



Eric, diagnosed with HCM



EMPOWERING
muscle
EMPOWERING
lives

Forward-Looking Statements

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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	Research	Pre-Clinical	Phase 1	Phase 2	Phase 3	Approval
 Myosin Myosin-Targeted Therapy	oHCM	Aficamten						U.S. PDUFA date 9/26/25 China NDA & EU MAA on file
	oHCM (Monotherapy*)	Aficamten						
	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.

Strong Financial Position

Strengthened balance sheet & access to capital to execute launch & advance R&D pipeline

~\$1.3B in cash, cash equivalents and investments as of September 30, 2024

Further access to capital through term loans^[1] with Royalty Pharma (RP)

Eligible to draw up to \$175m 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 4: Cytokinetics is eligible to draw up to \$75m by April 3, 2025. The minimum draw for tranche 4 is \$50m.

Tranche 5: Cytokinetics, at its option, is eligible to draw up to \$100m by November 24, 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.

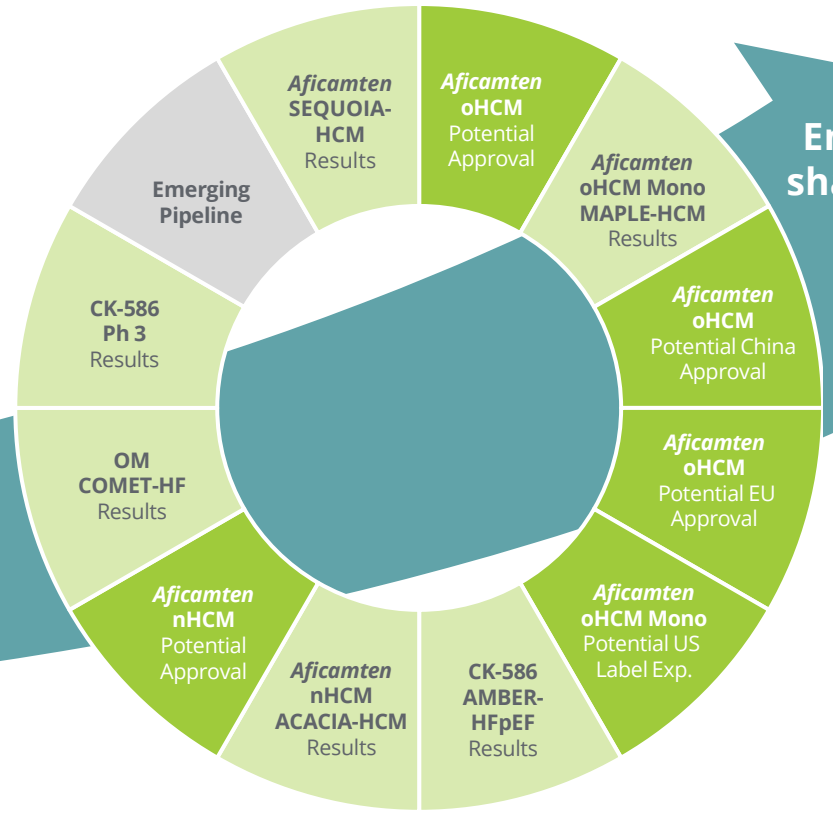
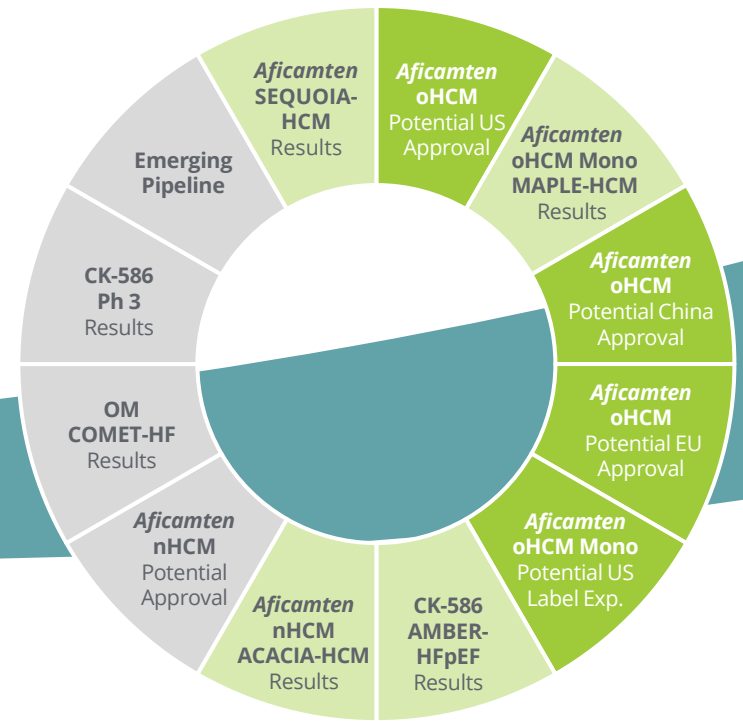
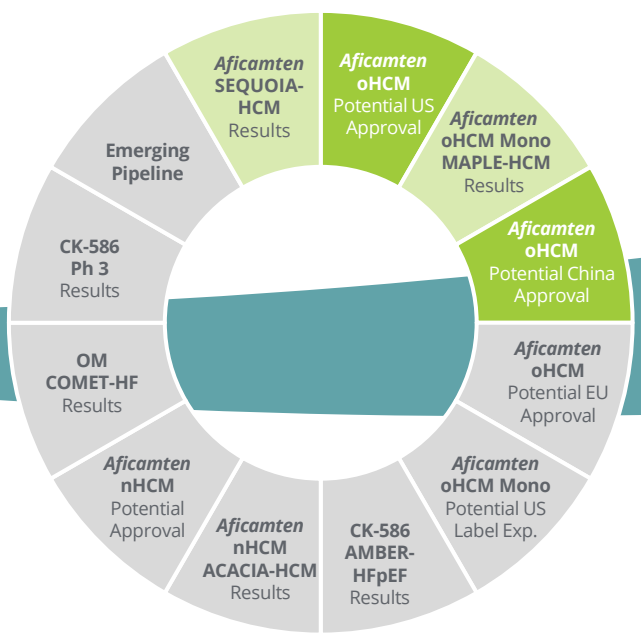
[4]Royalty Pharma currently has a revenue participation interest of 1.0% of worldwide net sales of CK-586.

Myosin Platform Fuels Multiple Milestones and Increased Value

Potential Regulatory Approval Results

For illustrative purposes only

U.S. PDUFA date of September 26, 2025, China NDA & EU MAA on file for *aficamten*



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.

VISION 2030

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

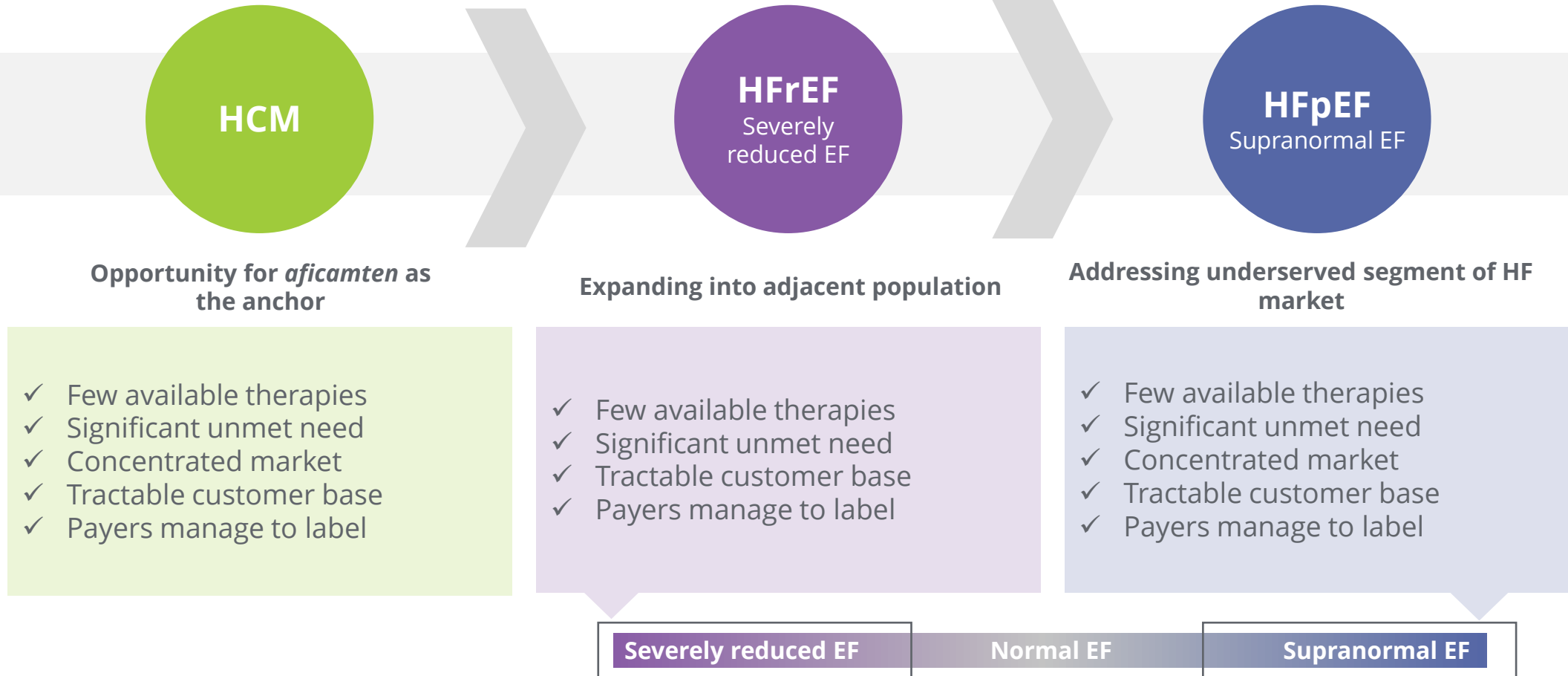
○ INGENUITY

Extend leadership in muscle biology deploying multiple therapeutic modalities

Building a Specialty Cardiology Franchise

Addressing Difficult to Treat Populations Within Heart Failure

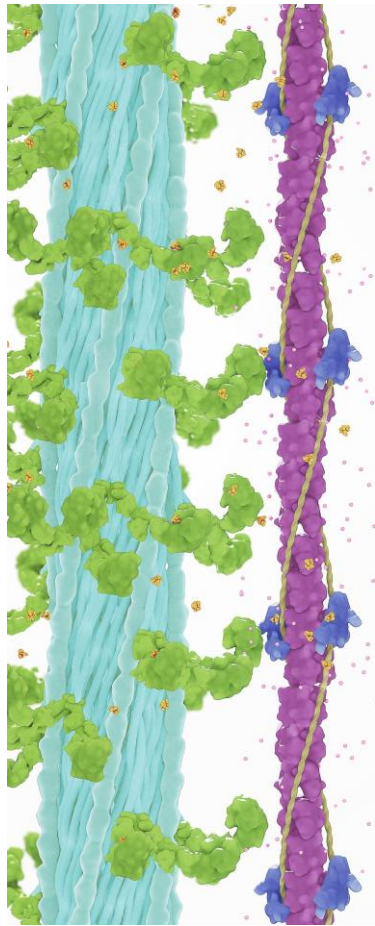
Specialty cardiology franchise strategy applies to markets with similar characteristics



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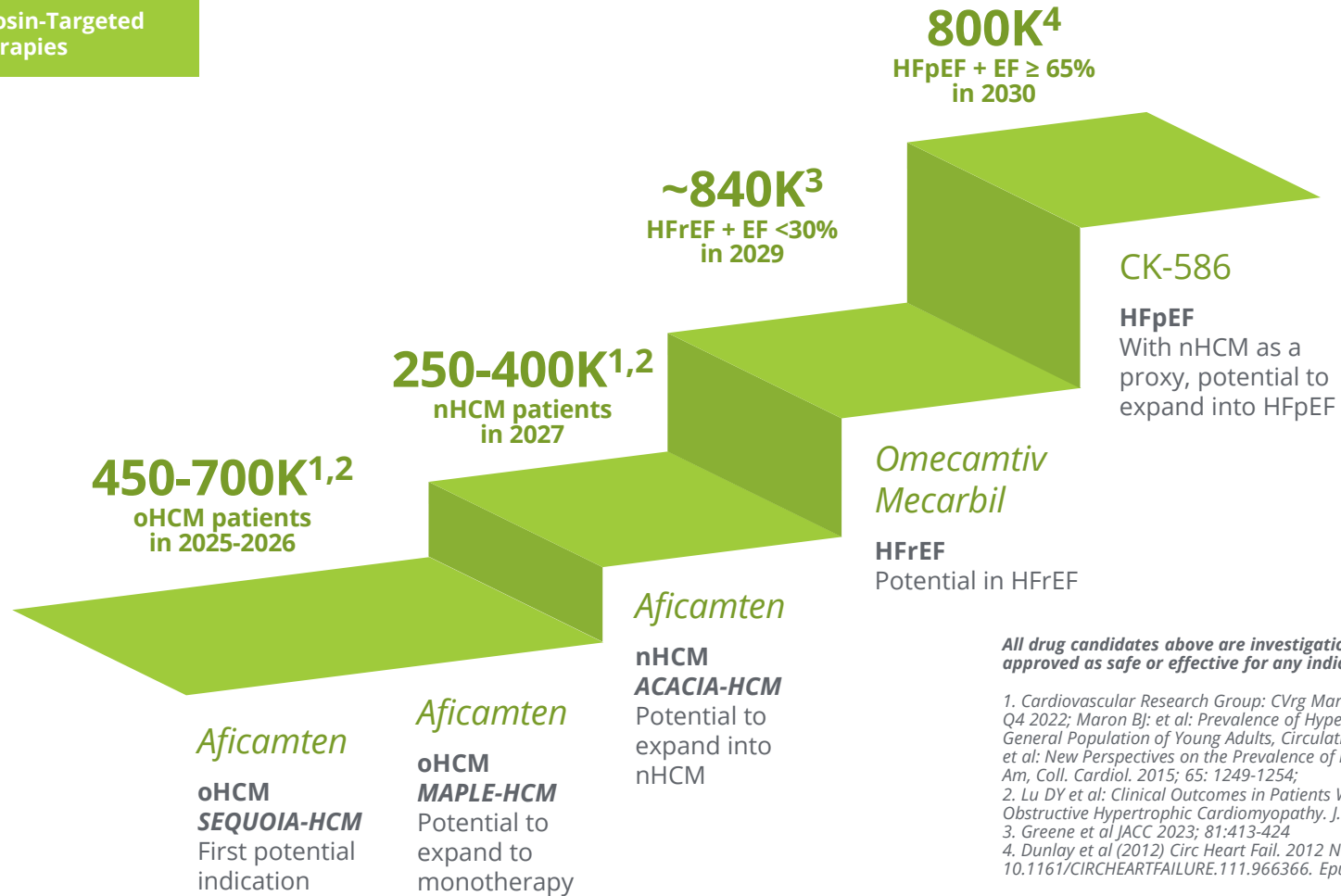
Building a Specialty Cardiology Franchise Anchored by *Aficamten*

Potential patient market for specialty cardiology franchise strategy



Myosin-Targeted Therapies

Estimated prevalence in US only



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

1. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ: et al: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, *Circulation* 1995;92:785-789; Semsarian C. et al: New Perspectives on the Prevalence of Hypertrophic Cardiomyopathy, *J. Am. Coll. Cardiol.* 2015; 65: 1249-1254;
 2. Lu DY et al: Clinical Outcomes in Patients With Nonobstructive, Labile, and Obstructive Hypertrophic Cardiomyopathy. *J. Am. Heart Assoc.* 2018;7:1-11
 3. 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.

