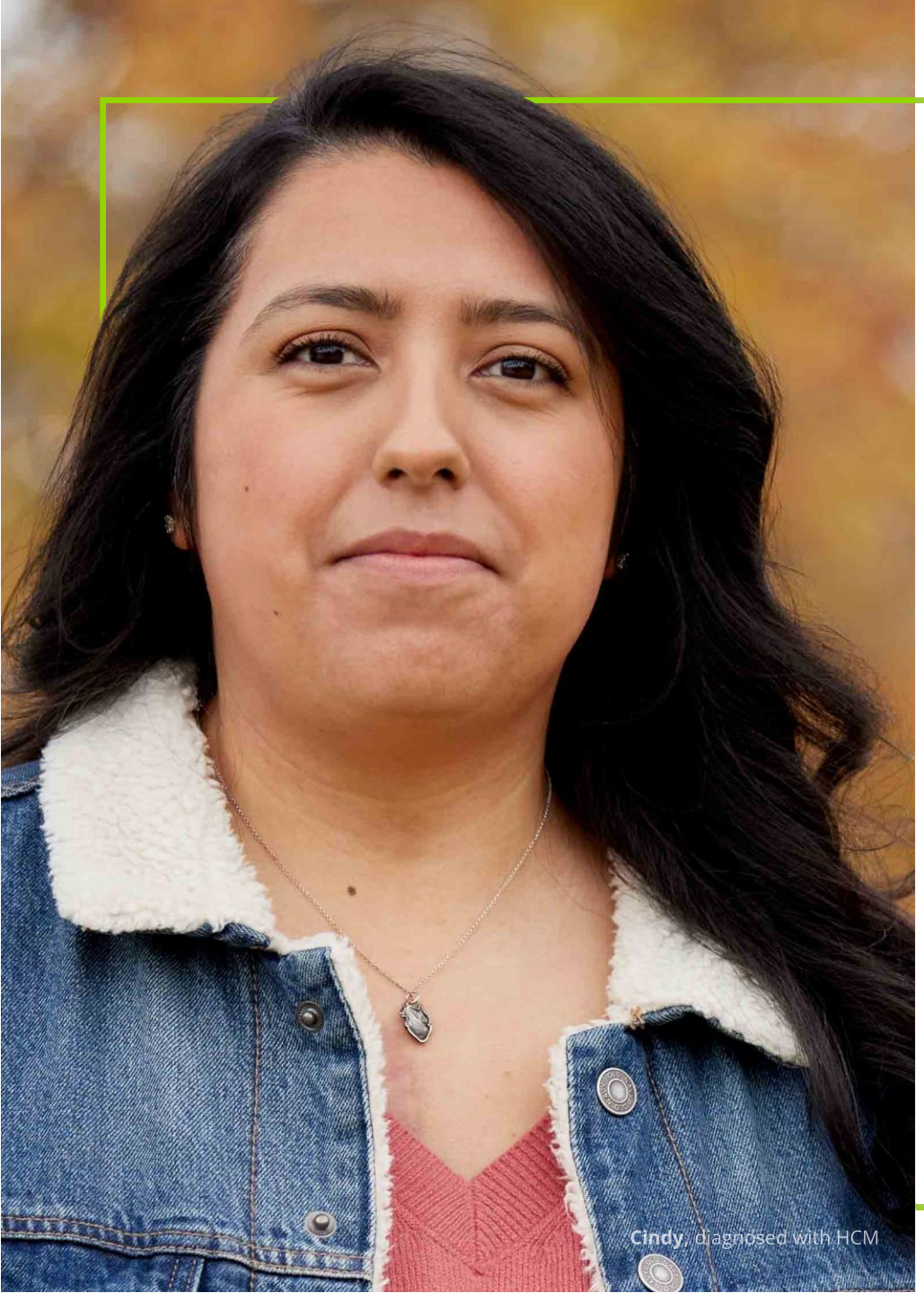
CK-586

- ○ **Complete first two patient cohorts of AMBER-HFpEF** in 2H 2025

CK-089

- ○ **Complete the Phase 1 study of CK-089** in 2025

Aficamten, omecamtiv mecarbil, CK-586 and CK-089 are investigational drugs and have not been approved. Their safety and efficacy have not been established.



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thank you