



EMPOWERING

muscle

EMPOWERING

lives



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

Forward-Looking Statements

This presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the “Act”). Cytokinetics disclaims any intent or obligation to update these forward-looking statements and claims the protection of the Act’s Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements express or implied related Cytokinetics’ research and development and commercial readiness activities, including the initiation, conduct, design, enrollment, progress, continuation, completion, timing and results of clinical trials, projections regarding growing prevalence, low survival rates and market opportunity in heart failure, hypertrophic cardiomyopathy (HCM) or heart failure with preserved ejection fraction (HFpEF); projections regarding the size of the addressable patient population for *aficamten*, *omecamtiv mecarbil*, CK-136, CK-586 or any of our other drug candidates; Cytokinetics’ commercial readiness for *aficamten* or *omecamtiv mecarbil*; our ability to submit a new drug application for *aficamten* with FDA in the third quarter 2024 or a marketing authorization application with EMA in the fourth quarter 2024, the likelihood and/or timing of regulatory approval for our planned new drug application for *aficamten*, *omecamtiv mecarbil* or any future new drug application for any of our other drug candidates or the anticipated timing of any interactions with FDA, EMA or any other regulatory authorities in connection thereto; the timing of our commencement of a new phase 3 clinical trial of *omecamtiv mecarbil*, the timing of completion of MAPLE-HCM, ACACIA-HCM, CEDAR-HCM, or any of our other clinical trials, the efficacy or safety of *aficamten*, *omecamtiv mecarbil*, CK-136, CK-586 or any of our other drug candidates, our ability to fully enroll or to announce the results of any of our clinical trials by any particular date; the properties, potential benefits and commercial potential of *aficamten*, *omecamtiv mecarbil*, CK-136, 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.

VISION 2025

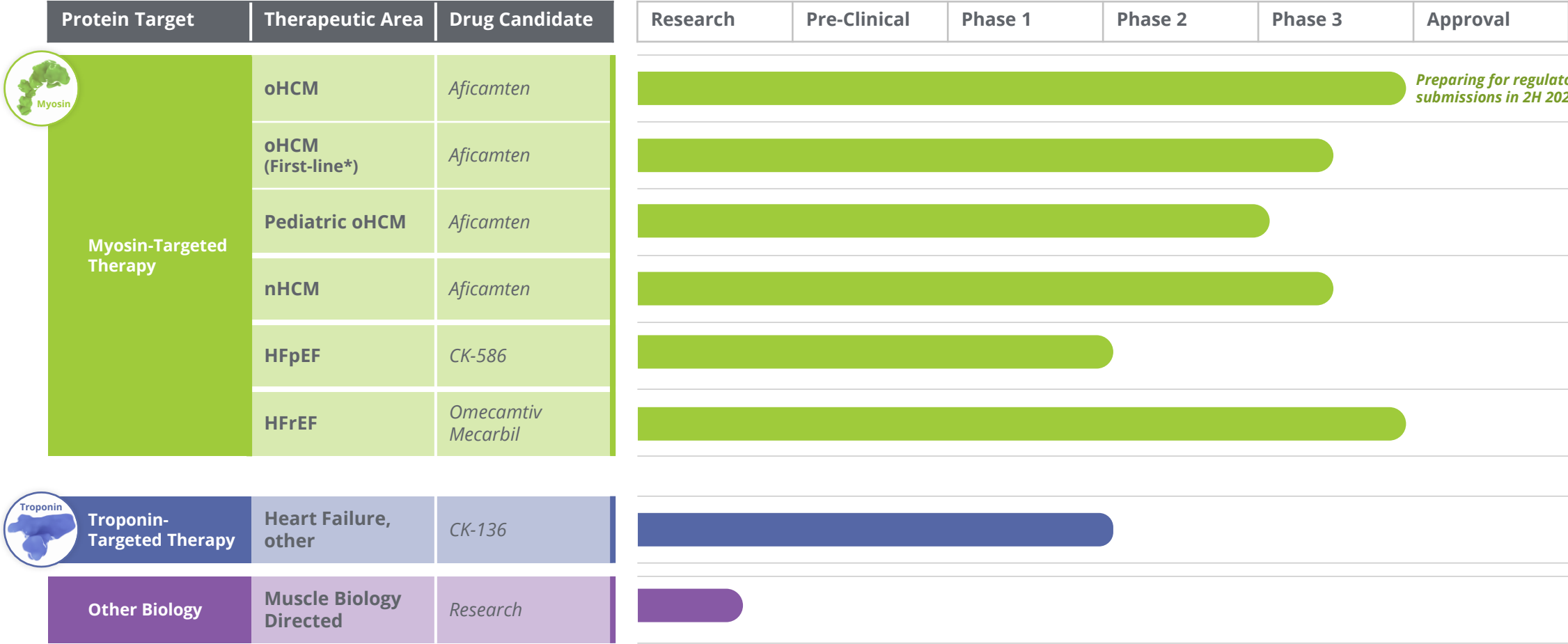
Leading with Science,
Delivering for Patients

As always, we will support disease advocacy groups elevating the patient voice and live by our values of integrity, fairness and compassion in all that we do.



A Commitment to Muscle-Directed Cardiac Medicines

Building a specialty cardiology franchise anchored by *aficamten*

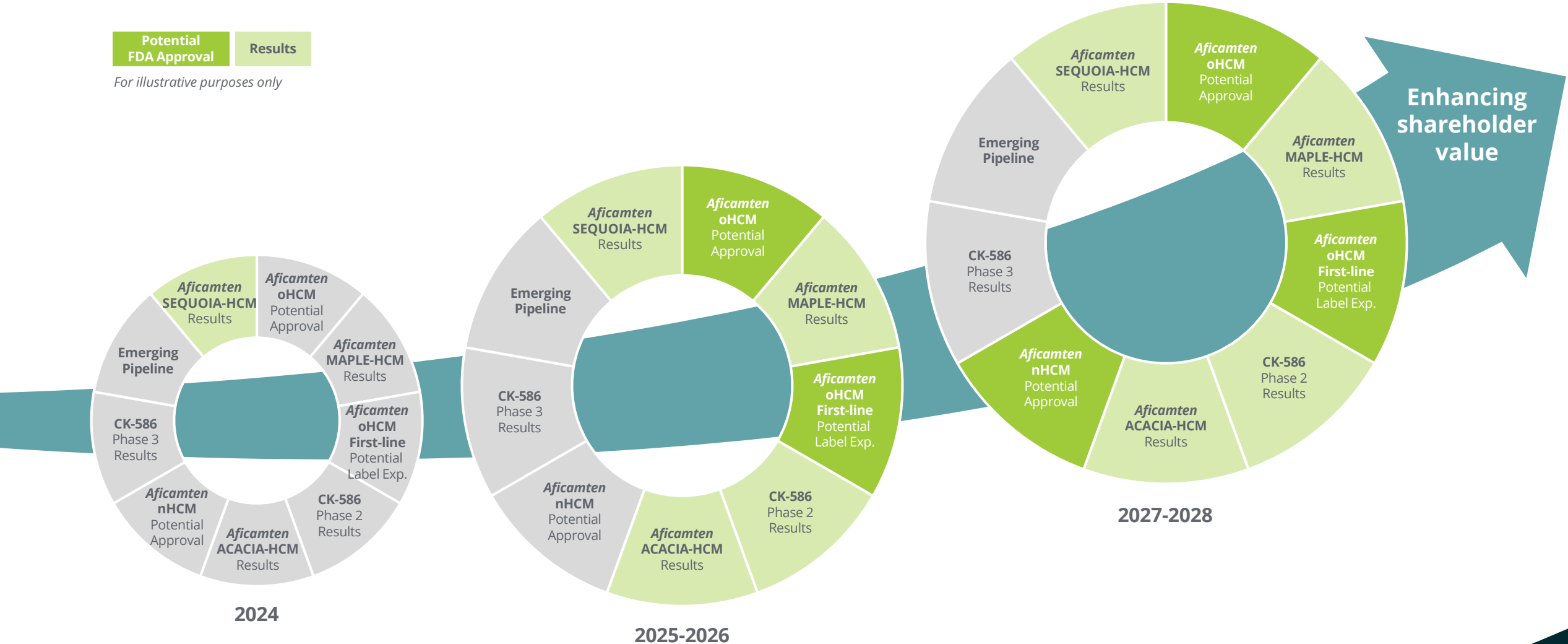


**Pending results from MAPLE-HCM, an ongoing Phase 3 clinical trial evaluating for the potential superiority of aficamten as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM.*
All drug candidates above are investigational products and are not approved as safe or effective for any indication.

Myosin Platform Fuels Multiple Milestones and Increased Value

Potential FDA Approval	Results
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For illustrative purposes only



Strong Financial Position

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

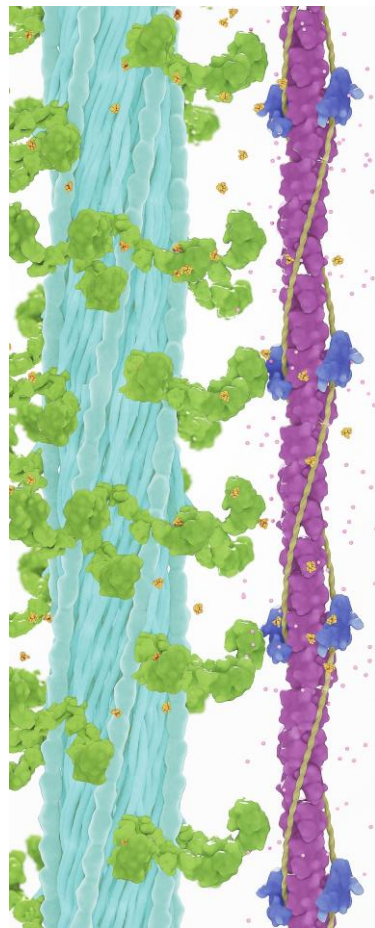
Q1 2024 cash and investments	~\$634M	>\$1B
Strengthened balance sheet with recent financings	>\$800M cash received through equity and structured financing transactions executed in May 2024	
Further access to capital through term loans with RP	Secured access to add'l \$175M* in term loan on top of \$175M** already secured with Royalty Pharma (RP); total available term loans \$350M	Add'l \$500M
Potential further funding through RP opt-in	RP, at its option, can invest up to \$150M in a Phase 3 trial of CK-586	

*Tranche 7 Loan: Cytokinetics, at its option, is eligible to draw up to \$175m during the 1-year period following the FDA approval of aficamten for oHCM provided that the NDA is accepted on or prior to December 31, 2025.