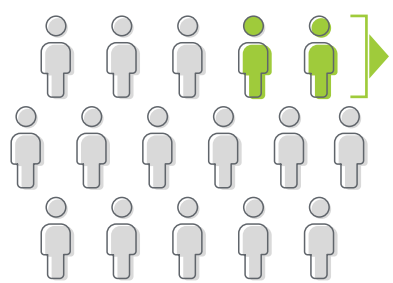
Potential for Multiple Specialty Cardiology Launches

Drug Candidate	Potential Indication	2024	2025	2026	2027	2028	2029	2030+
Aficamten	oHCM		★					
	oHCM Mono (MAPLE-HCM)			★				
	nHCM (ACACIA-HCM)					★		
Omecamtiv Mecarbil	HFrEF						★	
CK-586	HFpEF							★

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.

Specialty Cardiology Business Has Potential for High ROI

Concentrated Prescribers
~80K cardiologists/PCPs treat CV diseases

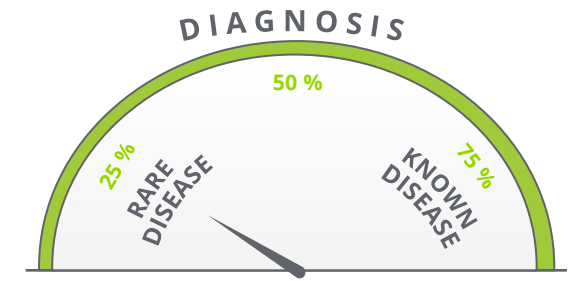


~10K
cardiologists
treat ~80%
HCM

Higher Revenue Per Prescriber



Opportunity To Grow Market Through Diagnosis

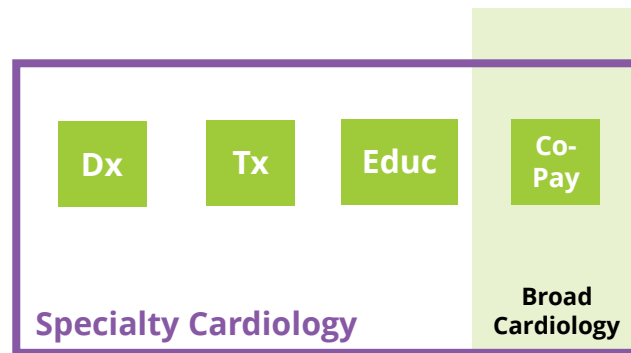


Distribution Limited to Specialty Retailers

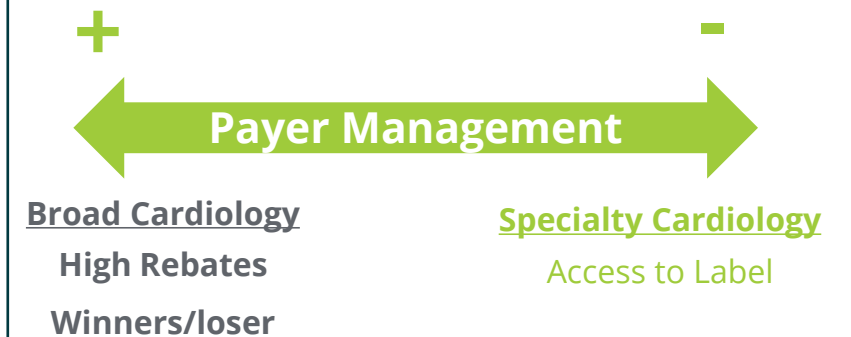


● Retail Pharmacy
● Limited Specialty Retailer

Differentiated Patient Experience



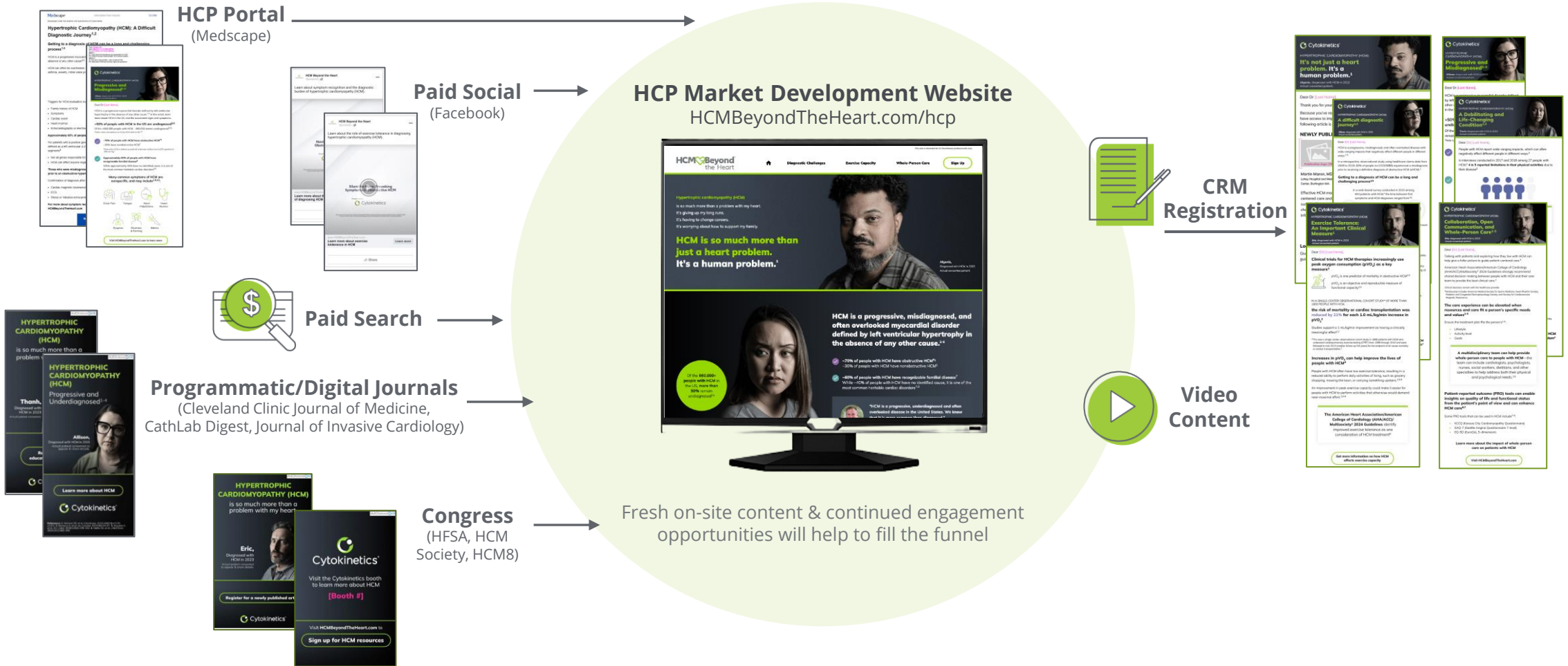
Path to Reimbursement



Potential Benefits of a Specialty Cardiology Franchise

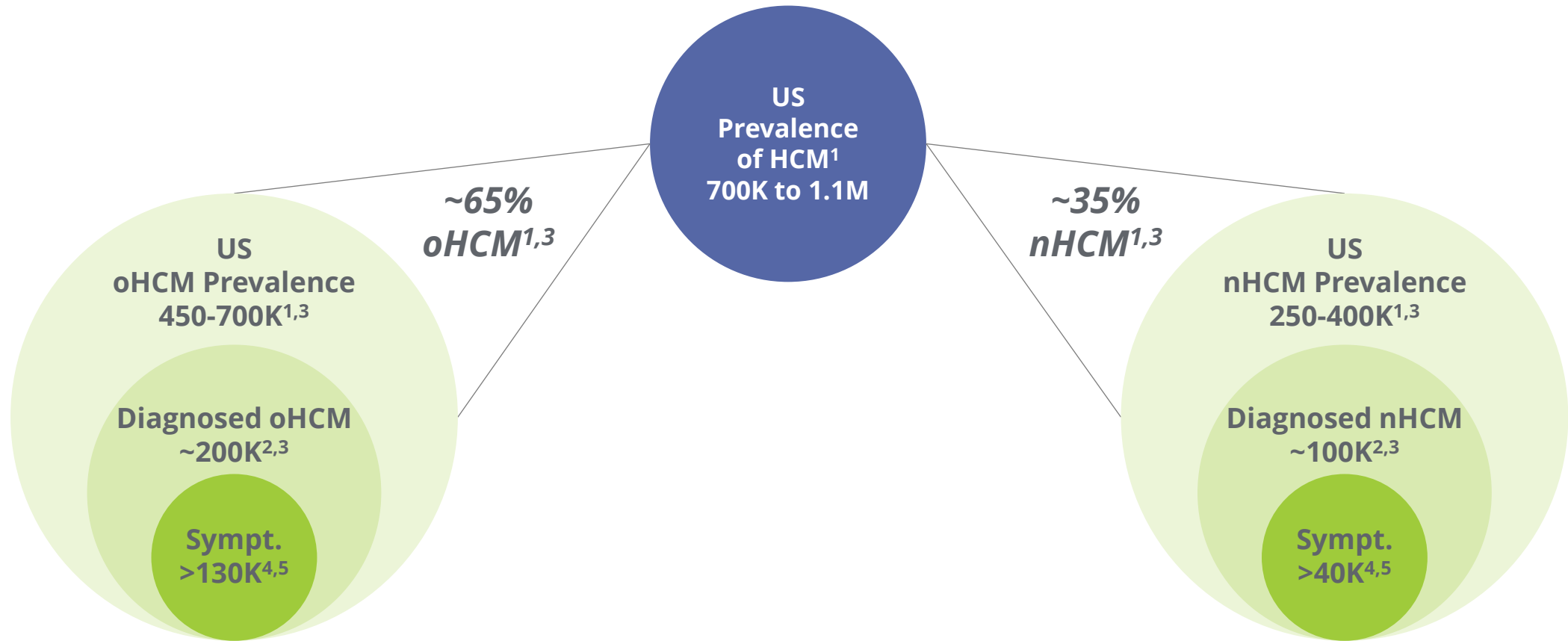


HCP-Directed HCM Awareness Campaign Launched



Aficamten

Opportunity for CMI in Diagnosed, Symptomatic HCM Patients



Projections and forecasts for illustration.

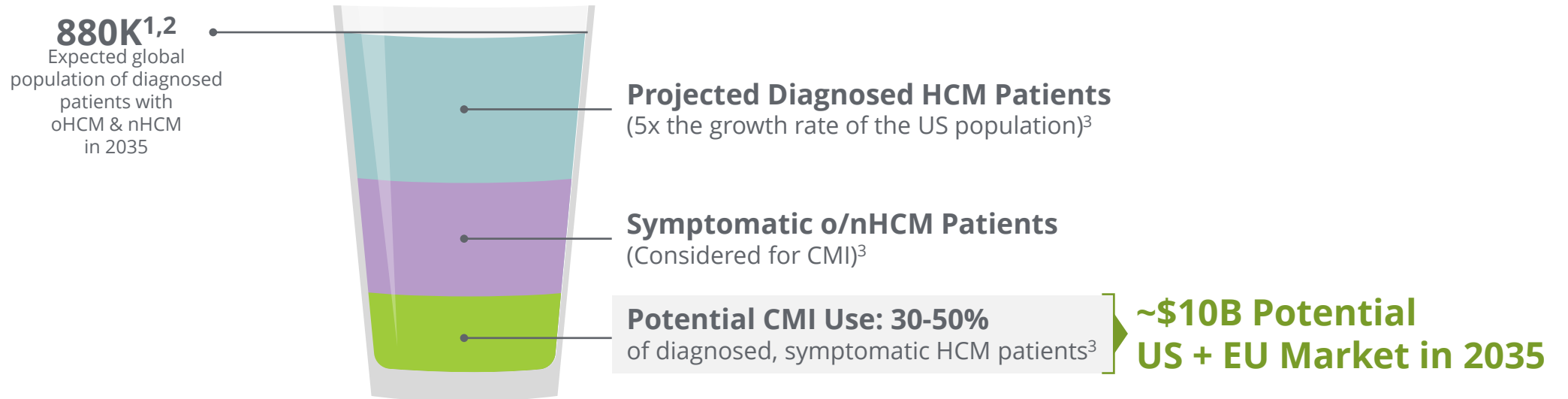
1. Cardiovascular Research Group: CVrg Market Strategies: Heart Failure, p 48, Q4 2022; Maron BJ; et al.: Prevalence of Hypertrophic Cardiomyopathy In A General Population of Young Adults, Circulation 1995;92:785-789; Semsarian C. et al: New Perspectives on the Prevalence of Hypertrophic Cardiomyopathy,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

\$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](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.

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.

SEQUOIA-HCM: Pivotal Phase 3 Trial



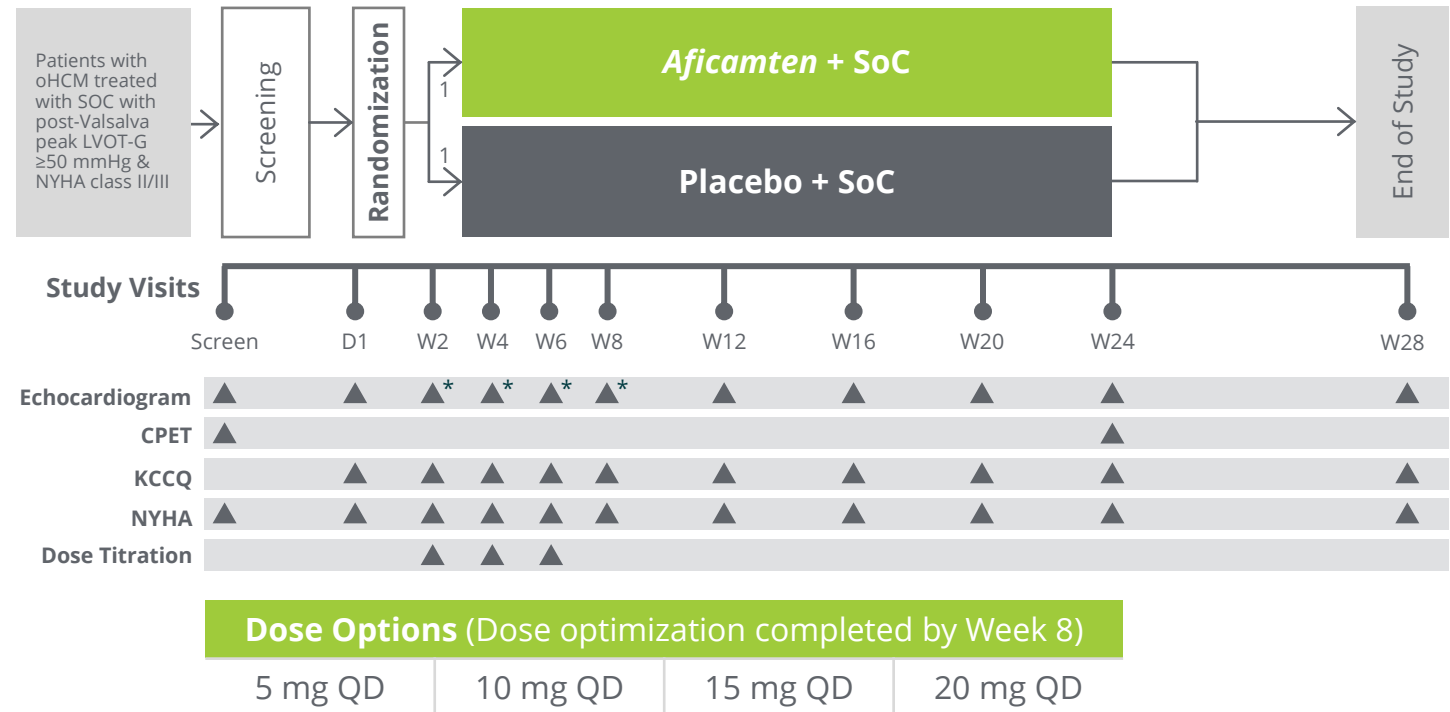
Primary endpoint: **Change in pVO₂ by CPET from baseline to Week 24**

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

Enrolled 282 patients treated with standard of care with:

- **resting LVOT-G ≥30 mmHg,**
- **post-Valsalva LVOT-G ≥50 mmHg,**
- **NYHA Class II or III,**
- **exercise performance <80% predicted**

Individualized dose up-titration based on echocardiography: LVEF ≥55%, post-Valsalva LVOT-G ≥30 mmHg



SOC: standard of care
* Focused echocardiogram

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

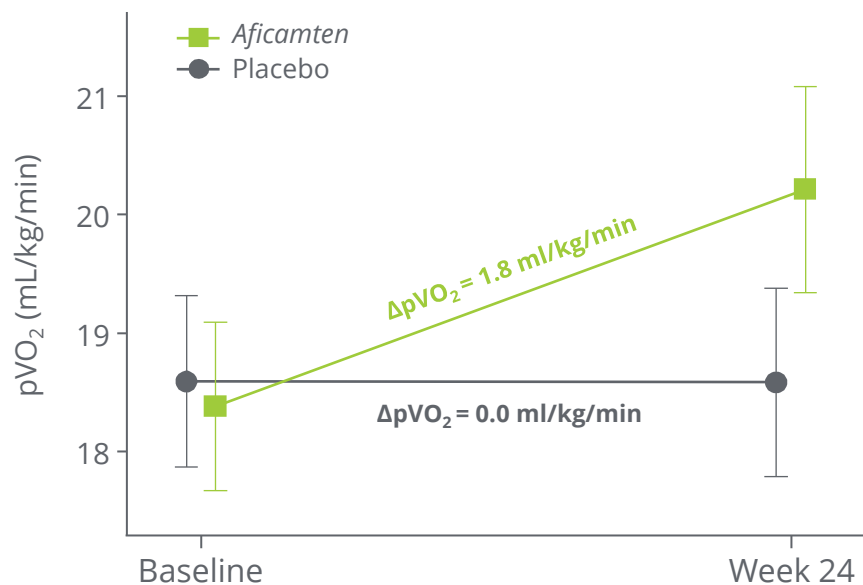
SEQUOIA-HCM: Primary Endpoint

Significant improvement in exercise capacity compared to placebo

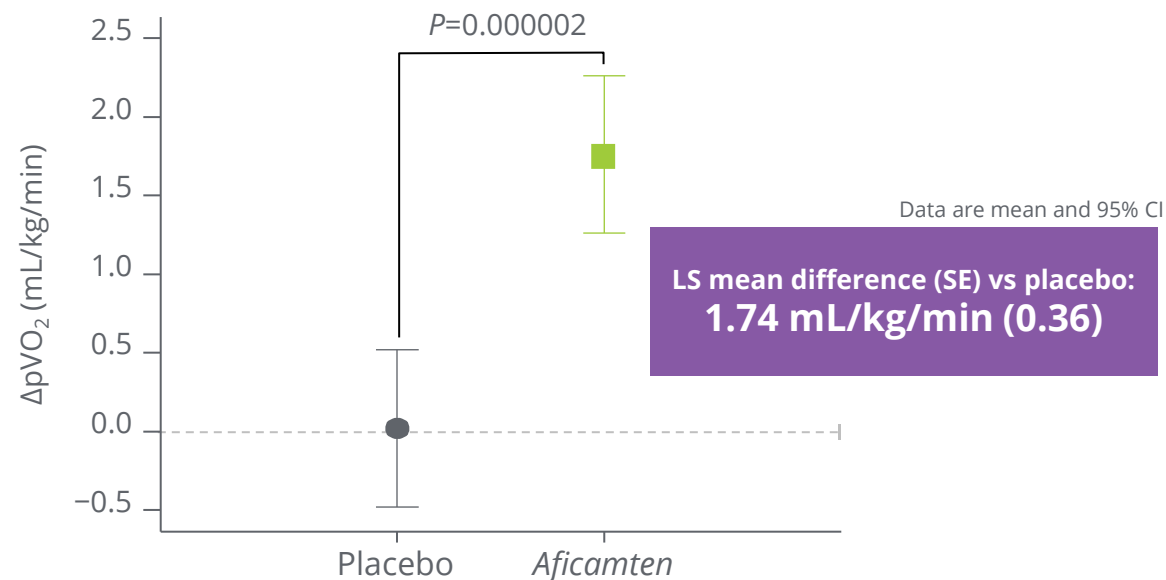


Results presented at Heart Failure 2024 and published in *NEJM*

Absolute Change from Baseline to Week 24



LS mean Change from Baseline to Week 24



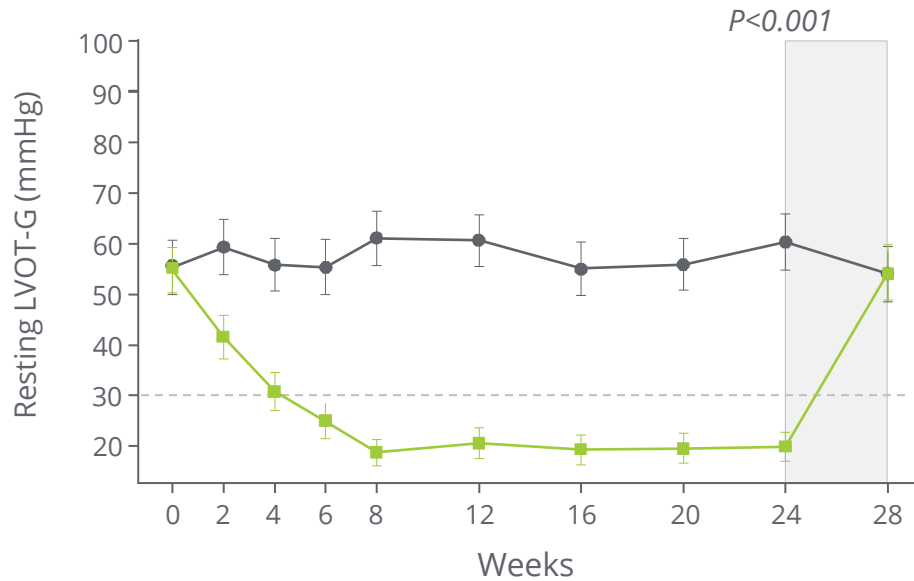
Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024. Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: Secondary & Exploratory Endpoints

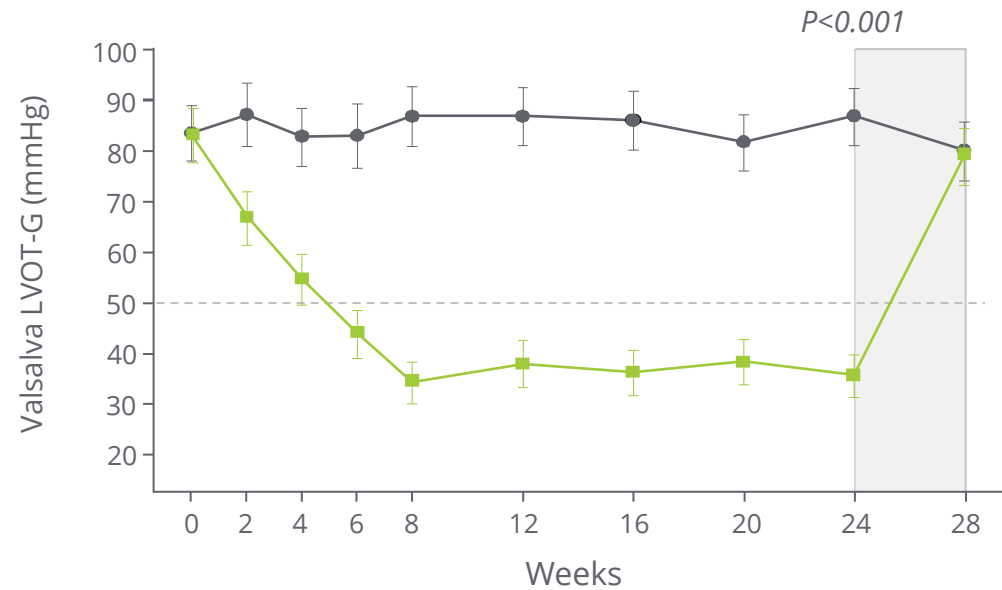


Significant improvement in gradients by ~60% with no significant adverse change in LVEF

Resting LVOT-G



Valsalva LVOT-G



LS mean difference: - 50 mmHg

- Aficamten
- Placebo
- Washout

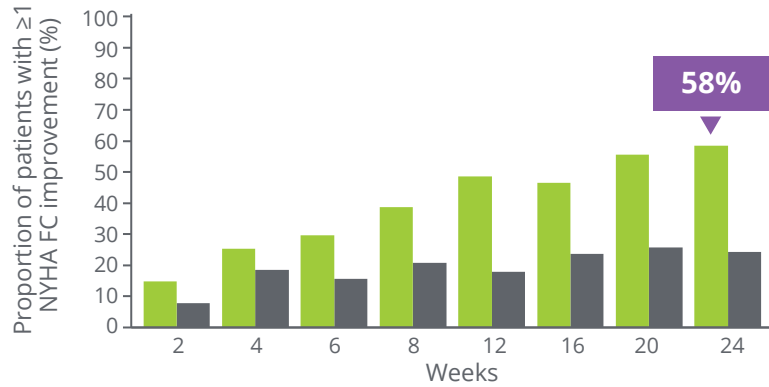
Error bars are 95% CI
 Hegde S, et al. Impact of Aficamten on Echocardiographic Cardiac Structure and Function in Symptomatic Obstructive Hypertrophic Cardiomyopathy. JACC. 2024.
 Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

SEQUOIA-HCM: Secondary & Exploratory Endpoints



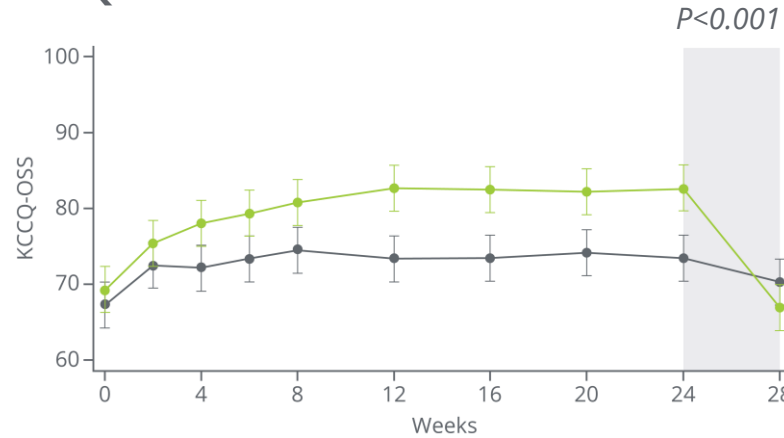
Significant improvement in patient symptom burden and quality of life

≥1 NYHA FC Improvement¹



■ Aficamten
● Placebo
■ Washout

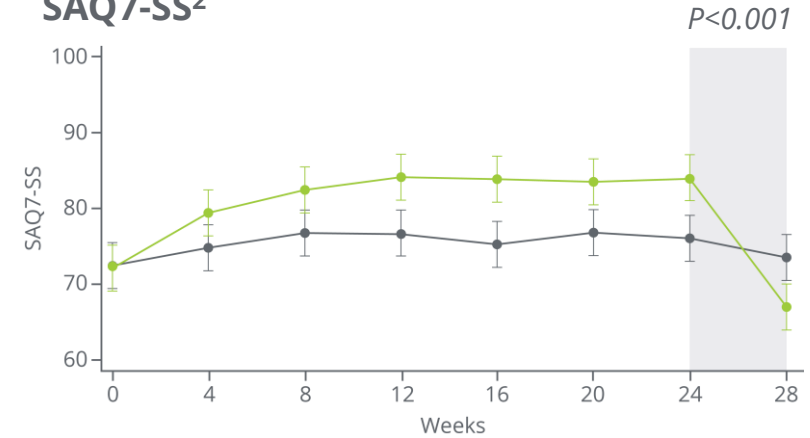
KCCQ-OSS²



Mean difference between *aficamten* & placebo = 7.9 points

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

SAQ7-SS²



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.