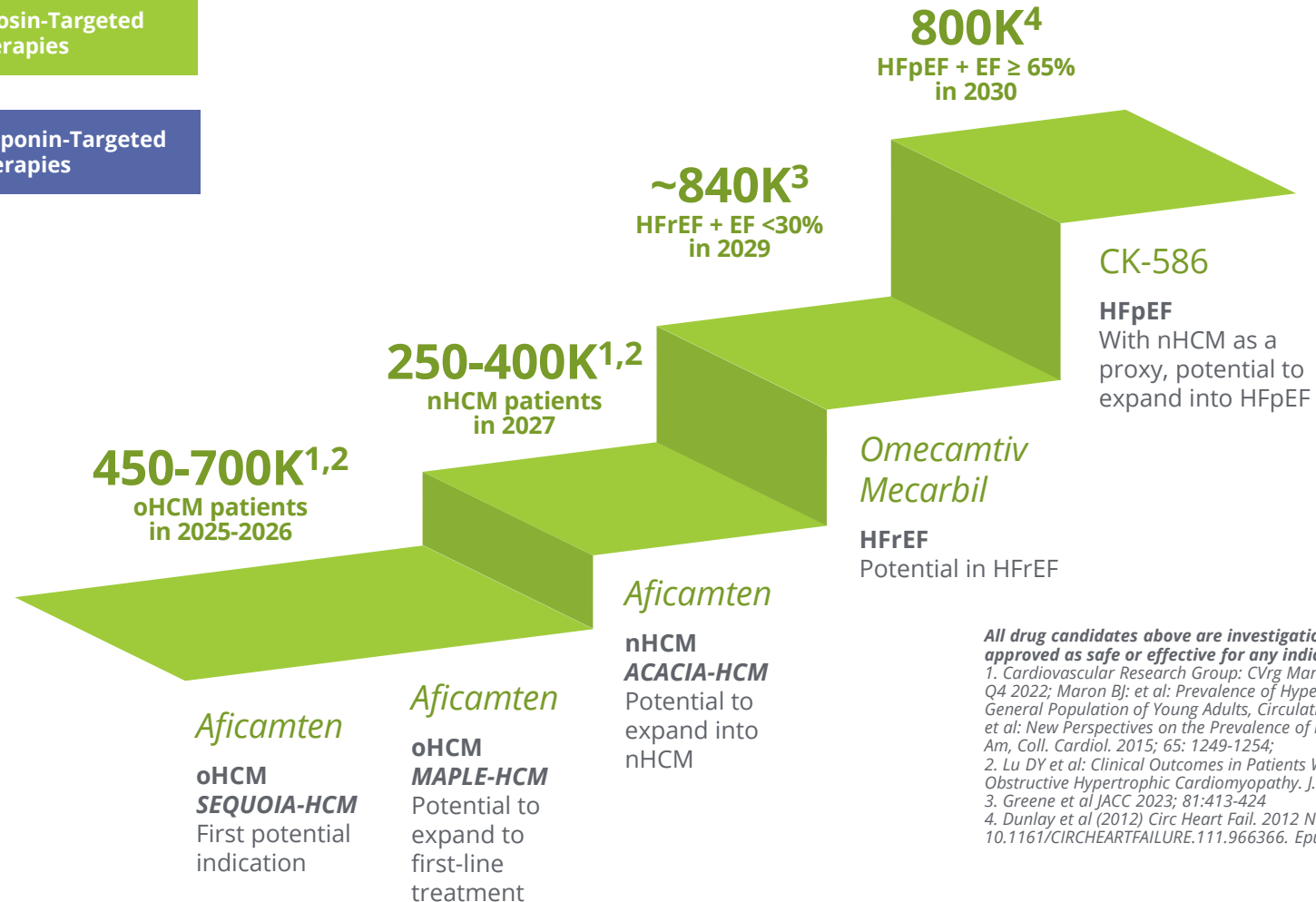
**Tranche 4 & 5 Loans: Cytokinetics is eligible to draw up to \$75m by April 30, 2025 from tranche 4. The minimum draw for tranche 4 is \$50m. Cytokinetics, at its option, is eligible to draw up to \$100m during the 1-year period following the acceptance of the NDA filing for aficamten provided that the NDA filing is accepted on or prior to March 31, 2025.

Building a Specialty Cardiology Franchise Anchored by *Aficamten*

Potential patient market for specialty cardiology franchise strategy



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.

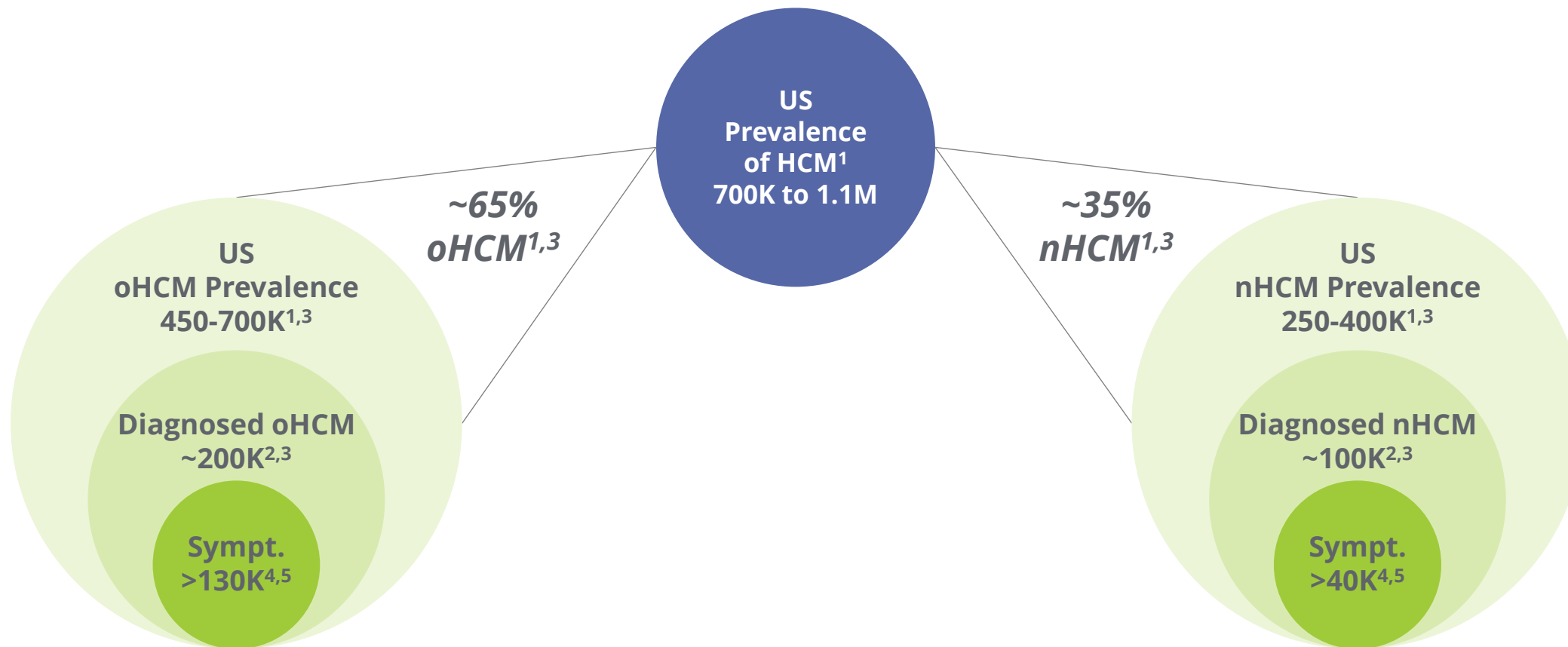
Cytokinetics Poised to Compete in the Specialty Cardiology Business

Potential for high return on investment

	Broad Cardiology	Specialty Cardiology
Example Therapies	Heart failure, cholesterol, blood thinner	HCM, TTR amyloidosis
Prescribers	<i>Broad:</i> Cardiologists, PCPs (50K+)	<i>Concentrated:</i> Subset of cardiologists (~10K)
ROI / Prescriber	Limited	High
Distribution	Retail	Limited, specialty distributor
Customer-Facing Reps	Entry level	Highly experienced
Support Services	<i>Standard:</i> Affordability / copay	<i>High-touch:</i> Financial, education, journey
Managed Care	Competitive/high rebates	Managed to label
Diagnosis	High awareness and diagnosis rate	Limited awareness with high % undiagnosed
HCP – Rep Interactions	Brief features/benefits	Comprehensive broad-based discussion

Aficamten

Opportunity for CMLs 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.

Aficamten: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor



**Rapid
onset**



**Rapid
reversibility**



**Speed to
optimal dose**



**Predictable
dose response**



**No
teratogenicity**



**No clinically
meaningful
P450 liabilities**

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

SEQUOIA-HCM: Phase 3 Trial



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

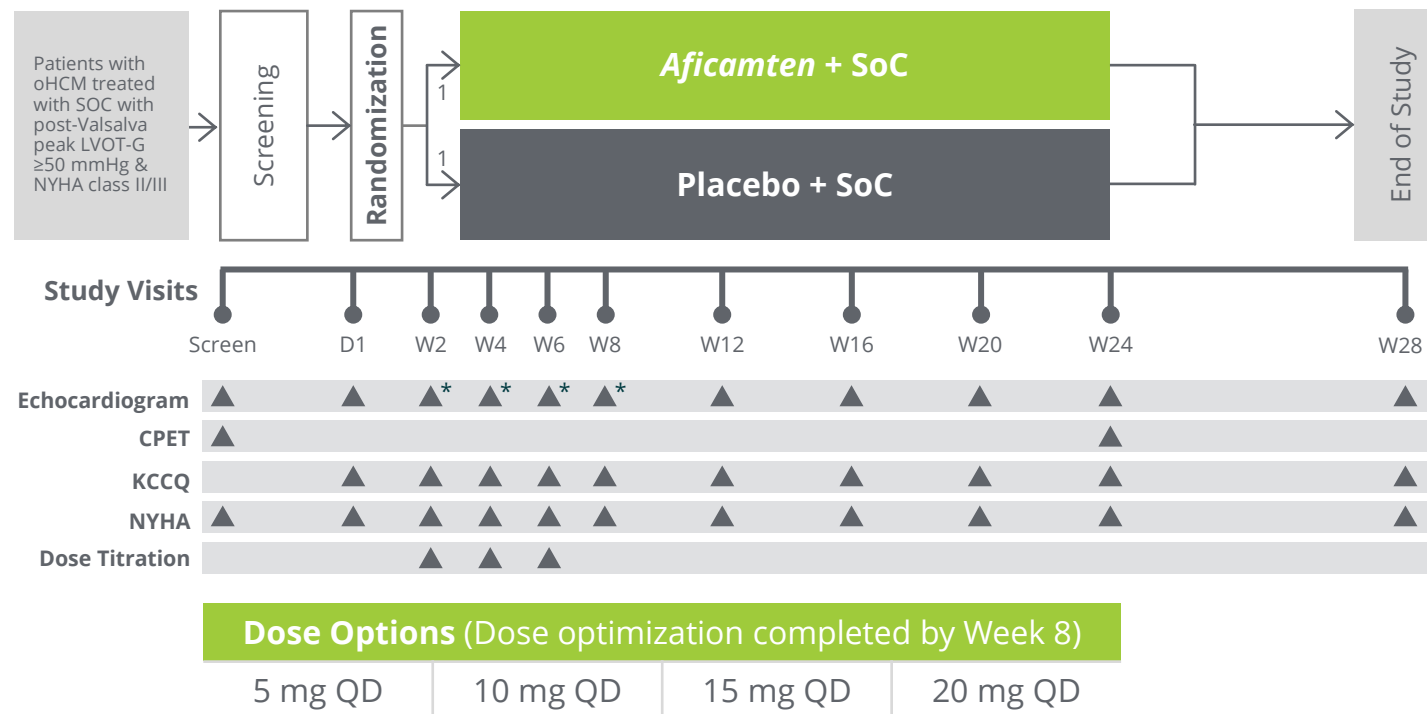
Secondary objectives include measuring **change in KCCQ & improvement in NYHA class at week 12 and 24**

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 $\geq 55\%$, post-Valsalva LVOT-G ≥ 30 mmHg

SOC: standard of care
* Focused echocardiogram



SEQUOIA-HCM: Baseline Characteristics



Baseline characteristics reflect highly symptomatic patient population with reduced exercise capacity

- Significant **symptom burden** despite background therapy
- 61% of patients on **beta-blockers**
- Baseline pVO_2 reflects patient population with **reduced exercise capacity**

	Aficamten n=142	Placebo n=140
Age, y	59.2 ± 12.6	59.0 ± 13.4
Female sex, n (%)	56 (39.4)	59 (42.1)
Race, n (%)		
White	108 (76.1)	115 (82.1)
Geographic region, n (%)		
North America	49 (34.5)	45 (32.1)
China	24 (16.9)	22 (15.7)
Europe and Israel	69 (48.6)	73 (52.1)
Medical history, n (%)		
Hypertension	75 (52.8)	70 (50.0)
Paroxysmal atrial fibrillation	21 (14.8)	20 (14.3)
Permanent atrial fibrillation	2 (1.4)	1 (0.7)
CPET		
pVO_2 (mL/kg/min)	18.5 (4.5)	18.6 (4.5)
Percent of predicted pVO_2 (%)	58 (13)	57 (12)

Values are the mean ± SD unless otherwise indicated.

	Aficamten n=142	Placebo n=140
Background HCM therapy, n (%)		
Beta-blocker	86 (60.6)	87 (62.1)
Calcium channel blocker	45 (31.7)	36 (25.7)
Disopyramide	16 (11.3)	20 (14.3)
None	19 (13.4)	22 (15.7)
KCCQ-CSS	76 ± 18	74 ± 18
NYHA FC, n (%)		
II	108 (76.1)	106 (75.7)
III/IV	34 (23.9)	34 (24.3)
Median NT-proBNP (IQR), pg/mL	818 (377–1630)	692 (335–1795)
Median hs-cTnI (IQR), ng/L	12.9 (7.6–33.6)	11.5 (7.7–25.0)
Echocardiographic parameters		
Valsalva LVOT-G, mmHg	82.9 ± 32	83.3 ± 33
Resting LVOT-G, mmHg	54.8 ± 27	55.3 ± 32
LVEF, %	74.8 ± 5.5	74.8 ± 6.3
Maximal LV wall thickness, mm	20.7 ± 3.0	21.0 ± 3.0

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

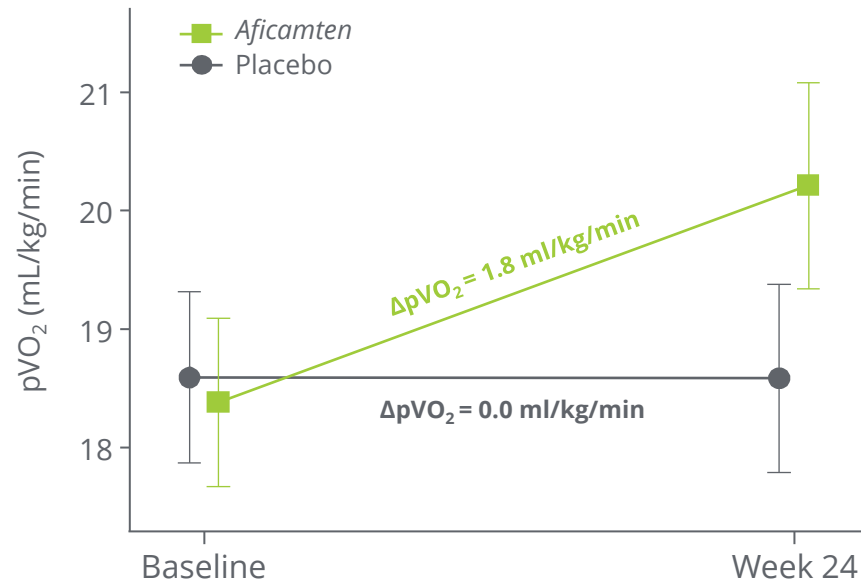
SEQUOIA-HCM: Primary Endpoint

Significant improvement in exercise capacity compared to placebo

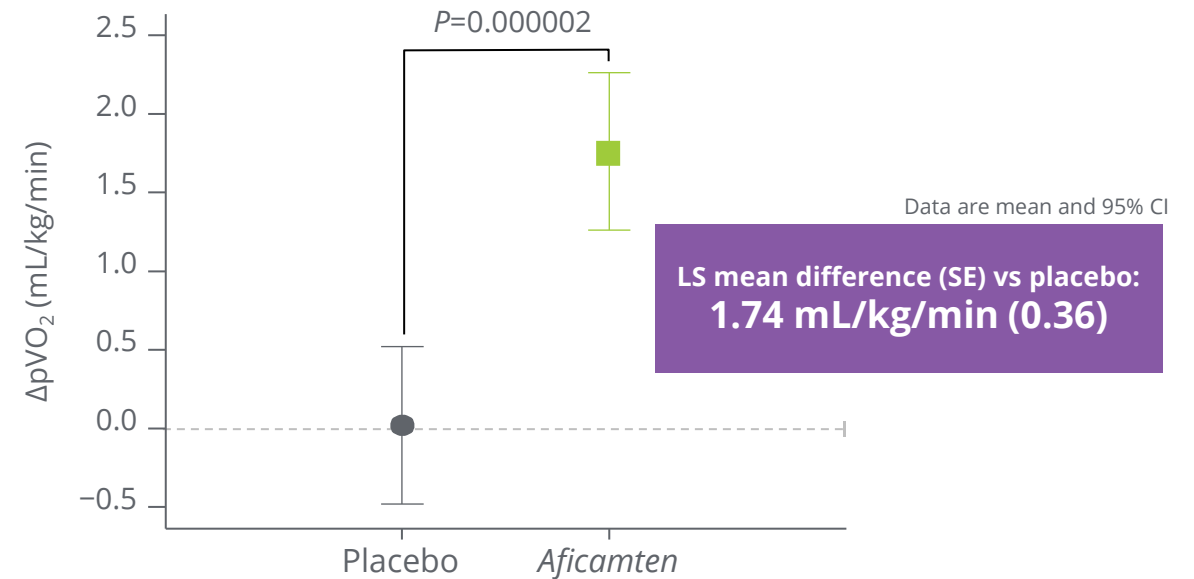


Results presented at Heart Failure 2024 and published in *NEJM*

Absolute Change from Baseline to Week 24



LS mean Change from Baseline to Week 24



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SEQUOIA-HCM: Subgroup Analysis



Results consistent across all prespecified subgroups including patients receiving or not receiving background beta-blockers

	n (Afi/Plb)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)		n (Afi/Plb)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)
Age					Baseline NT-proBNP (median)				
<65 y	85/84	2.4	0.4	2.0 (1.1, 2.8)	≤ 788 pg/mL	66/73	2.2	0.6	1.7 (0.7, 2.7)
≥65 y	57/56	0.9	-0.5	1.4 (0.3, 2.5)	> 788 pg/mL	73/65	1.4	-0.6	2.0 (1.0, 2.9)
Sex					CPET Modality				
Male	86/81	2.5	0.7	1.8 (0.9, 2.7)	Treadmill	78/77	2.5	0.2	2.3 (1.4, 3.2)
Female	56/59	0.6	-0.8	1.4 (0.4, 2.5)	Bicycle	64/63	0.9	-0.1	1.0 (-0.0, 2.1)
Baseline BMI					Baseline Median pVO₂				
<30 kg/m ²	97/94	1.9	0.1	1.8 (1.0, 2.7)	≤18.4 mL/kg/min	74/67	1.5	-0.1	1.6 (0.6, 2.5)
≥30 kg/m ²	45/46	1.4	-0.2	1.6 (0.3, 2.8)	>18.4 mL/kg/min	68/73	2.0	0.1	1.9 (1.0, 2.9)
Baseline Median LVEF					Baseline Beta-Blocker Use				
≤75.6%	73/68	1.9	0.0	1.8 (0.8, 2.8)	Yes	86/87	1.4	-0.2	1.6 (0.7, 2.5)
>75.6%	69/72	1.7	0.0	1.6 (0.6, 2.6)	No	56/53	2.2	0.2	1.9 (0.8, 3.1)
Baseline NYHA FC					Baseline Resting LVOT (median)				
Class II	108/106	2.0	0.3	1.7 (0.9, 2.5)	≤51.1 mmHg	72/69	1.8	0.5	1.3 (0.3, 2.3)
Class III /IV	34/34	1.0	-0.9	1.9 (0.5, 3.3)	>51.1 mmHg	70/71	1.7	-0.4	2.1 (1.2, 3.1)
Baseline Median KCCQ-CSS					Genotype				
≤78.1	67/75	1.7	-0.1	1.8 (0.8, 2.8)	Positive	20/22	1.6	-1.0	2.6 (0.9, 4.2)
>78.1	75/65	1.8	0.1	1.7 (0.7, 2.6)	Negative	71/70	1.4	-0.1	1.4 (0.5, 2.3)

Interaction P values were >0.05 for all prespecified subgroups

← Favors Placebo Favors Treatment →

← Favors Placebo Favors Treatment →

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

SEQUOIA-HCM: Secondary Endpoints



Statistically significant improvements in all 10 pre-specified secondary endpoints

Endpoints	P value
Primary Endpoint	
pVO ₂ change from baseline to Week 24	<0.0001
Secondary Endpoints	
1. KCCQ-CSS change from baseline to Week 24	<0.0001
2. NYHA Class Improvement by at least 1 class at Week 24	<0.0001
3. Valsalva LVOT-G change from baseline to Week 24	<0.0001
4. % Valsalva LVOT-G <30 mmHg at Week 24	<0.0001
5. Duration of SRT Eligible during 24 Weeks of Treatment	<0.0001
6. KCCQ-CSS change from baseline to Week 12	<0.0001
7. NYHA Class Improvement by at least 1 class at Week 12	<0.0001
8. Valsalva LVOT-G change from baseline to Week 12	<0.0001
9. % Valsalva LVOT-G <30 mmHg at Week 12	<0.0001
10. Total workload change from baseline to Week 24	<0.0001

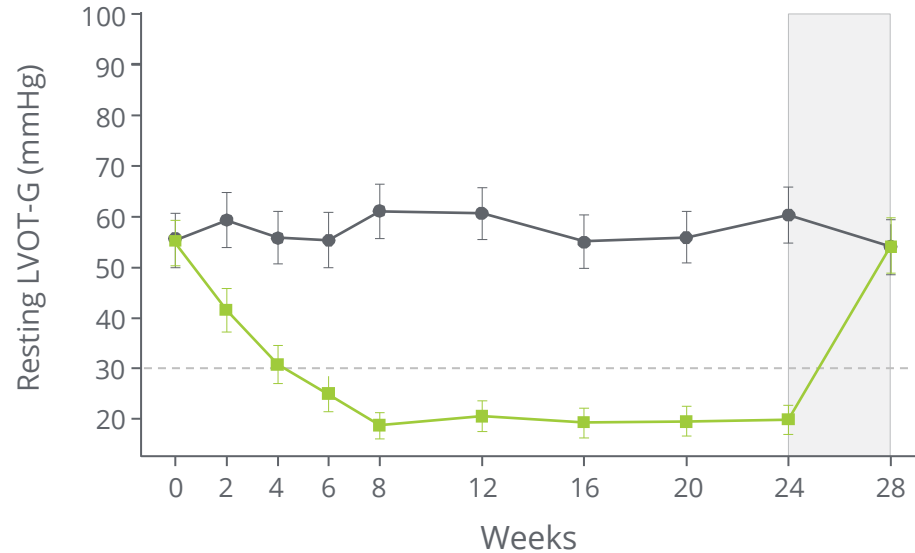
*Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.*

SEQUOIA-HCM: Secondary & Exploratory Endpoints

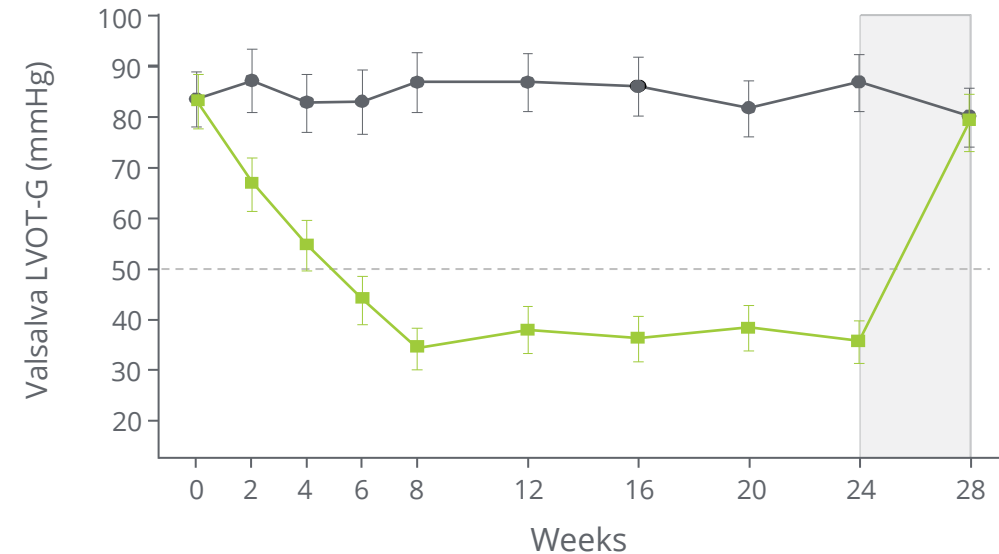


Significant improvement in post-Valsalva left ventricular outflow tract gradient (LVOT-G)

Resting LVOT-G



Valsalva LVOT-G



LS mean difference:
- 50 mmHg

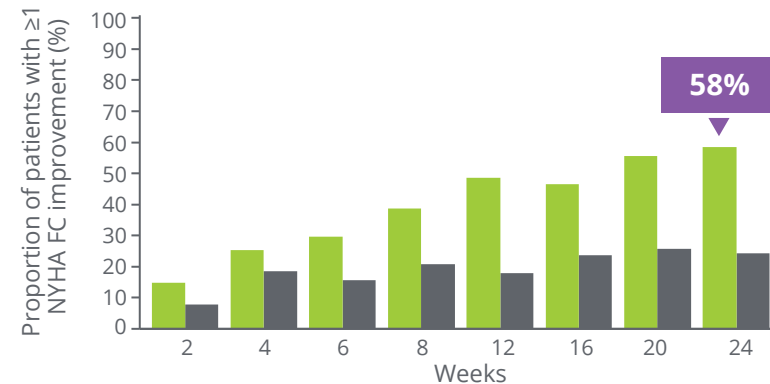
■ Aficamten
● Placebo
■ Washout

Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
Error bars are 95% CI
Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.