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)	<i>Aficamten</i> (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%.



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.

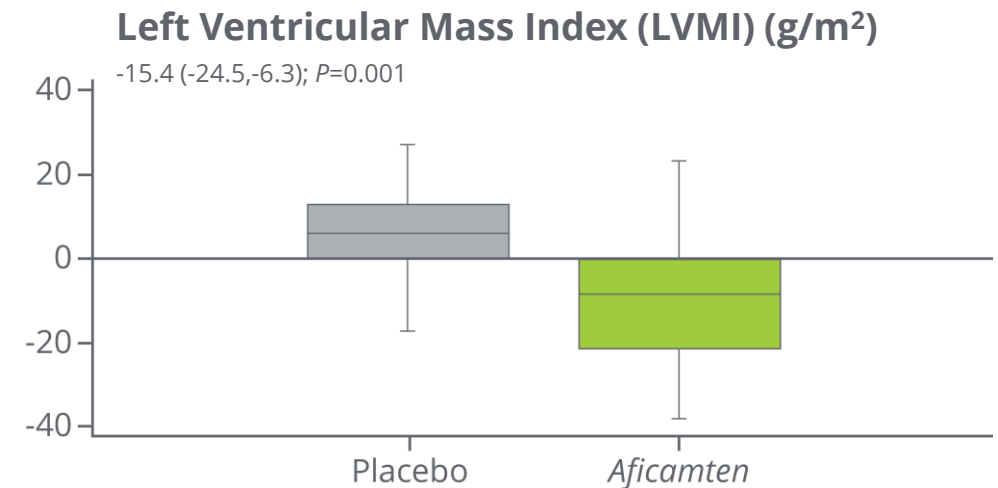
SEQUOIA-HCM: CMR Sub-Study



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.

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 <i>aficamten</i> -treated pool	Placebo-controlled pool ^b	
	<i>Aficamten</i>	<i>Aficamten</i>	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.

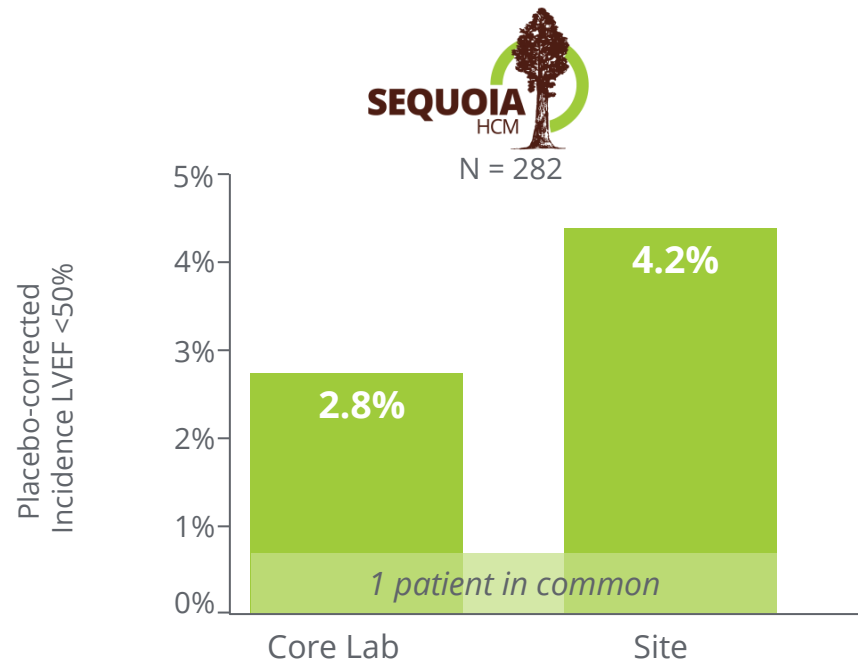
*Median exposure: 6-months, range of exposure: 0-32 months

Integrated Safety Analysis to reflect real world clinical application.

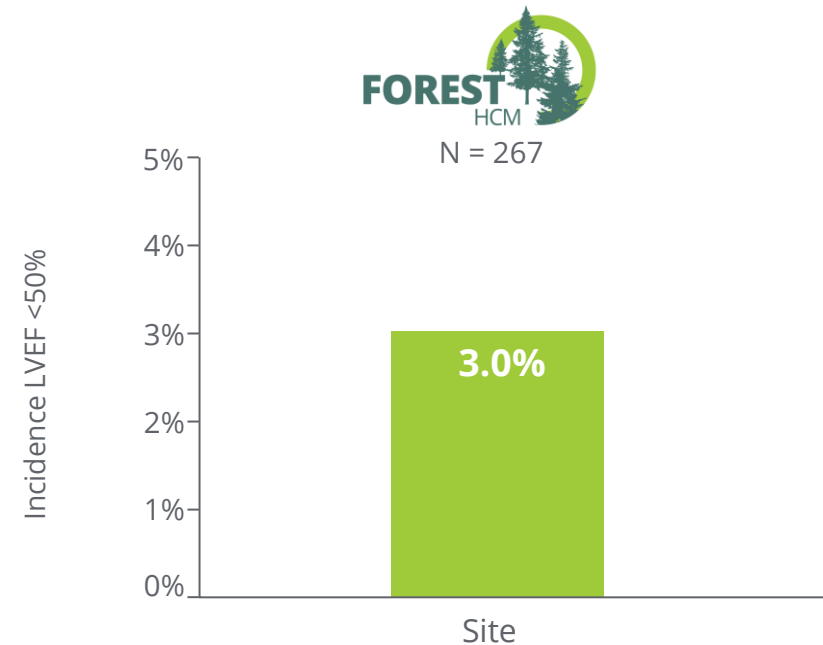
Imasri A. Aficamten in Patients with Obstructive Hypertrophic Cardiomyopathy: An Integrated Safety Analysis. ESC 2024. Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

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



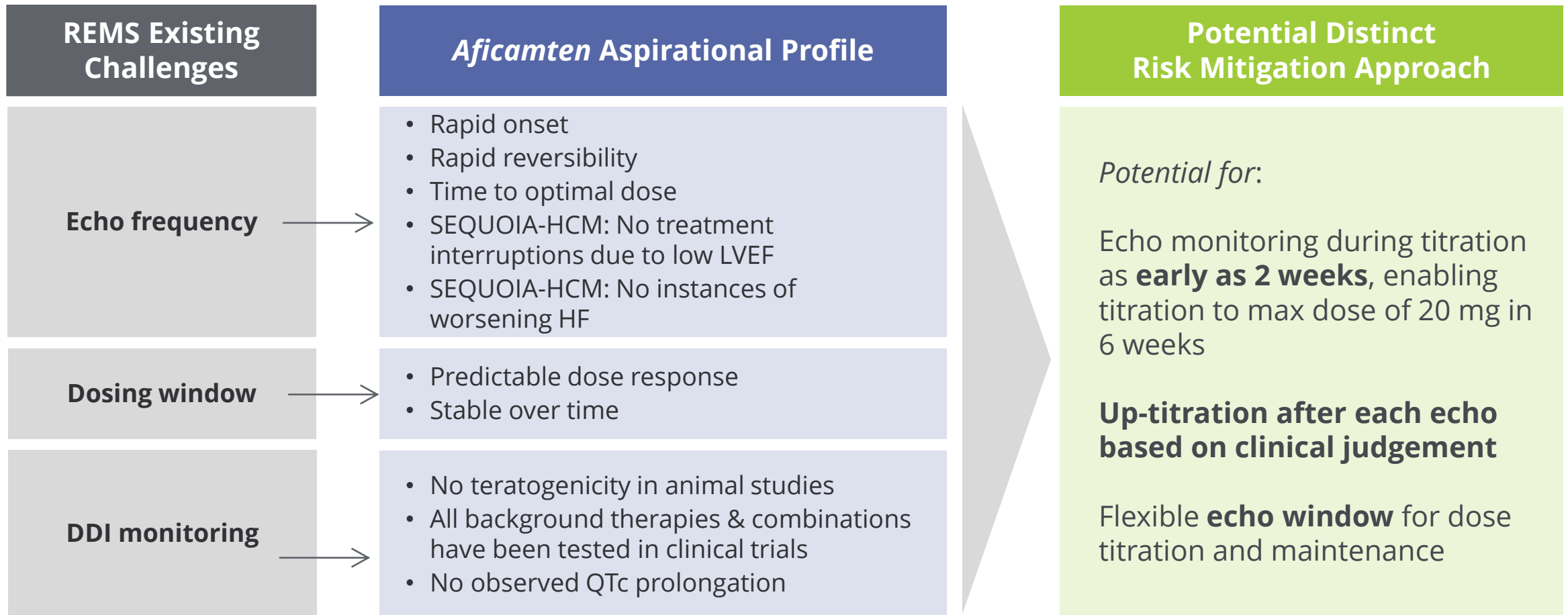
- ✓ No treatment interruptions
- ✓ No heart failure events
- ✓ All reversible
- ✓ Great majority of patients on highest doses



- ✓ 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.

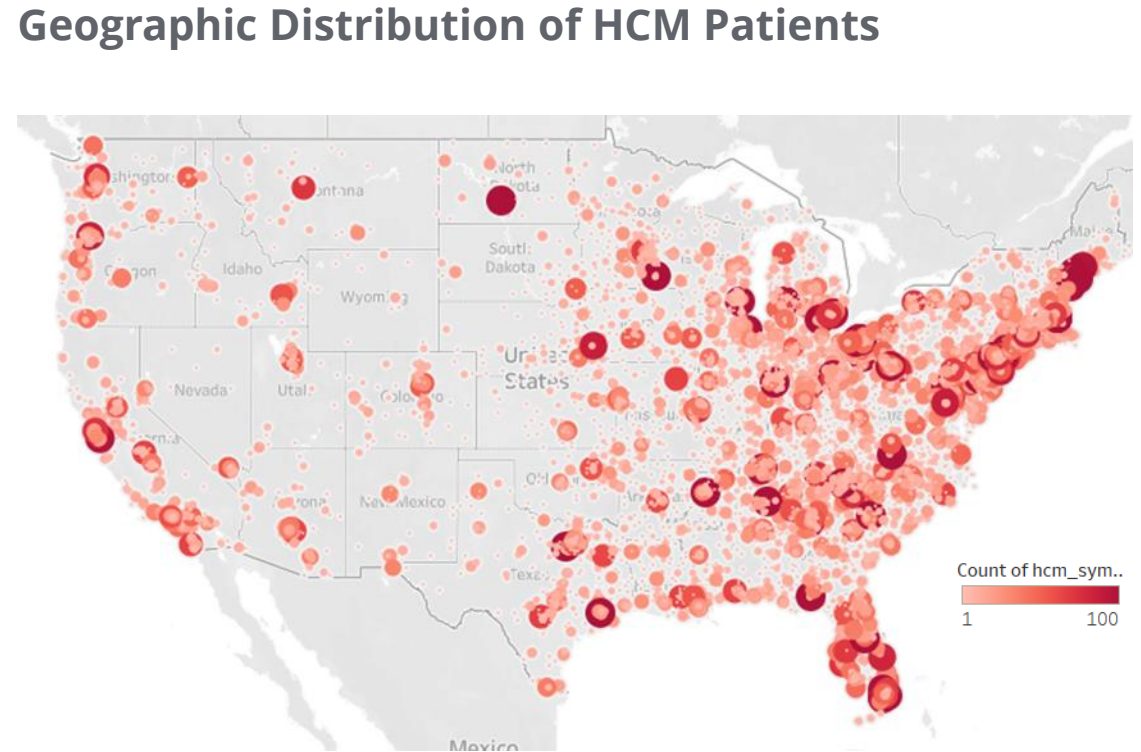
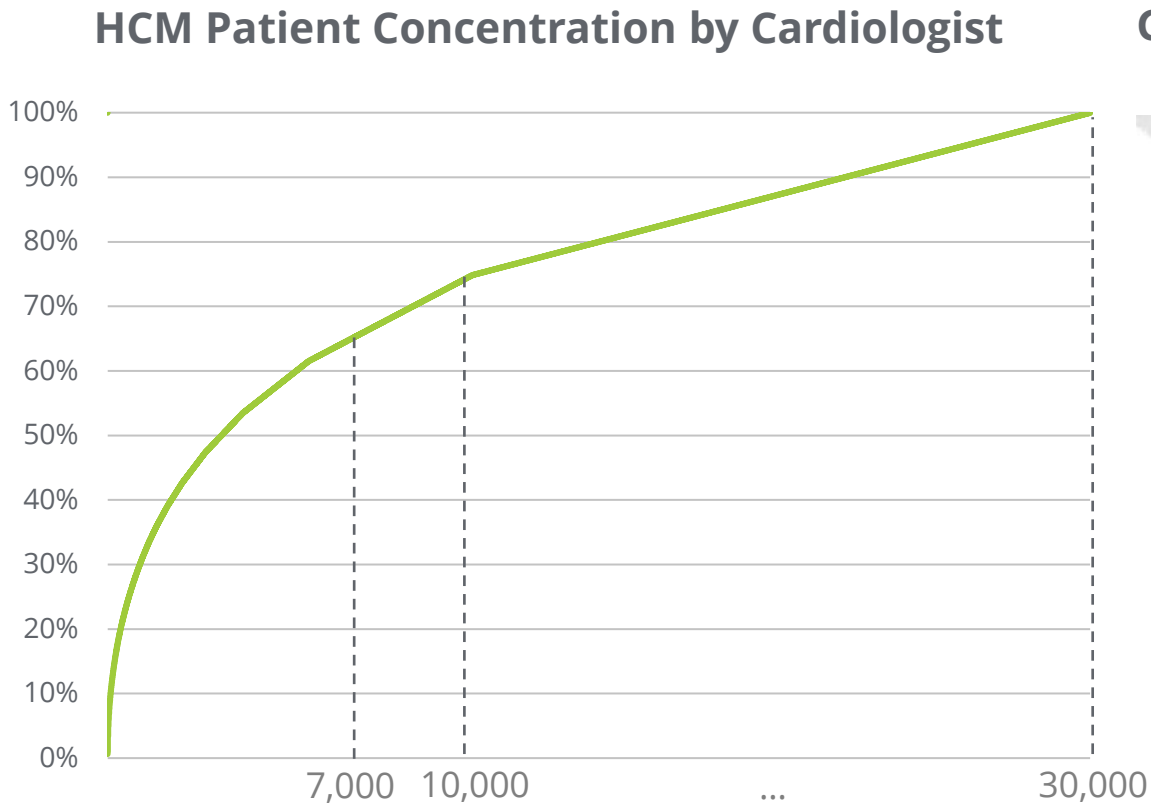
Aspirational Profile of *Aficamten* & Results from SEQUOIA-HCM Inform Potential Distinct Risk Mitigation



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

Cardiologists Located in Concentrated Geographic Clusters Across the US

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

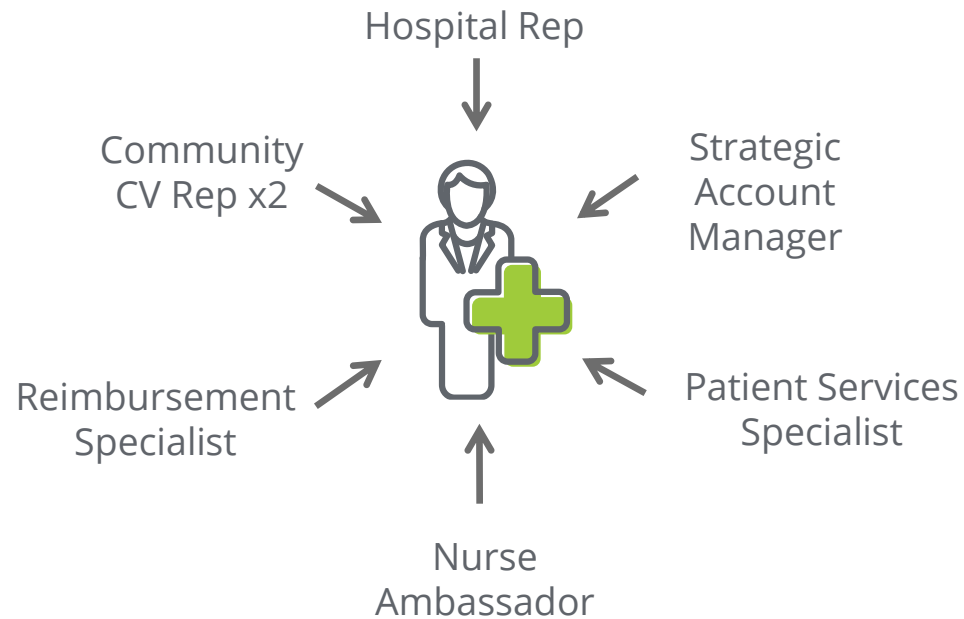


Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients
Source: Symphony PTD (Patient Transaction Data); mapping of HCPs to HCOs using Definitive Healthcare Data 2023 and 7/2023 mapping; Patient volume by dominant Cardiologist Location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

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

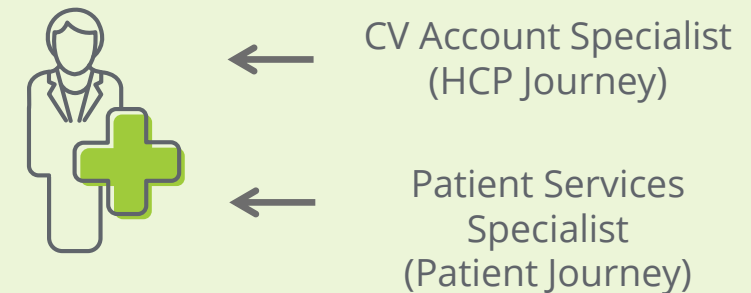
Traditional Models

Several functions with very focused roles
Overwhelmed customers, "It's too much"

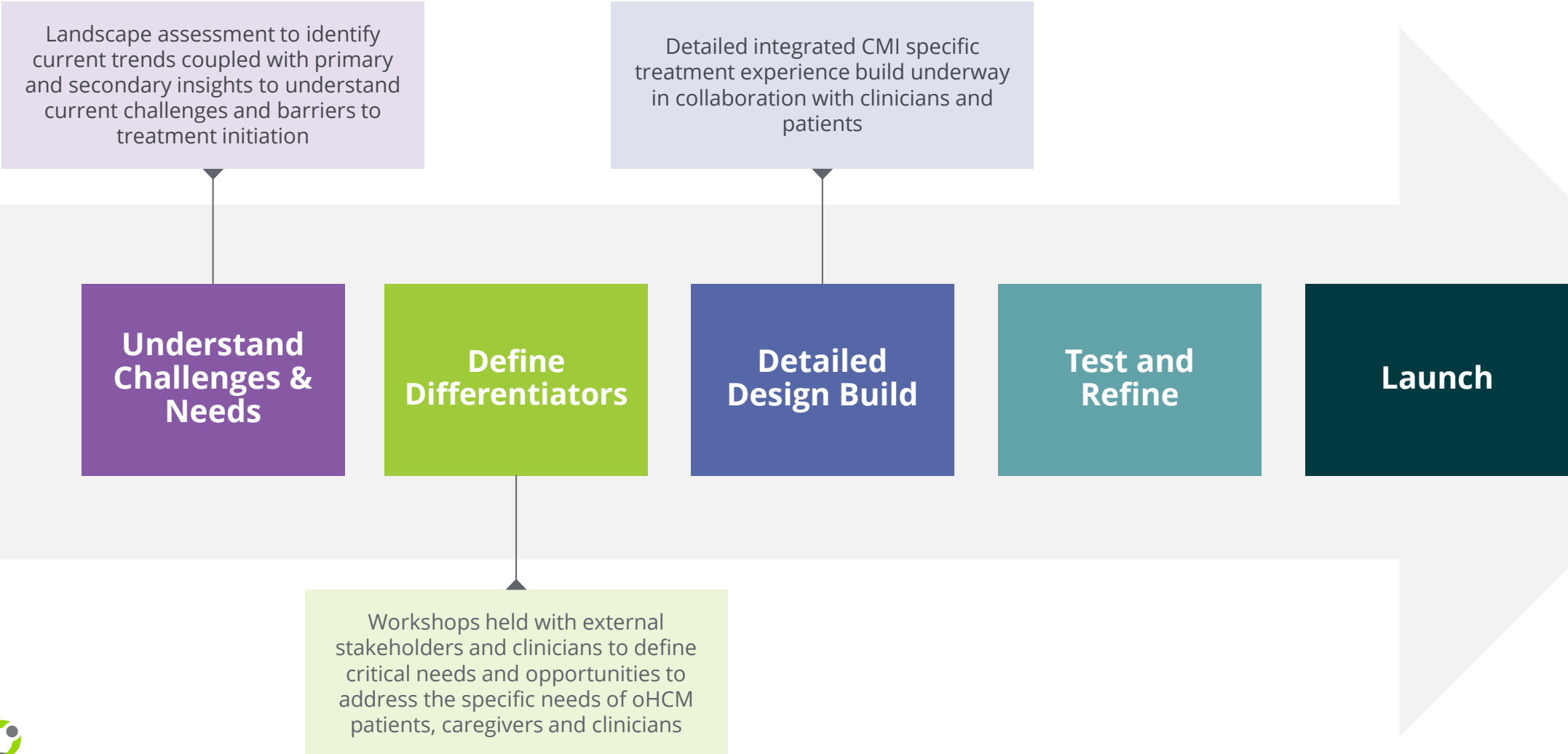


Our Design Principles

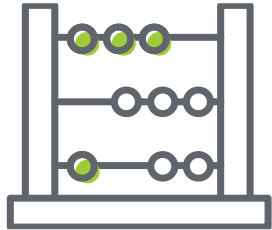
Simple model creating quality experience
Hire team with deep experience in specialty



Building a Bespoke Treatment Experience



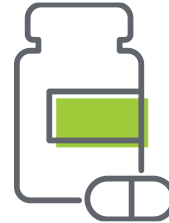
Strategy in Place to Support Market Access at Launch



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

Advancing EU Launch Readiness Activities

Key Hires in Zug & Munich



Highly experienced hires in Zug, Switzerland in Regulatory, Medical Affairs, Commercial, Market Access



Highly experienced hires in Munich, Germany including General Manager, Medical Director



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



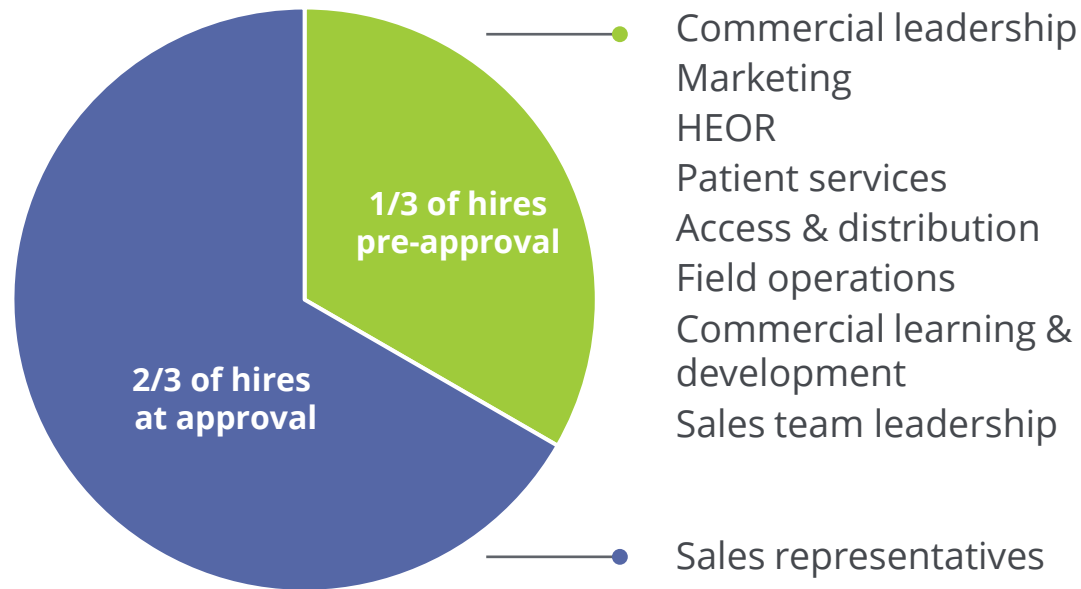
Start implementing all needed processes to support German launch:

- Market understanding (prescribers concentration curves, patient journey...)
- HTA Dossier writing for P&R process

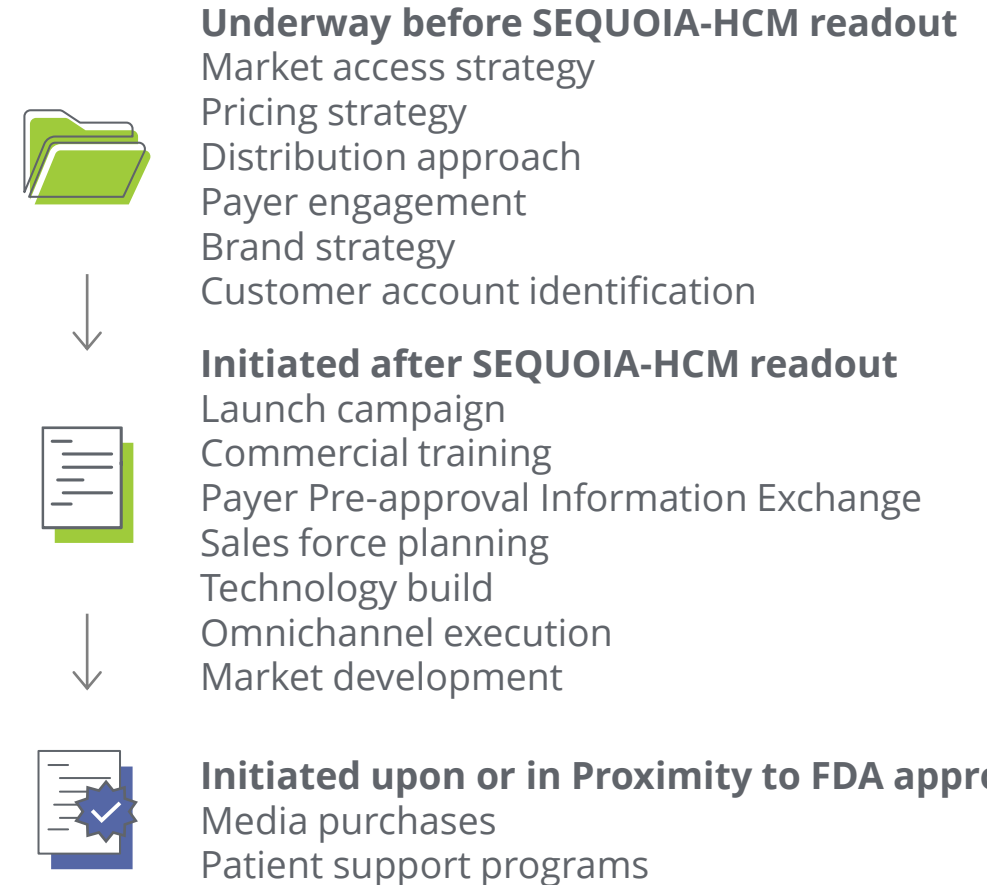
Gated Build of Commercial Infrastructure

Sales representative hiring to occur in proximity to approval

2/3 of hiring to occur at-approval

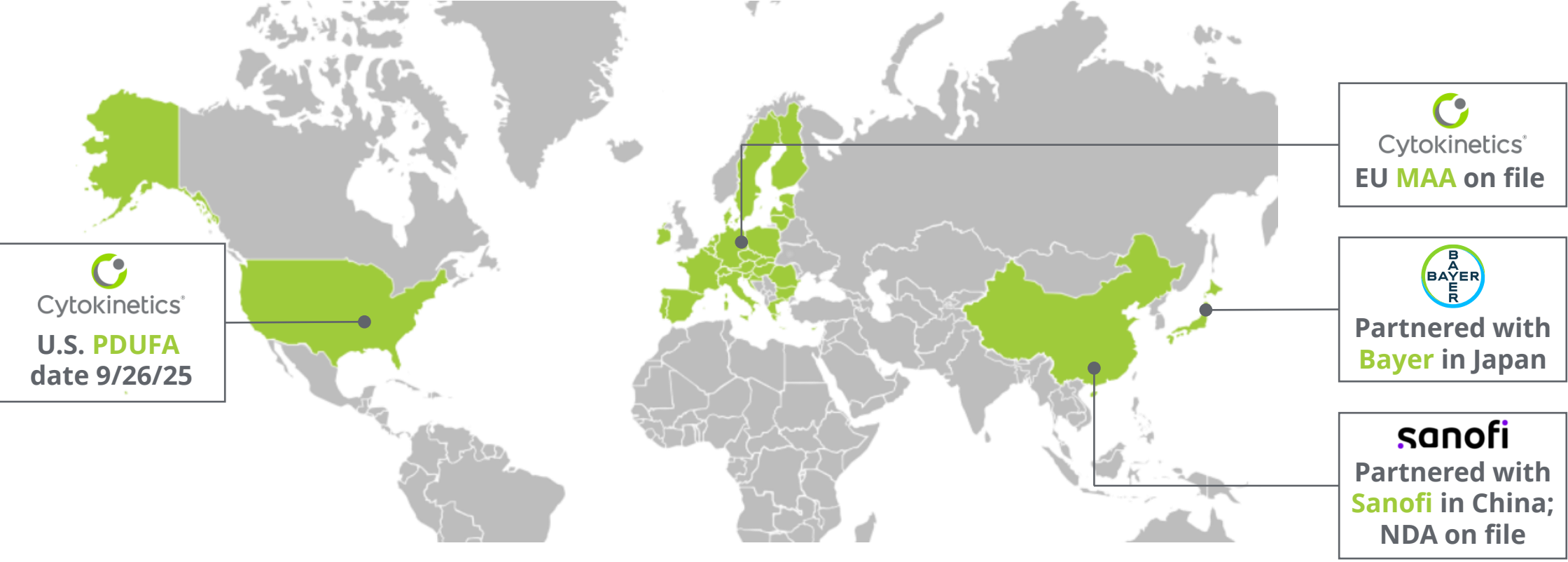


Activities initiated upon key de-risking events



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

Expected Global Presence of *Aficamten* in Major Markets



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 of *aficamten* as monotherapy vs. metoprolol in oHCM

Enrollment complete; data expected 1H 2025



Pivotal Phase 3 clinical trial in nHCM

Expect to complete enrollment in 2H 2025



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

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Omecamtiv Mecarbil

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. Buring-Sorensen, M. Böhm, D. Bondarman, 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 (32.0%) 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; IsradrCT 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@va.gov.