SEQUOIA-HCM: Secondary & Exploratory Endpoints

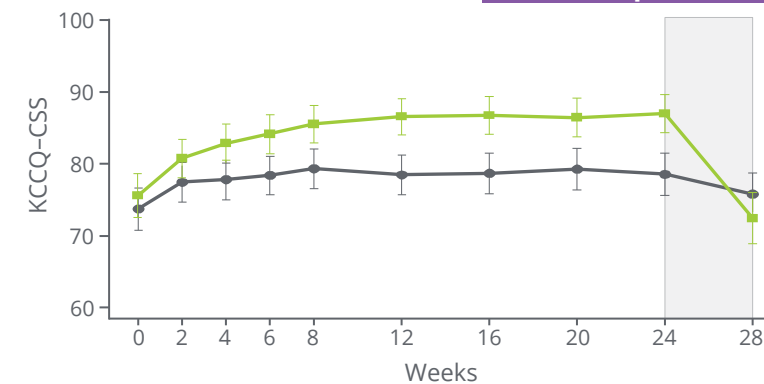


≥1 NYHA FC Improvement



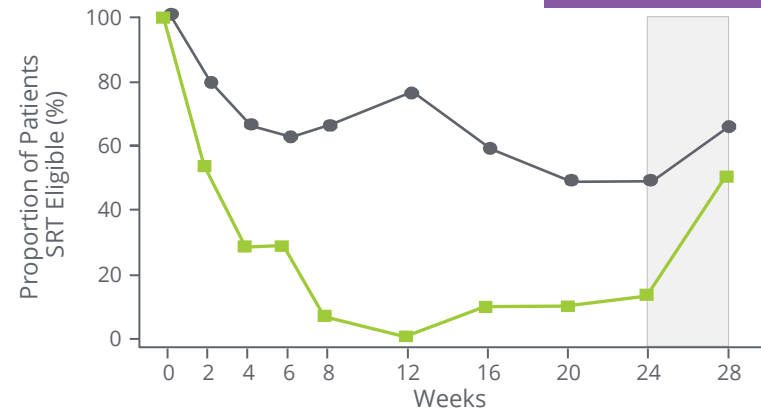
KCCQ-CSS

LS mean difference:
7 points



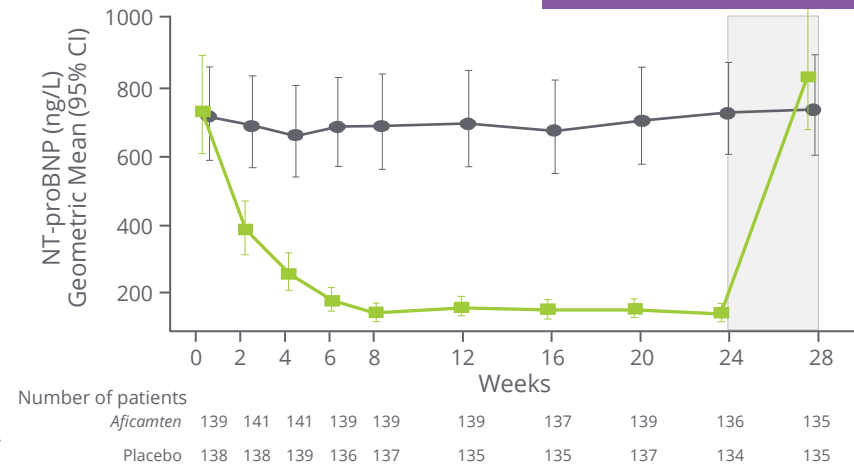
Guideline Eligibility for SRT

78 fewer days
spent SRT-eligible



NT-proBNP

80% reduction
from baseline to Wk 24



■ Aficamten
● Placebo
■ Washout

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Error bars are 95% CI
Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.

SEQUOIA-HCM: Responder Analysis



Significant improvement in exercise capacity and symptoms in composite responder endpoint

	Aficamten n=142	Placebo n=140
≥1.5 mL/kg/min increase in pVO₂ and ≥1 NYHA FC improvement or ≥3.0 mL/kg/min increase in pVO₂ and no worsening of NYHA FC, n (%)	60 (42)	19 (14)
≥1.5 mL/kg/min increase in pVO ₂ and ≥1 NYHA class improvement	44 (31)	9 (6)
≥3.0 mL/kg/min increase in pVO ₂ and no worsening of NYHA class	37 (26)	13 (9)
Both ≥3.0 mL/kg/min increase in pVO ₂ and ≥1 NYHA class improvement	21 (15)	3 (2)
Common rate difference vs placebo (95% CI) P value	28.7 (18.8, 38.6) <0.0001	

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

SEQUOIA-HCM: Safety Data



	Event, n (%)	Placebo (n=140)	<i>Aficamten</i> (n=142)
	Overall AEs	99 (70.7)	105 (73.9)
<div data-bbox="433 539 1044 639"> <p>AEs with ≥5% incidence</p> </div> <div data-bbox="433 658 1059 1006"> <p>There were no serious adverse cardiovascular events associated with <i>aficamten</i> treatment in SEQUOIA-HCM</p> </div>	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%.

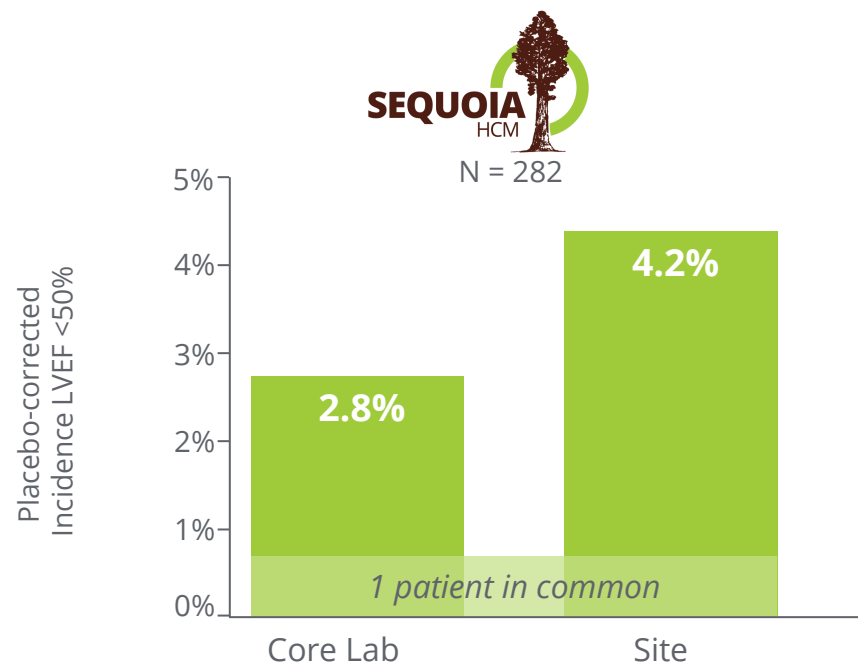
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

AE, adverse event; SAE, serious adverse event.

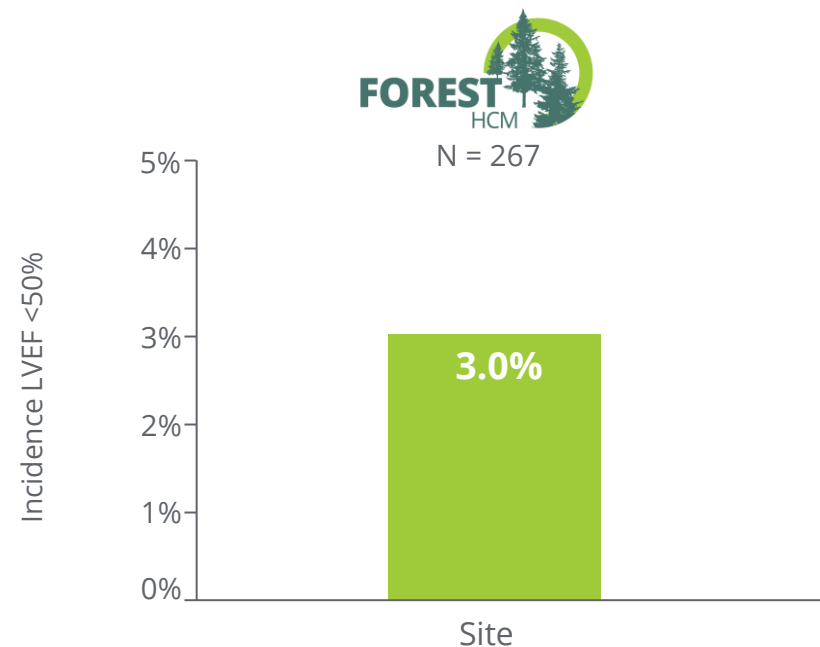
Coats CJ. Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

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

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

Preparing for Regulatory Submissions to FDA, EMA



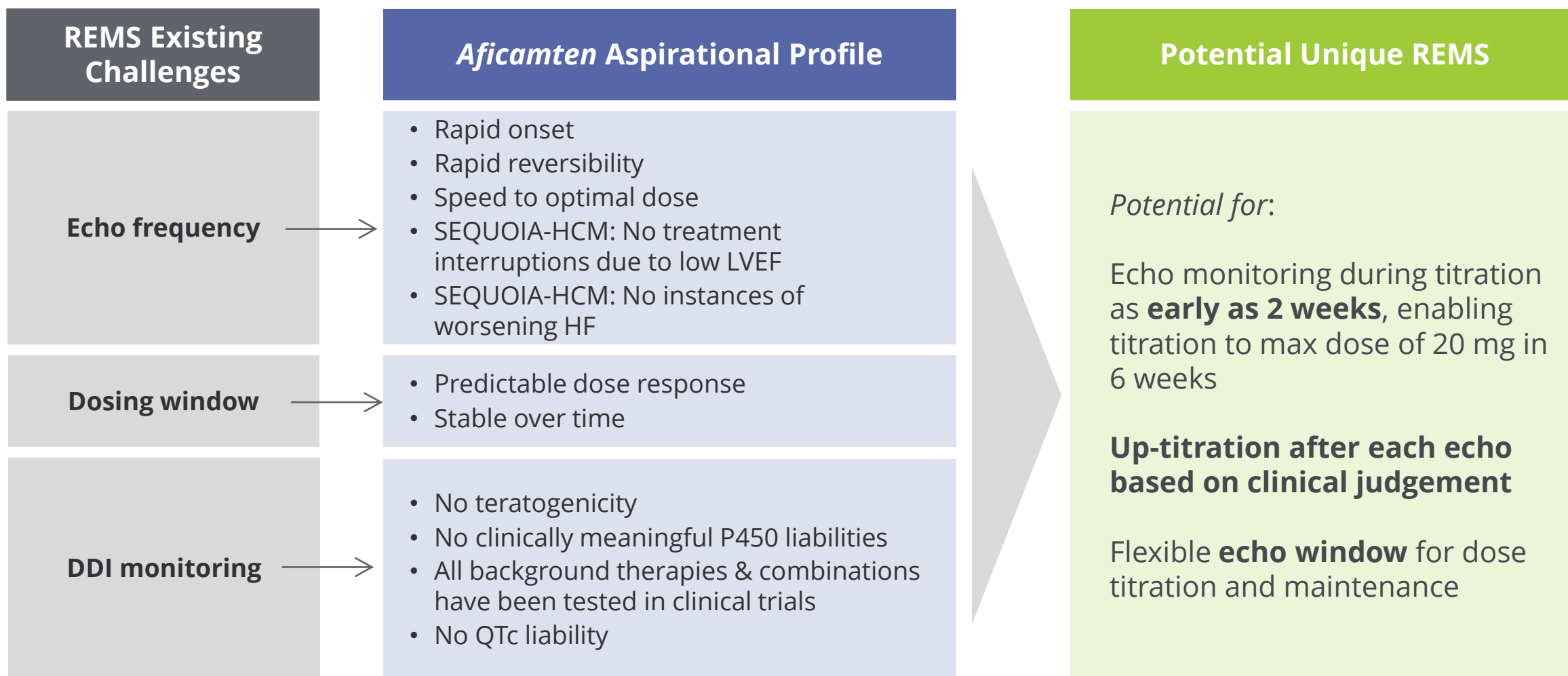
Positive Results from
SEQUOIA-HCM

2024

- Participated in
 - **Two meetings with FDA** in Q1 2024
 - **Type B meeting with FDA** in Q2 2024
 - **Meetings with EMA** in Q2 2024
- **Expect to submit NDA to FDA** in Q3 2024 and **MAA to EMA** in Q4 2024: development of all modules underway and manufacturing activities on track