*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.

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DOI: 10.1056/NEJMoa2022797
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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

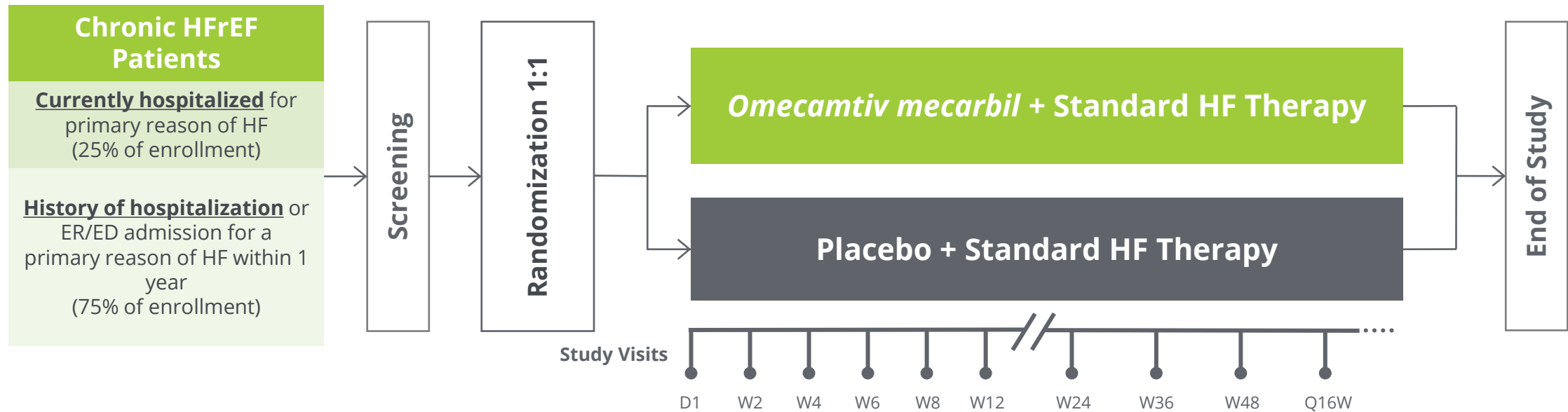
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

GALACTIC-HF: Clinical Trial Overview

Phase 3 clinical trial

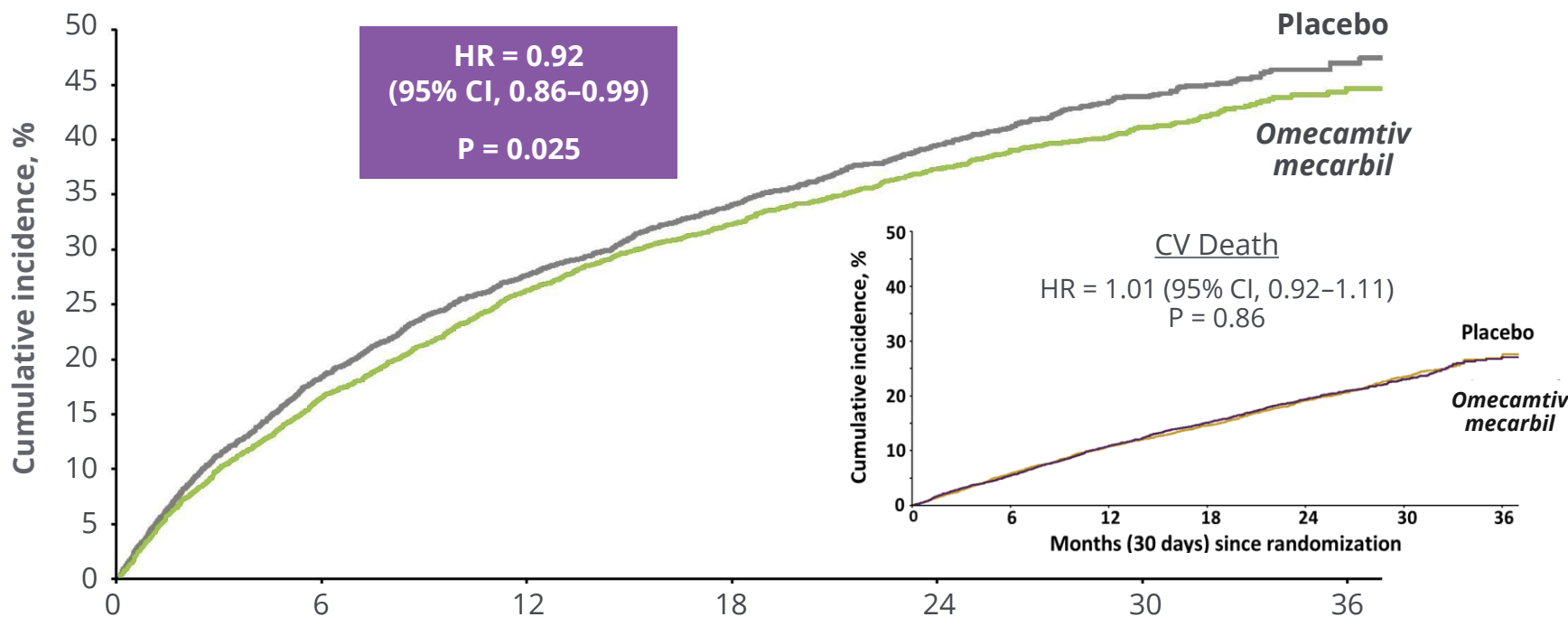


Event-driven clinical trial; 8,256 patients randomized in 35 countries at 944 clinical trial sites



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Primary Composite Endpoint



	Months (30 days) since randomization						
Patients at risk, n	0	6	12	18	24	30	36
Placebo	4112	3310	2889	2102	1349	647	141
OM	4120	3391	2953	2158	1430	700	164

Time to first HF event or CV death

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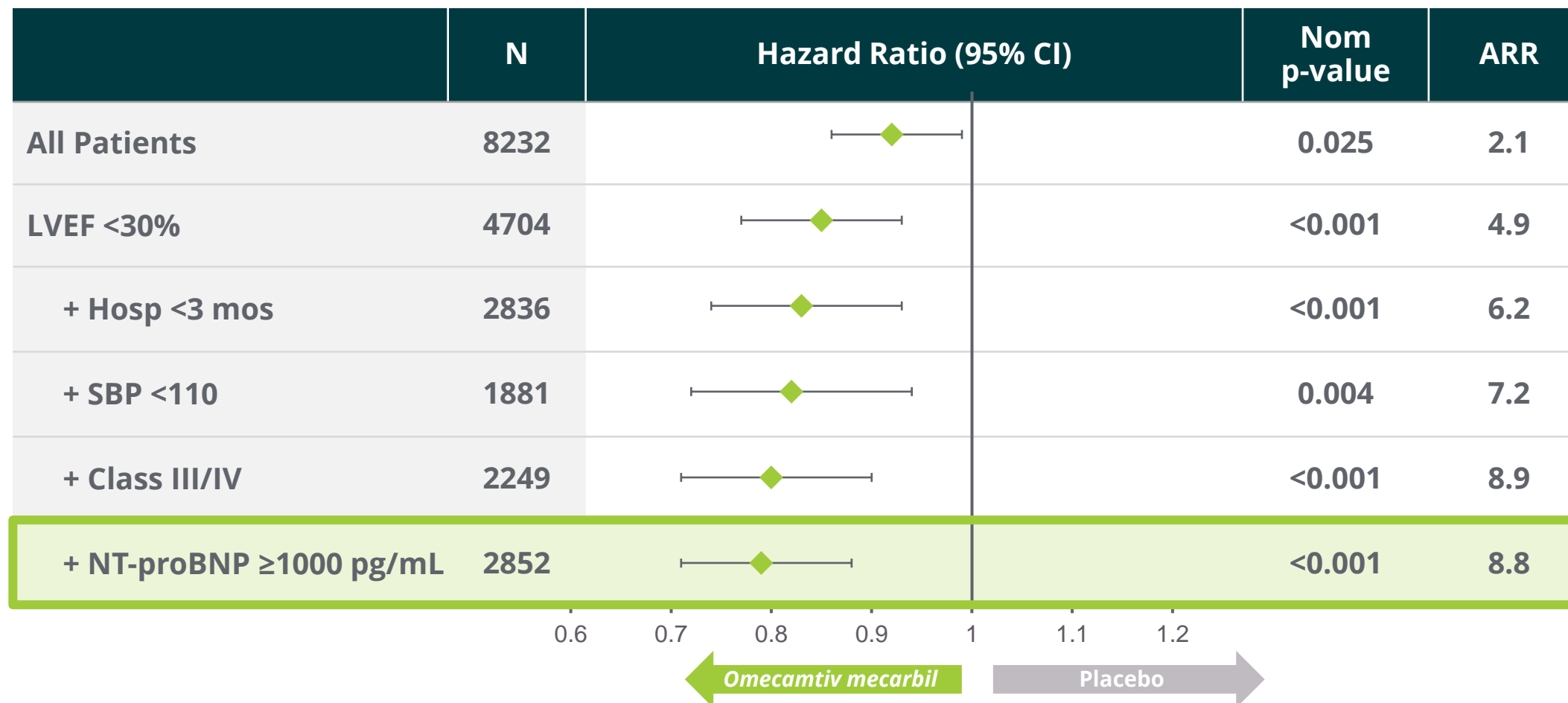
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We randomly assigned 8256 patients (inpatients and outpatients) with symptomatic chronic heart failure and an ejection fraction of 35% or less to receive omecamtiv mecarbil (using pharmacokinetic-guided doses of 25 mg, 37.5 mg, or 50 mg twice daily) 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.

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N Engl J Med 2021;384:102-14.
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Large Treatment Effect in Easily Defined HF Population



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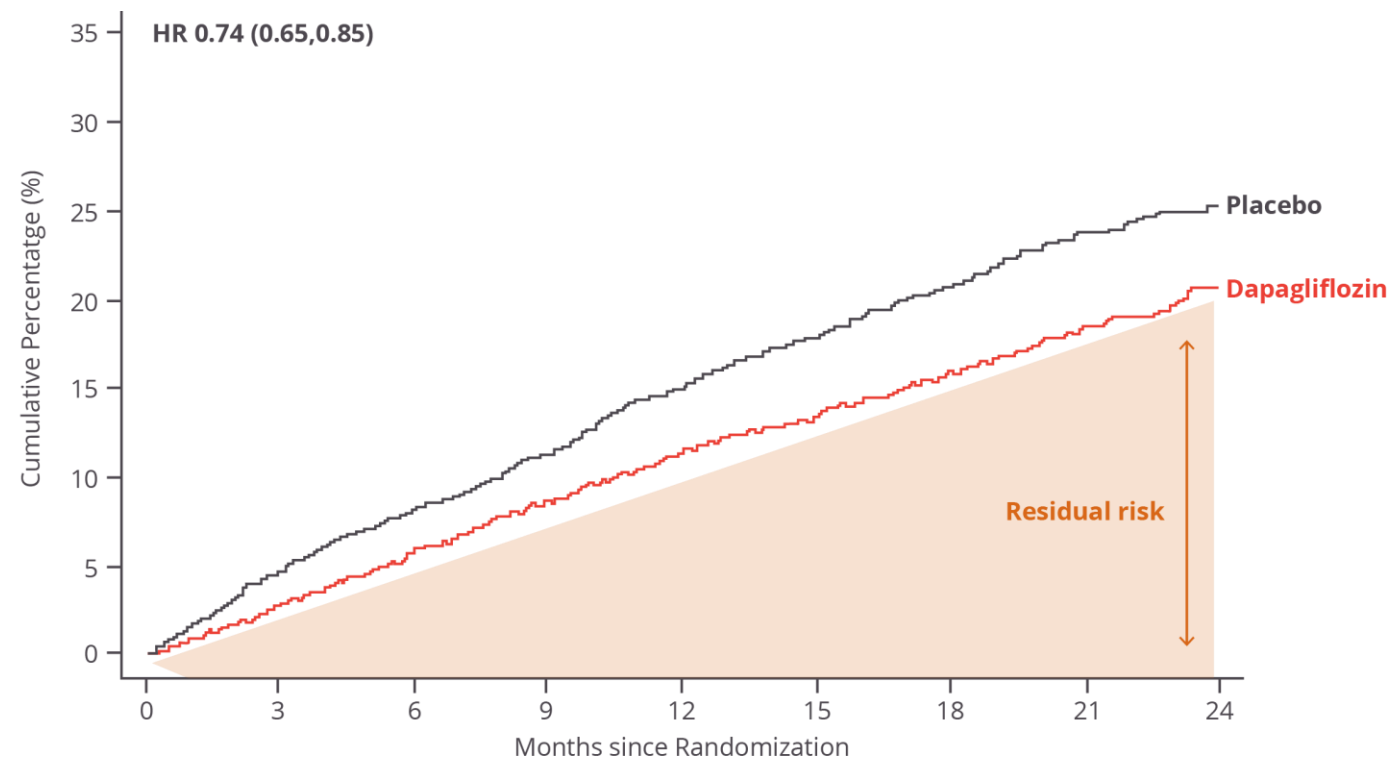
Residual Risk is High Despite Best Therapy