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 Risk Mitigation



Ongoing Clinical Trials of *Aficamten*



Pivotal Phase 3 clinical trial of *aficamten* as monotherapy vs. metoprolol in oHCM



Pivotal Phase 3 clinical trial in nHCM



Clinical trial in a pediatric population with oHCM



Open-label extension clinical study in HCM

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

Upcoming Presentations to Expand on Safety, Efficacy of *Aficamten*

Four late breaking clinical trial presentations & two oral presentations at ESC 2024



**ESC Congress
2024 London**

Onsite & Online, 30 August - 2 September



Late Breaking Clinical Trial Update

Effect of *Aficamten* on Patient-Reported Health Status in oHCM: Results From SEQUOIA-HCM

John A. Spertus

Late Breaking Clinical Trial Update

Impact of *Aficamten* on Echocardiographic Cardiac Structure & Function in Adults with Symptomatic oHCM

Sheila M. Hegde

Late Breaking Clinical Trial Update

Effect of *Aficamten* on Cardiac Structure & Function in Patients With oHCM: The SEQUOIA-HCM CMR Trial

Ahmad Masri

Oral Presentation

Clinical Application of Biomarkers in oHCM: Insights From SEQUOIA-HCM

Caroline J. Coats



Late Breaking Clinical Trial Update

Safety & Outcomes of Standard of Care Medications Withdrawal in Patients with oHCM Treated with *Aficamten* in FOREST-HCM Trial

Ahmad Masri

Oral Presentation

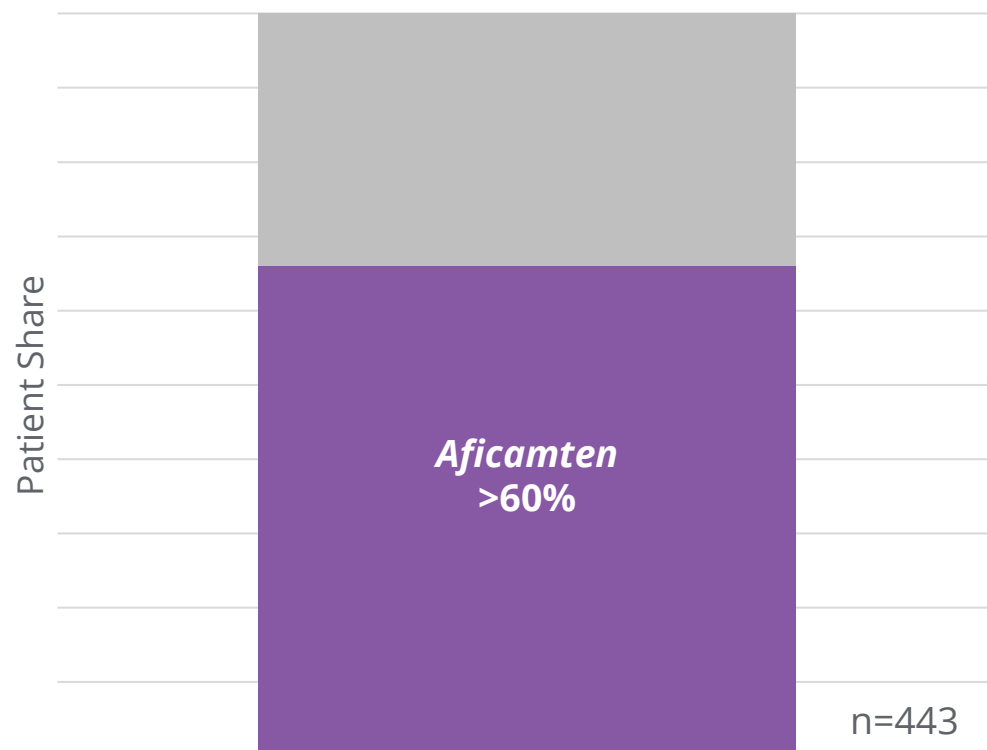
***Aficamten* in Patients with oHCM: an Integrated Safety Analysis**

Ahmad Masri

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

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

oHCM CMI Preference Shares in Eligible Patient Population*



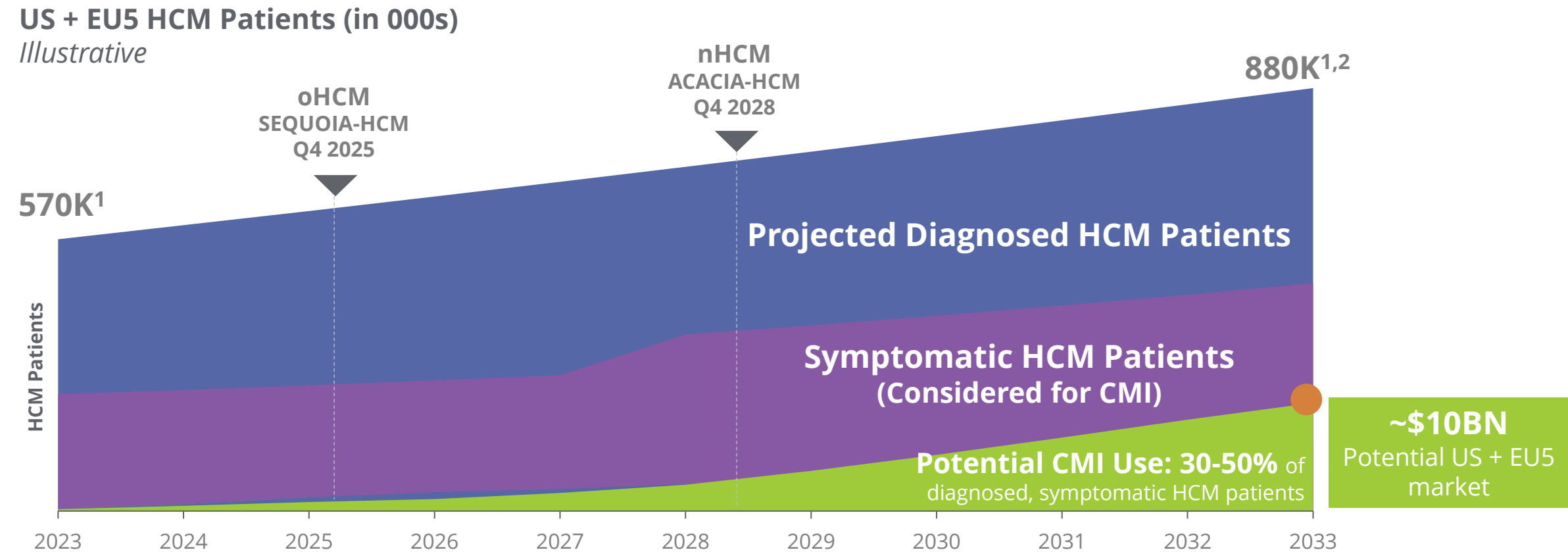
Survey results are based on the aspirational profile of *aficamten* and if approved, the actual profile could vary materially.

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

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

If Aficamten is Approved, Expect Majority of CMI-Eligible Patients Available at Launch

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



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Projections and forecasts for illustration

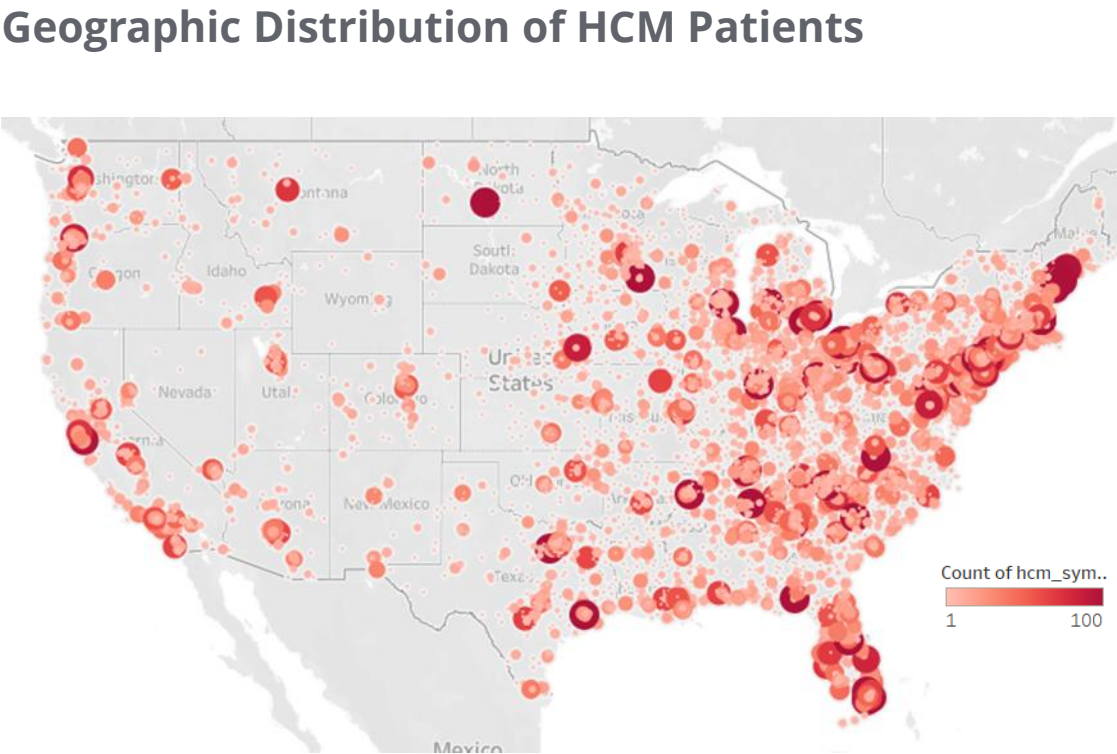
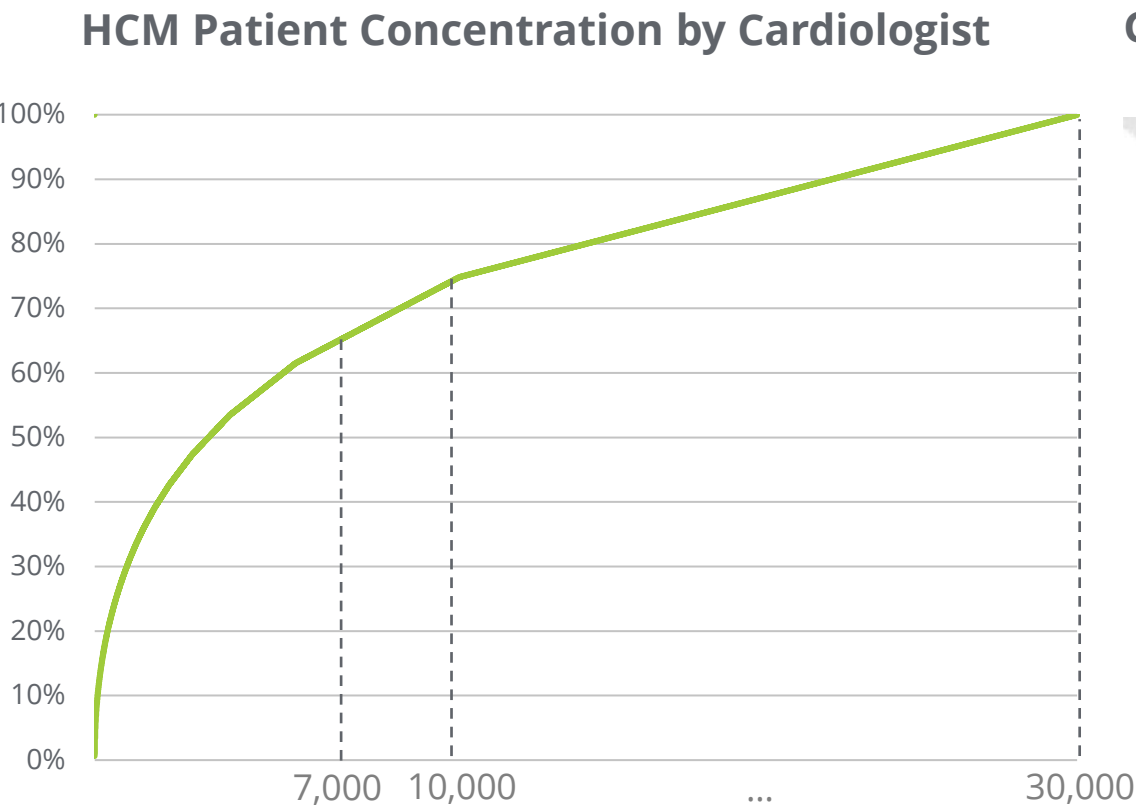
1. DoF internal projections based on Maron B., Ethan J. R., Maron M.: Global Burden of Hypertrophic Cardiomyopathy, JACC: Heart Failure, Volume 6, Issue 5, 2018, Pages 376-378. <https://doi.org/10.1016/j.jchf.2018.03.004>; SHA; Symphony PTD (Patient Transaction Data): Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023);

2. DoD; Butzner et al 2021 estimates a 8% growth rate in diagnosed HCM patients between 2013-2019 in the US [https://www.qjconline.org/article/S0002-9149\(21\)00783-9/fulltext](https://www.qjconline.org/article/S0002-9149(21)00783-9/fulltext); CYTK is forecasting a 5 % diagnosis rate increase in the US and a more conservative 4% growth rate in Europe due to a lack of growth of the overall populations in EU5 countries;

3. Internal forecasts

Cardiologists Located in Concentrated Geographic Clusters Across the US

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

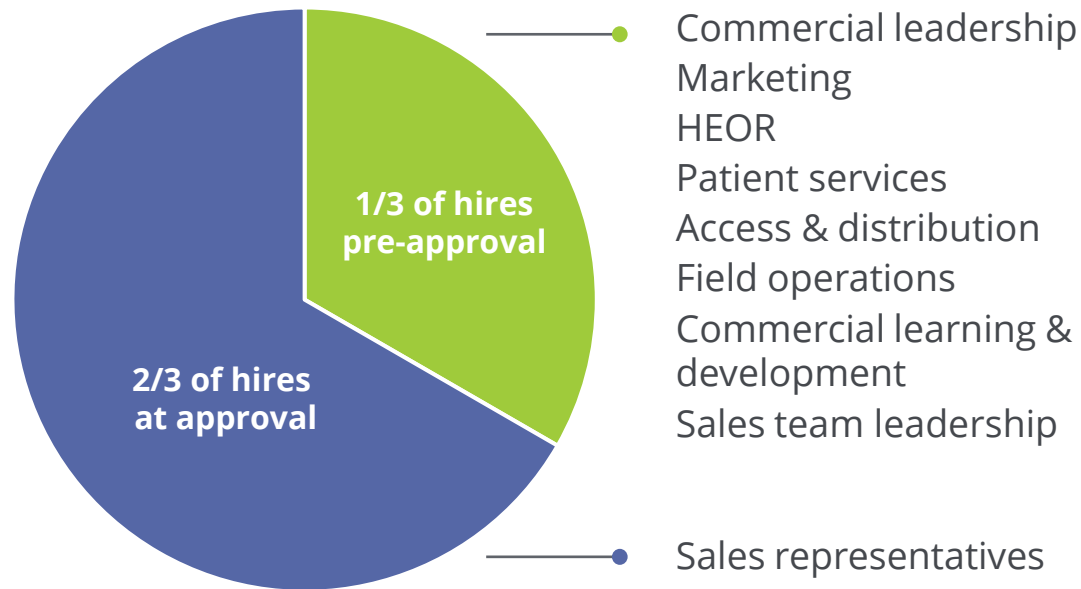


Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients
Source: Symphony PTD (Patient Transaction Data); mapping of HCPs to HCOs using Definitive Healthcare Data 2023 and 7/2023 mapping; Patient volume by dominant Cardiologist Location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

Gated Build of Commercial Infrastructure

Majority of spending to occur closer to potential approval in 2025

2/3 of hiring to occur at-approval



Key activities after SEQUOIA-HCM readout

Continued insight generation

Market access strategy validation

Pricing strategy finalization

Distribution approach

Payer engagement

Brand strategy evolution

Customer account identification

Launch campaign development

Customer Experience

Payer Pre-approval Information Exchange

Sales force planning

Data & Technology Infrastructure build

Omnichannel execution

Market development rollout

Initiated upon FDA approval

Media purchases

Patient support programs

Peer to peer engagement

HCP Omnichannel launched



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Omecamtiv Mecarbil

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

Advancing efficient, pragmatic Phase 3 clinical trial

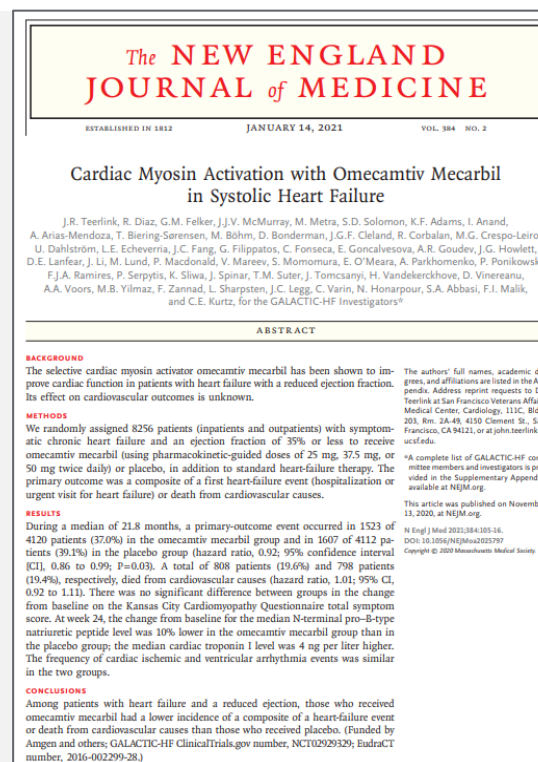
High Unmet Need

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



Ph 3 clinical trial results in 8,000 patients point to important treatment benefit

Planning confirmatory Ph 3 trial, **n= ~2,000, ~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

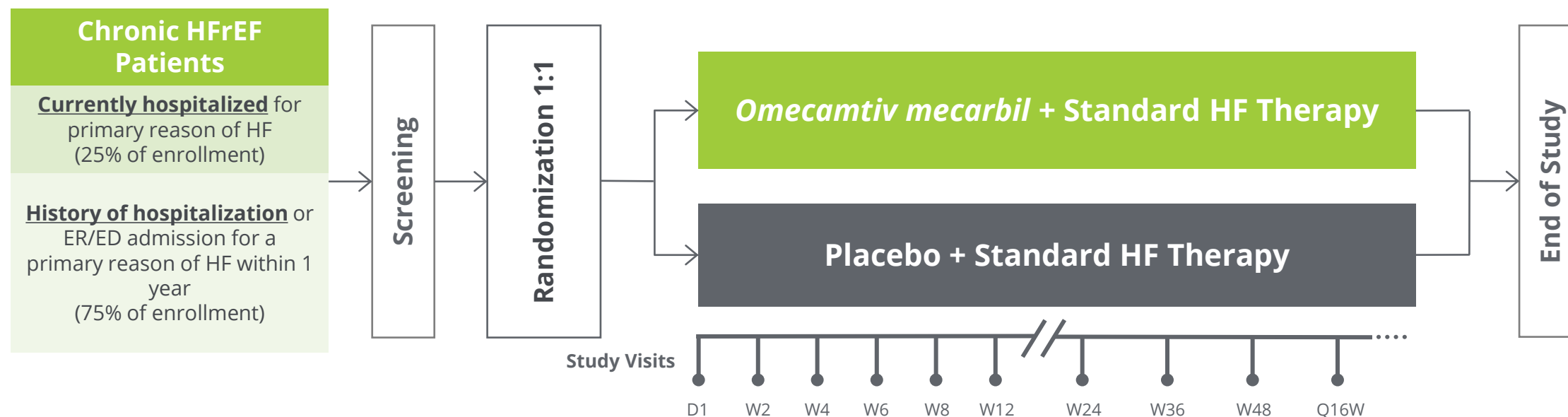
Pragmatic design elements including EHR screening, limited monitoring visits, remove visits, and limited safety labs & AE reporting