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%**

DAPA-HF Trial Residual Risk



Number at Risk

Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

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

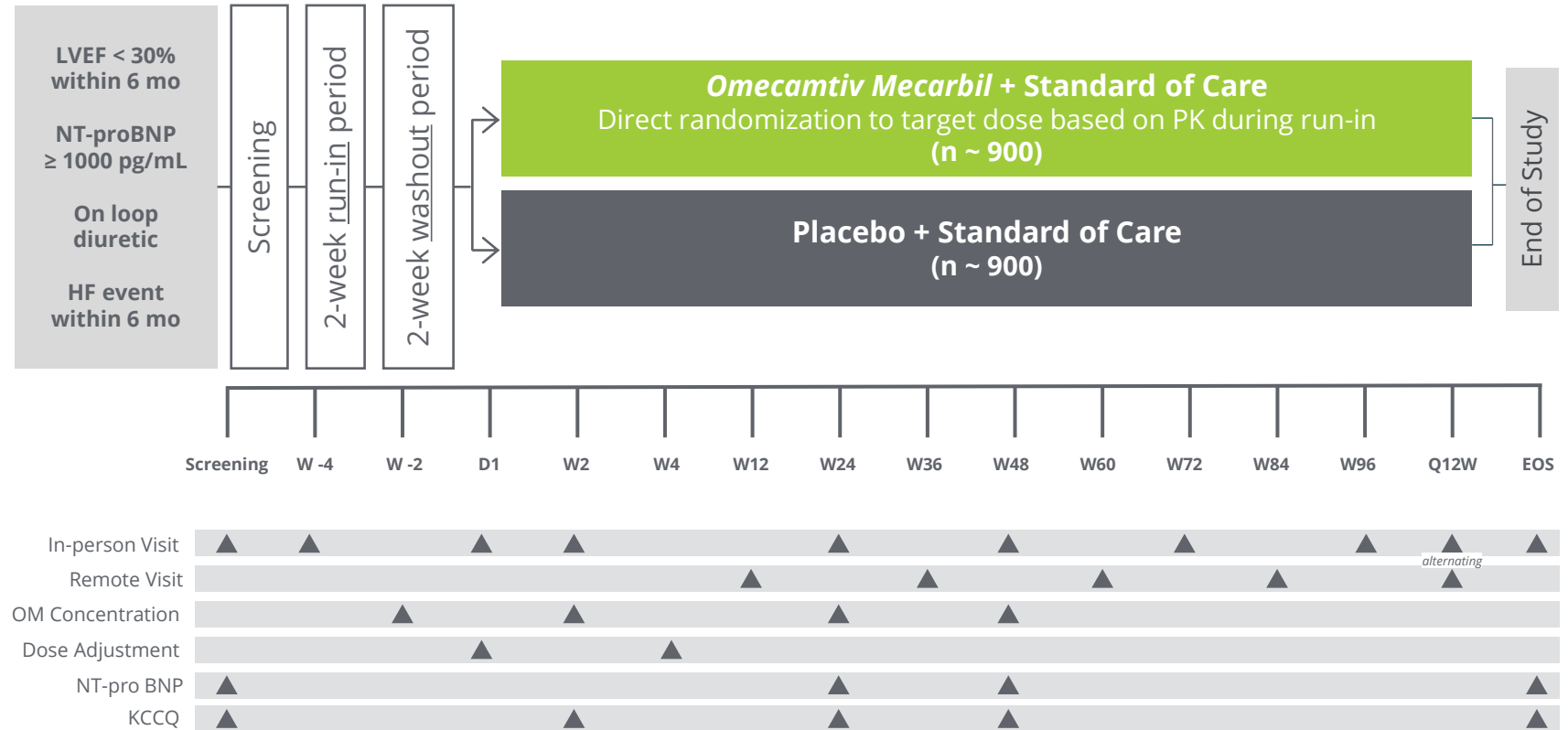
Phase 3 Confirmatory Clinical Trial Design

Currently enrolling



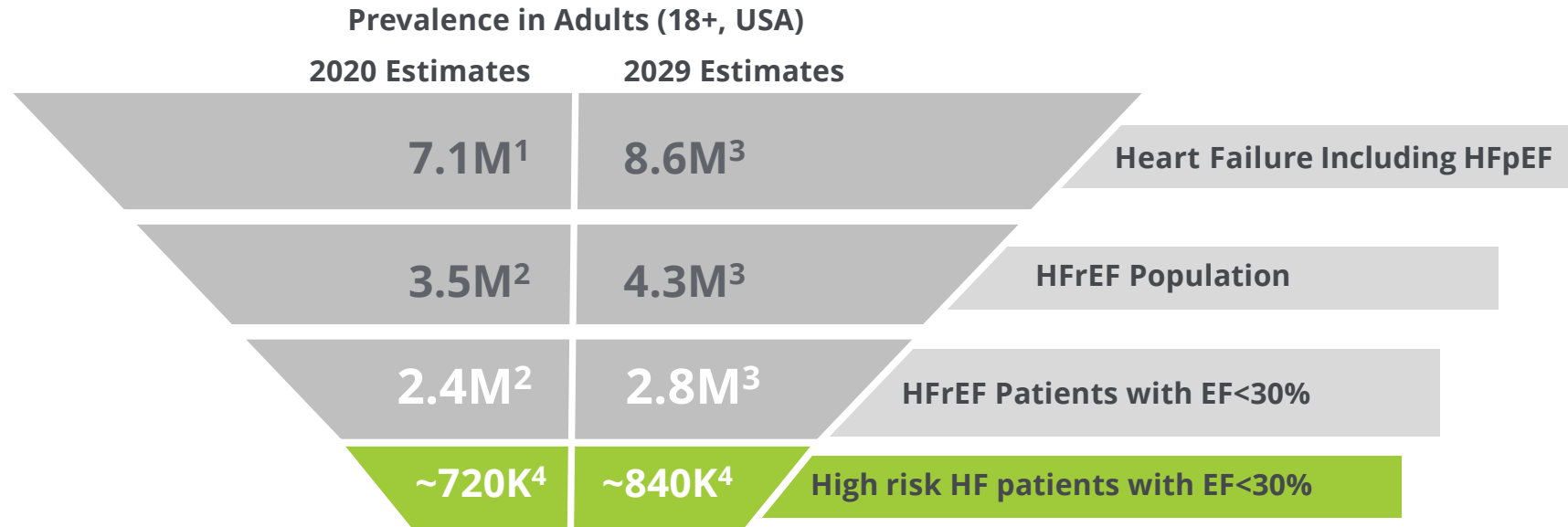
COMET-HF: Confirmation of *Omecamtiv Mecarbil* Efficacy Trial in Heart Failure

- 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



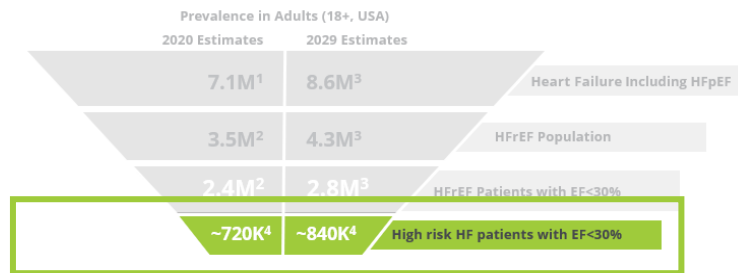
LVEF < 30%

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.

Higher Event Rate & Costs in Patients with Severely Reduced EF



Accounts for **~60%** of HFrEF hospitalizations⁵



35% of patients with severely reduced EF re-hospitalized within 1 year⁶



\$15,493 per HF re-hospitalization⁷



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.

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

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 Margin¹	+20% incremental improvement in brand margin*
	Cost Savings¹	+70% cost avoidance driven by portfolio synergies*

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

Heart Failure with Preserved Ejection Fraction (HFpEF)

Despite broad use of standard treatments & advances in care, the prognosis for patients with HF is poor¹



~75%

HFpEF patients will die within five years of initial hospitalization²



~84%

HFpEF patients will be rehospitalized²



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 2018⁶



Lifetime healthcare costs for HFpEF are ~ \$126,819 per patient⁵, 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, Hsieh E, Ibrahim NE, Jones LM, Khan SS, Khazanie P, Koelling T, Krumholz HM, Khush KK, Lee C, Morris AA, Page RL 2nd, Pandey A, Piano MR, Stehlik J, Stevenson LW, Teerlink JR, Vaduganathan M, Ziaeian B; Writing Committee Members. Heart Failure Epidemiology and Outcomes Statistics: A Report of the Heart Failure Society of America. *J Card Fail*. 2023 Oct;29(10):1412-1451. doi: 10.1016/j.cardfail.2023.07.006. Epub 2023 Sep 26. PMID: 37797885; PMCID: PMC10864030.

3. Dunlay SM, Roger VL, Weston SA, Jiang R, Redfield MM. Longitudinal changes in ejection fraction in heart failure patients with preserved and reduced ejection fraction. *Circ Heart Fail*. 2012 Nov;5(6):720-6. doi: 10.1161/CIRCHEARTFAILURE.111.966366. Epub 2012 Aug 30. PMID: 22936826; PMCID: PMC3661289.

4. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240-e327.

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.

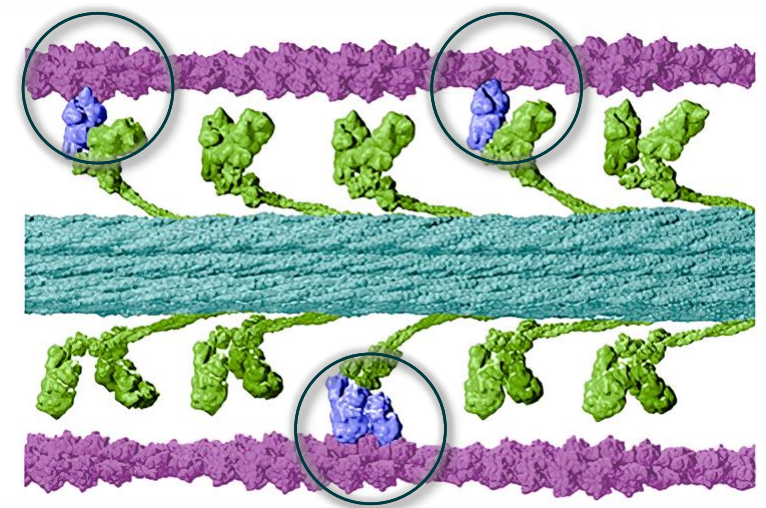
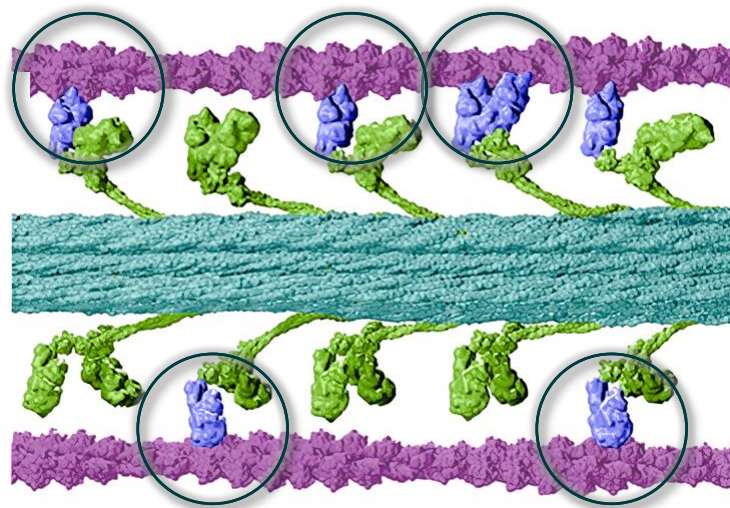
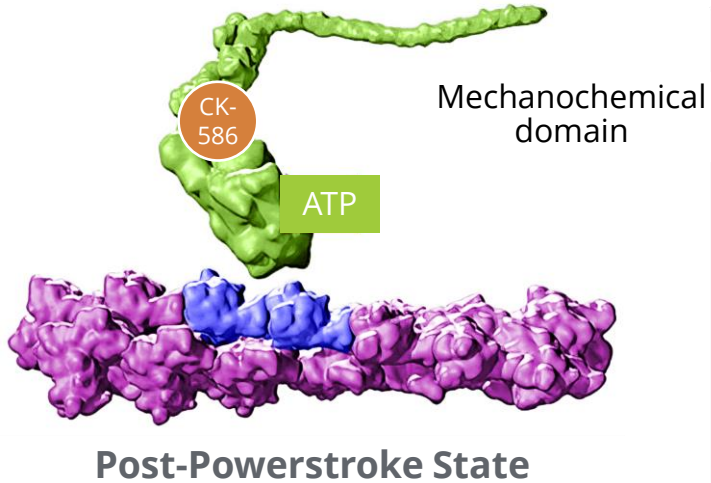
7. Lam CSP, Wood R, Vaduganathan M et al (2021) Contemporary economic burden in a real-world heart failure population with Commercial and Medicare supplemental plans. *Clin Cardiol* 44(5):646-655.