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

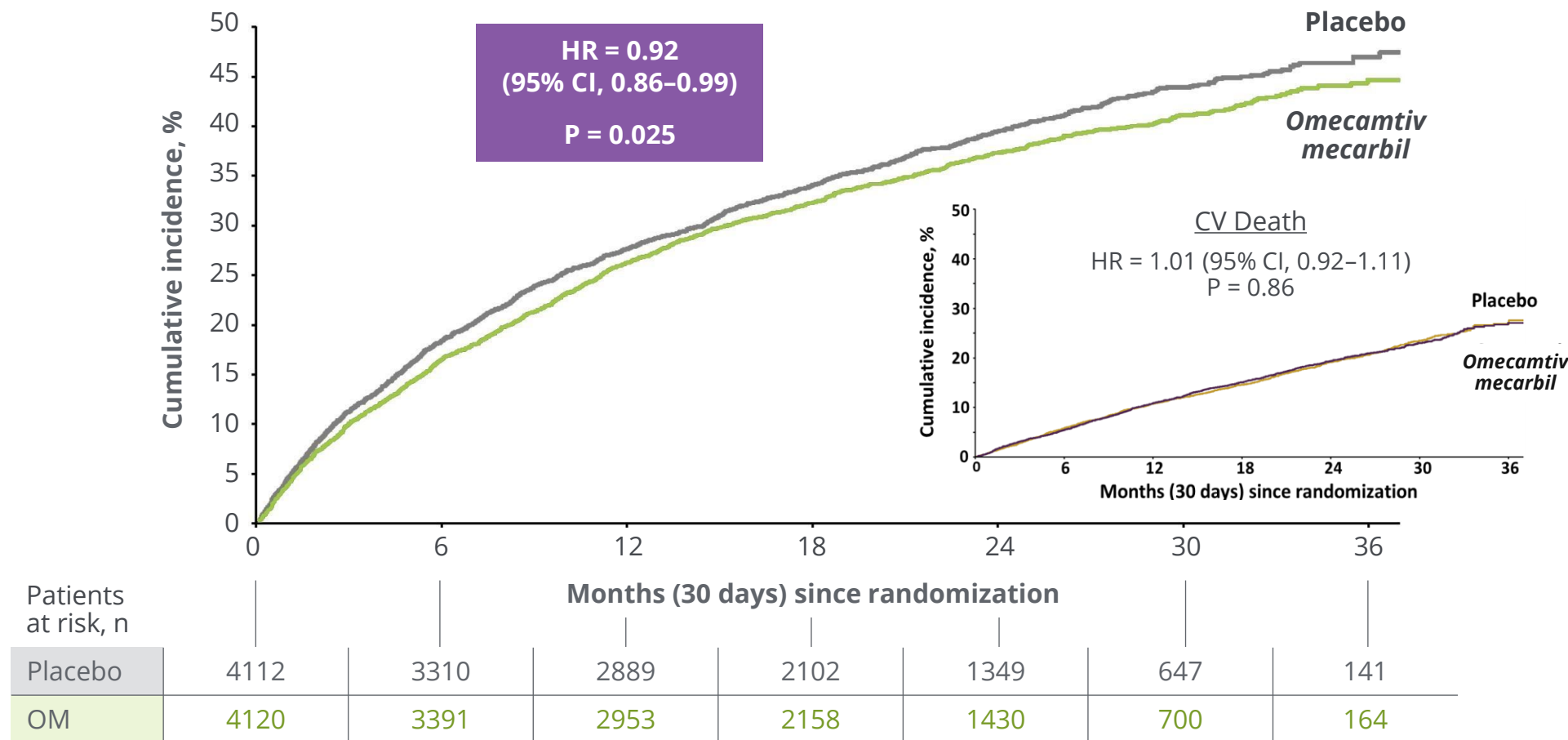
Phase 3 clinical trial

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



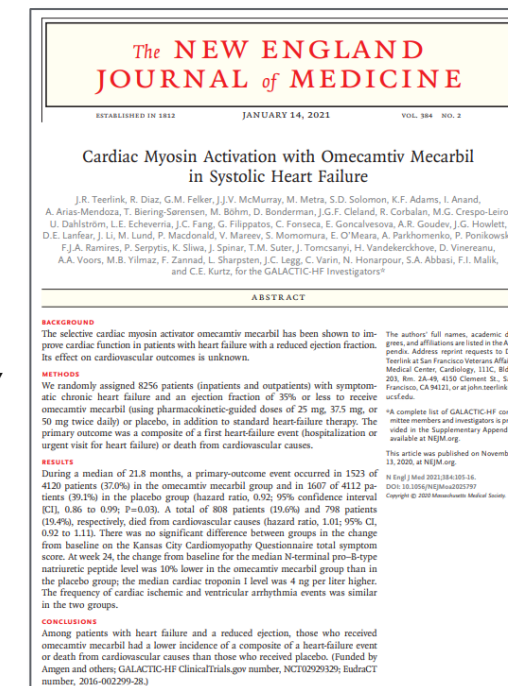
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Primary Composite Endpoint

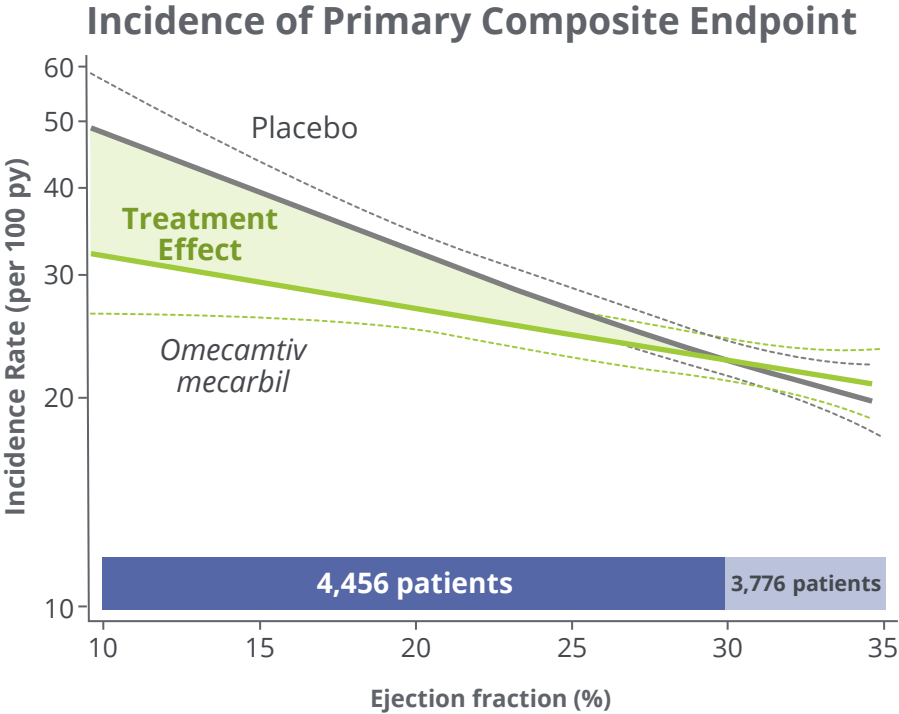


Time to first HF event or CV death

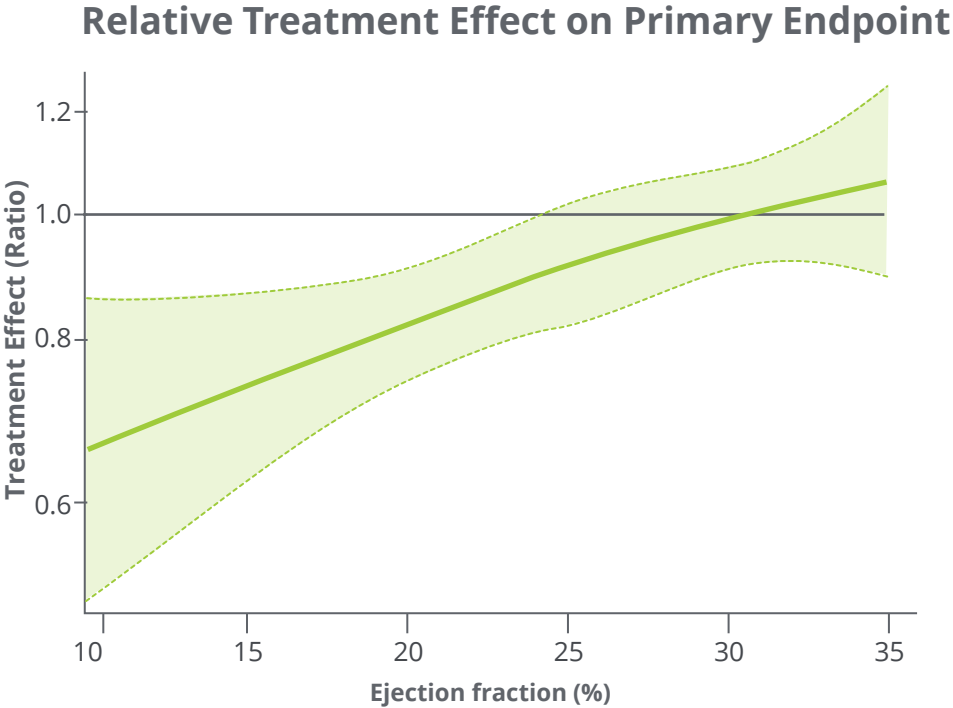
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.



Benefit Observed to Increase as Baseline LVEF Decreased

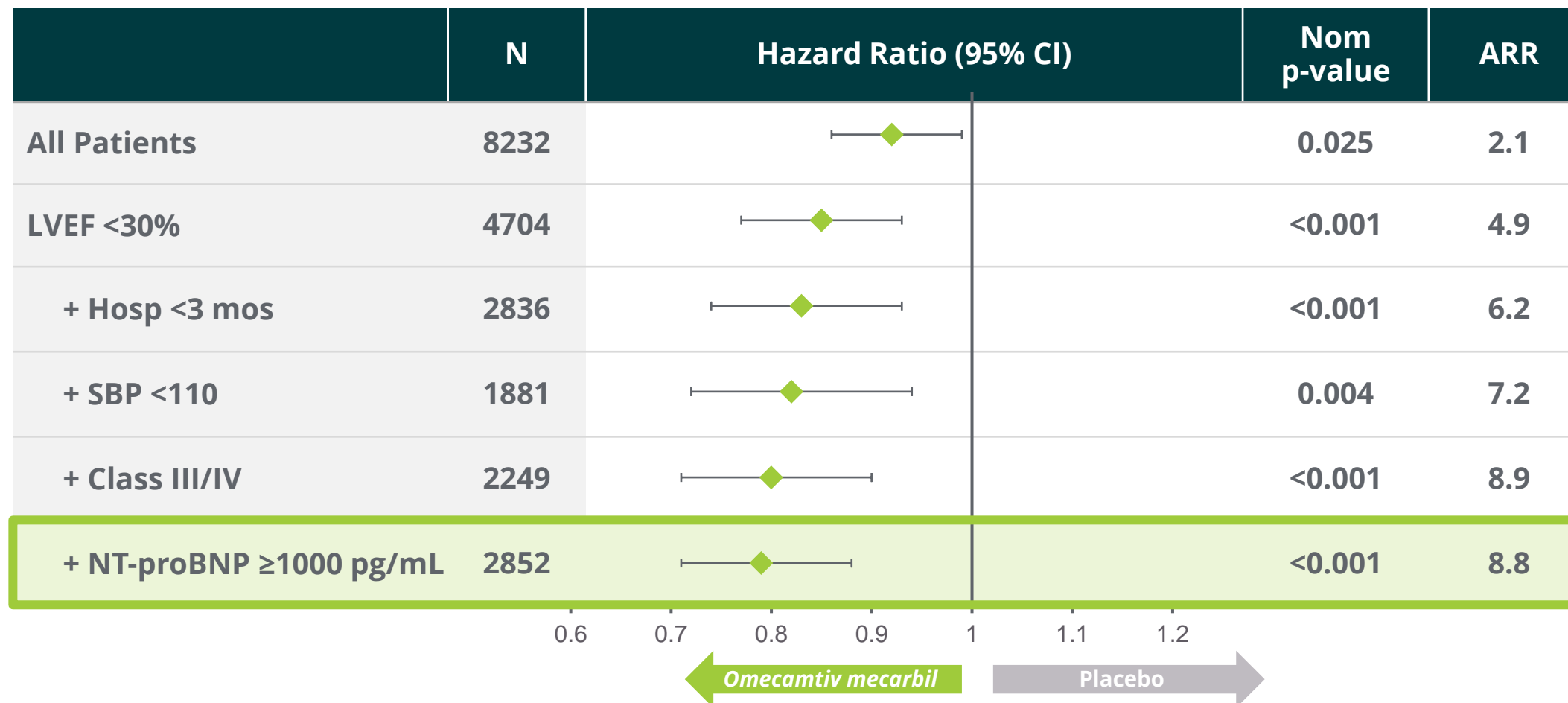


Pre-specified Subgroup	Baseline LVEF	≤ median (28%)	0.84 (0.77, 0.92)
	> median (28%)		1.04 (0.94, 1.16)
Interaction P-value = 0.004			



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

Large Treatment Effect in Easily Defined HF Population



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

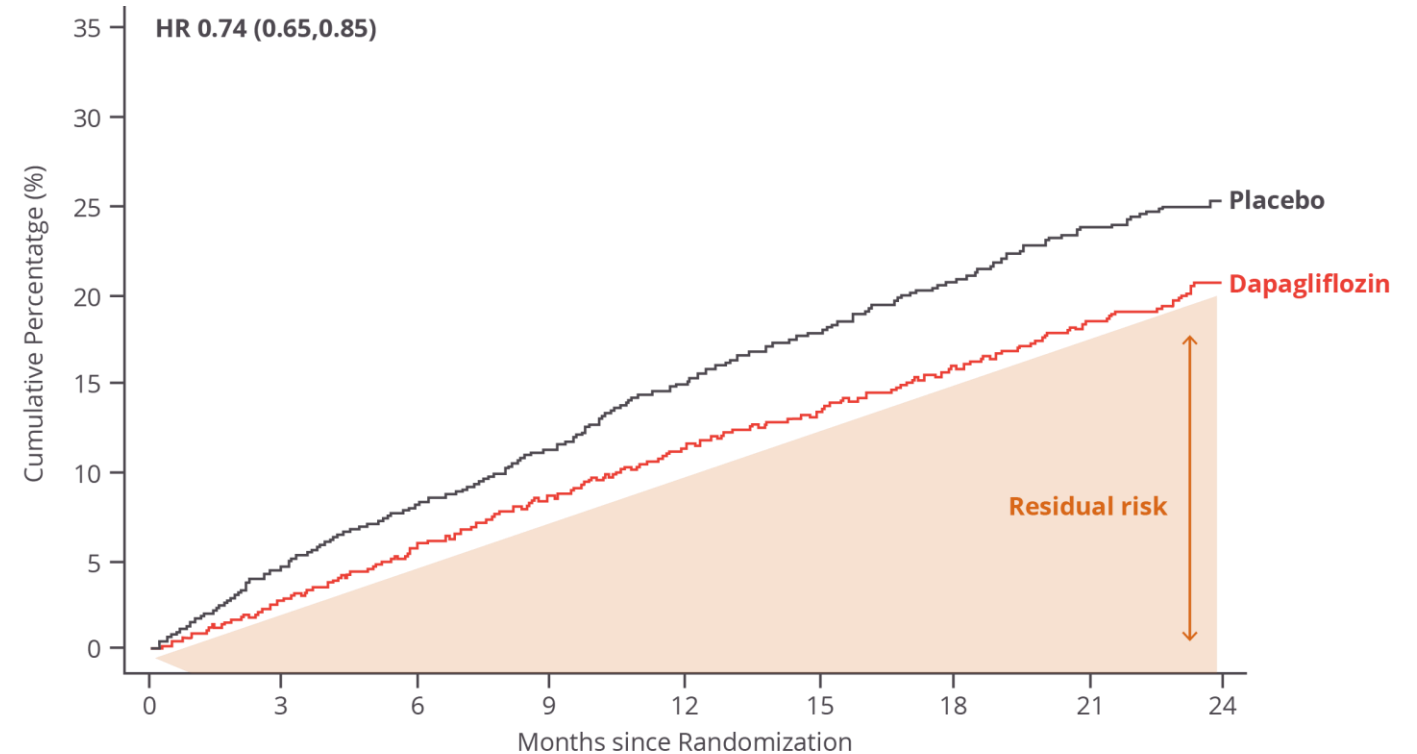
Residual Risk is High Despite Best Therapy