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

“Fewer hands pulling on the rope”

Before CK-586

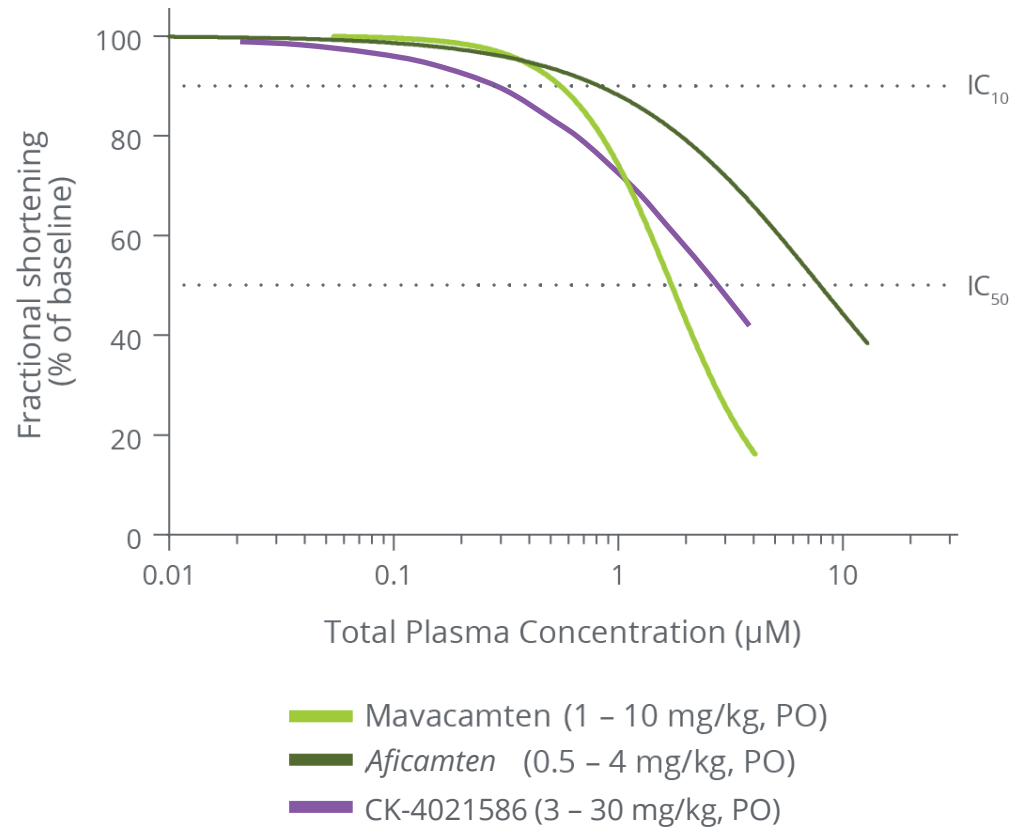
After CK-586



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

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

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



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

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

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

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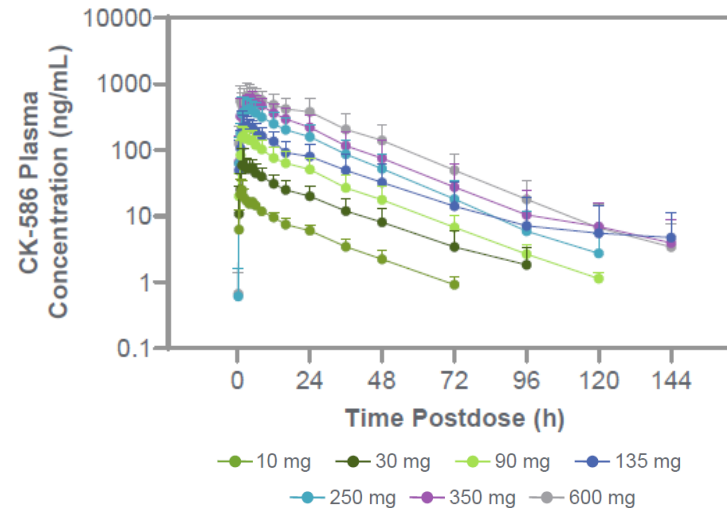
Phase 1 Data Support Advancement to Phase 2 Clinical Trial

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

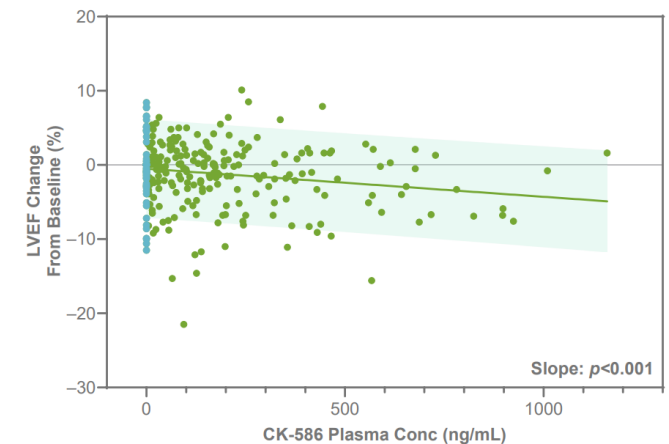
- **Less than 24-hour** half-life
- **Shallow and predictable** PK/PD relationship based on LVEF and LVFS
- **Well-tolerated** across all cohorts
- **No serious adverse events** were observed
- **Stopping criteria were not met**

Plasma Concentration

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

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Phase 2 Study Schema

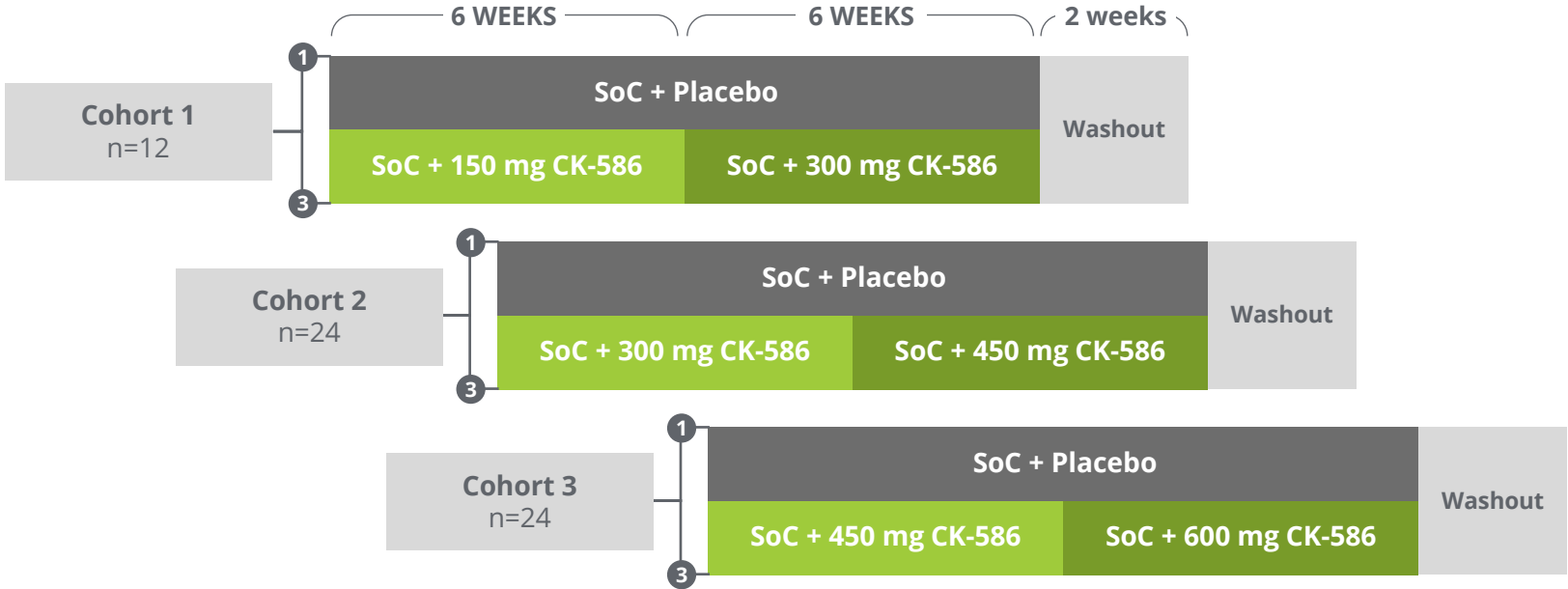
Currently enrolling



AMBER-HFpEF: Assessment of CK-586 in a Multi-Center, Blinded Evaluation of Safety and Tolerability Results in HFpEF

Enrolling HFpEF patients with:

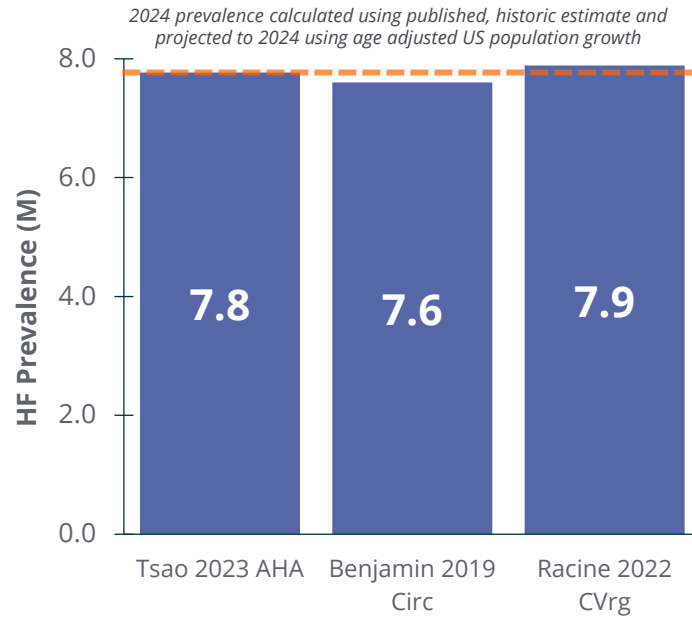
- LVEF \geq 60%
- Structural abnormality
- BMI < 40
- NYHA FC II or III
- NT-proBNP \geq 300 (or \geq 900 in AF)



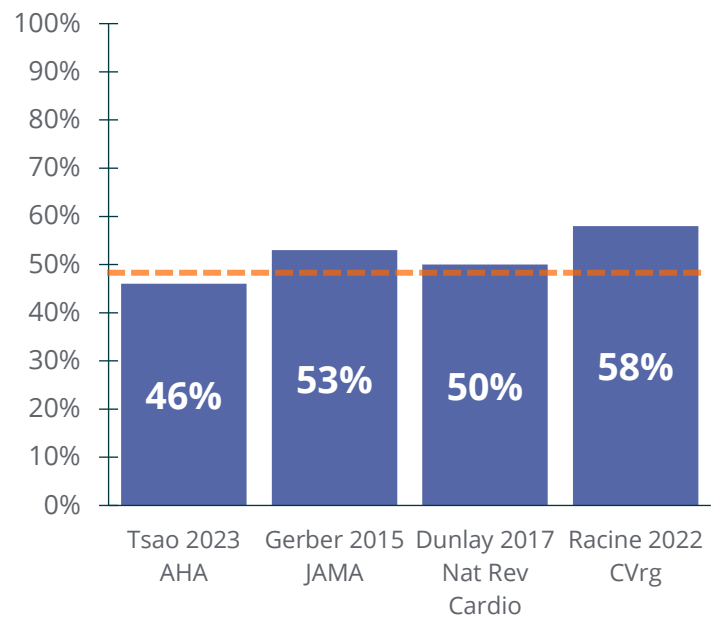
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CK-586: Focusing on Patients with HFpEF and EF ≥ 60

7.9M
Heart Failure Prevalence in 2024, US



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%

~10% of HF patients have EF ≥ 65
Additional ~10% of HF patients have EF between 60% and 65%

Study	% EF ≥ 65	% EF 60-65
Hsu 2017	10%	20%
Dunlay 2012	11%	22%
Kerwagen 2023	8%	16%
Delepaul 2017	14%	28%
TriNetX 2024	13%	26%

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. et 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/ehfj.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.

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

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

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Financials & Milestones

Strong Financial Position

Strengthened balance sheet & access to capital to execute launch & advance R&D pipeline

~\$1.3B in cash, cash equivalents and investments as of September 30, 2024

Further access to capital through term loans^[1] with Royalty Pharma (RP)

Eligible to draw up to \$175m 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 4: Cytokinetics is eligible to draw up to \$75m by April 3, 2025. The minimum draw for tranche 4 is \$50m.

Tranche 5: Cytokinetics, at its option, is eligible to draw up to \$100m by November 24, 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.

2024 Financial Guidance

	Current Guidance Issued on Aug. 8, 2024
GAAP Operating Expense ^[1]	\$555m to \$575m
Non-cash Expense ^[2] <u>Included</u> in GAAP Operating Expense	\$110m to \$105m
Non-GAAP Operating Expense ^[3]	\$445m to \$470m
Net Cash Utilization ^[4]	\$400m to \$420m

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.

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

^[2] Non-cash operating expense comprised of stock-based compensation and depreciation.

^[3] Non-GAAP operating expense comprised of R&D and G&A expenses but excludes non-cash operating expense.

^[4] Net cash utilization is a non-GAAP financial measure that we define as our ending 2023 cash, cash equivalents, and investments balance of \$655 million plus the net proceeds of \$707 million received from the sale of common stock (through the at-the-market facility, public offerings, and stock purchase agreement with Royalty Pharma) plus proceeds of \$200 million received from the structured financing agreement with Royalty Pharma announced on May 22, 2024 minus our projected ending 2024 cash, cash equivalents, and investments balance of between \$1,142 million and \$1,162 million.

Exclusive Licensing Collaboration with Bayer for *Aficamten* in Japan

Upfront payment, development & commercial milestone payments & tiered royalties

Collaboration leverages Bayer's regional capabilities & expertise in development & commercialization

Collaboration Financials:





- €50 million upfront payment
- Up to €90 million upon the achievement of milestones through commercial launch, €20 million of which are near-term payments
- Up to €490 million in commercial milestone payments upon the achievement by Bayer of certain sales milestones
- Tiered royalties ranging from the high teens to the low 30s on net sales of *aficamten* in Japan

Joint Development Program:

- Bayer will conduct a Phase 3 clinical trial in Japanese patients with oHCM
- Cytokinetics will expand ACACIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with nHCM, and CEDAR-HCM, the study of *aficamten* in a pediatric population, into Japan

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

Robust Pipeline, Upcoming Commercial Launch & Solid Financial Position

<p>Commercial</p>	 <p>U.S. PDUFA date of September 26, 2025 for <i>aficamten</i> U.S go-to-market strategies anchored in optimized market access & patient experience</p>		<p>China NDA and EU MAA on file European commercial readiness activities underway</p>			
<p>Pipeline</p>	<p><i>Aficamten</i> SEQUOIA-HCM: Positive Phase 3 results Ongoing clinical program with label-expanding opportunities including: MAPLE-HCM: Phase 3 mono. vs metoprolol ACACIA-HCM: Phase 3 nHCM CEDAR-HCM: Phase 2-3 pediatric oHCM FOREST-HCM: OLE in oHCM & nHCM</p>		<p><i>Omecamtiv mecarbil</i> Phase 3 confirmatory clinical trial COMET-HF ongoing</p>	<p>CK-586 Phase 2 AMBER-HFpEF clinical trial ongoing</p>	<p>CK-089 Phase 1 study ongoing in healthy participants</p>	 <p>Ongoing R&D Additional research in muscle biology, energetics & metabolism</p>
<p>Foundation</p>	 <p>R&D platform rooted in myosin modulation</p>	<p>Pioneers in muscle biology</p> 	<p>\$1.3B cash & investments* with further access to long-term capital, up to \$500M**</p>			

*As of September 30, 2024

** \$500M comprised of \$350M in term loan facilities with Royalty Pharma, and \$150M Royalty Pharma can, at its option, invest 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.*

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 1H 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.



Eric, diagnosed with HCM



thank you