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%**
- Beta-blocker **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

Omecamtiv Mecarbil: Regulatory Feedback

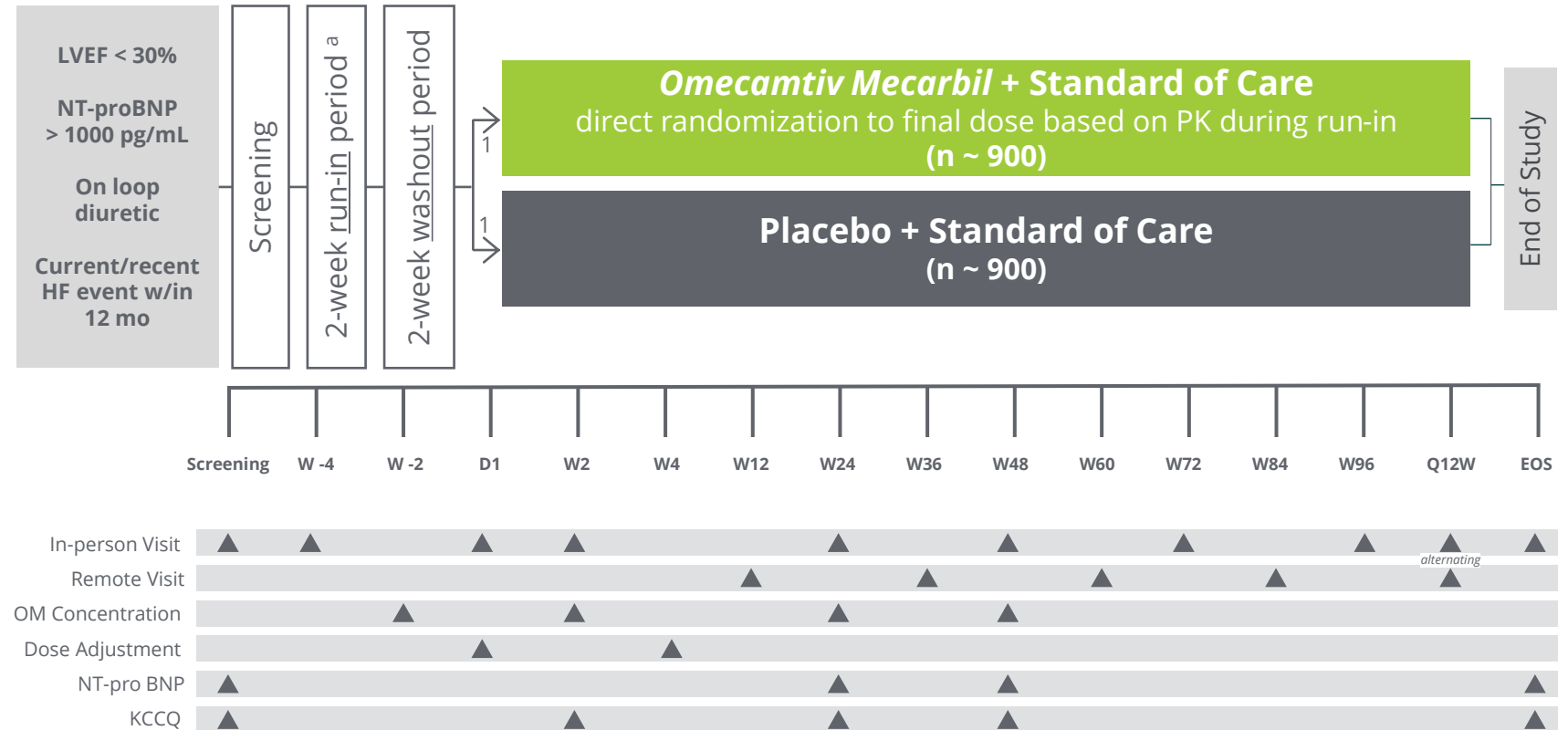


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Anticipated Phase 3 Confirmatory Clinical Trial Design

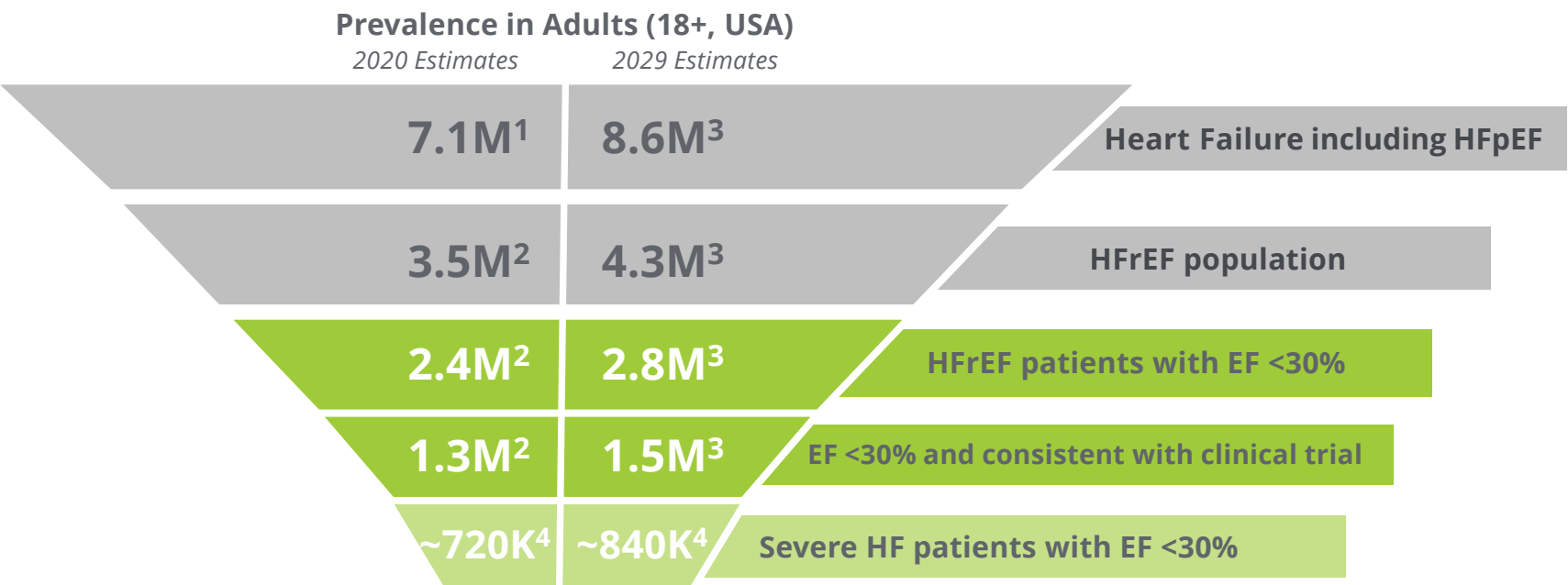
Trial design to be finalized

- Primary endpoint: **time to CV death, HF events, transplant/LVAD, or stroke**
- Enriched dosing for adherence**, with OM run-in period. Plan to randomize only those expected to land in therapeutic range
- Pragmatic design elements:**
 - EHR screening
 - Limit monitoring visits
 - Remote visits
 - Limited safety labs & 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%



Symptoms of Severe HF

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

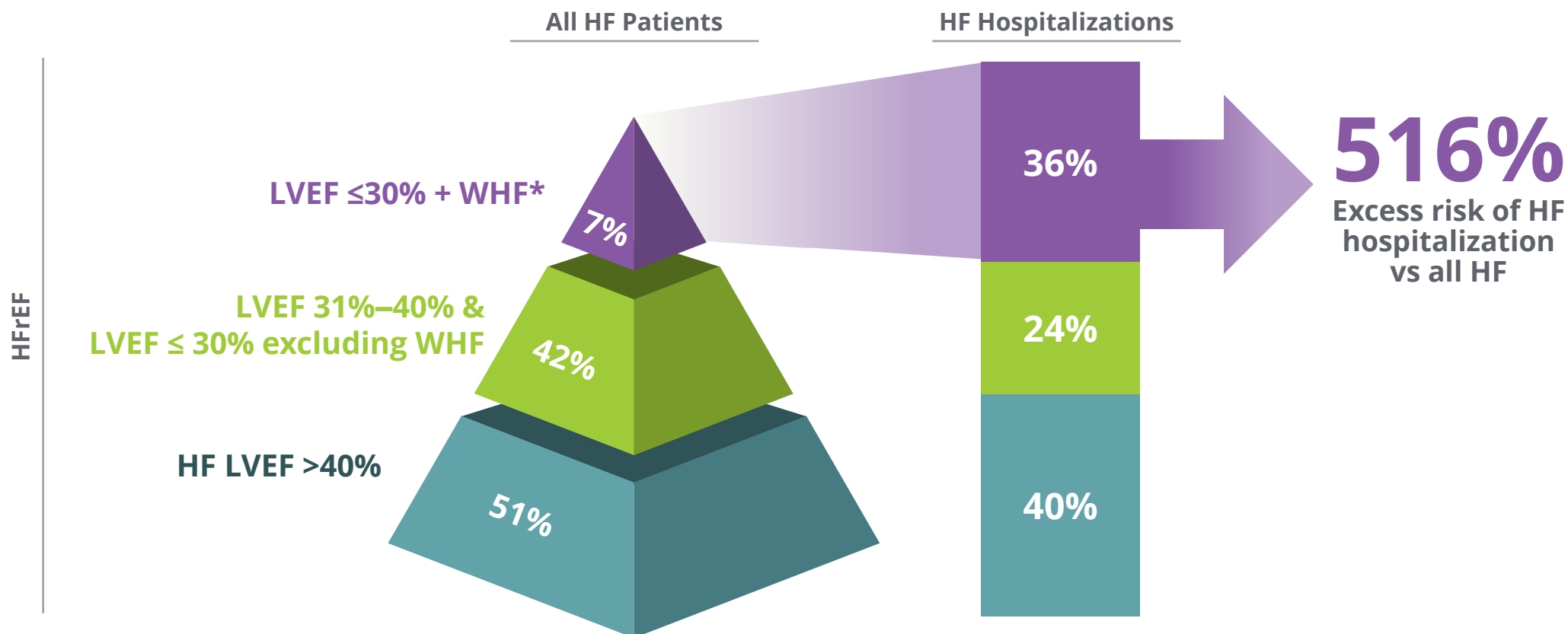
* HF event: urgent, unscheduled outpatient visit or hospitalization

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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

Patients with Severe HF at Excess Risk of Hospitalization

HF is #1 cause of 30-day readmission among Medicare beneficiaries¹



*Pyramid shows the proportion of patients with HF by subgroups with reduced LVEF. The purple section indicates the group with LVEF ≤30 and WHF. In this study, these patients make up 7% of the population with HF, yet account for an estimated 36% of hospitalizations for HF. WHF = worsening heart failure

1. 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.

Higher Price Potential in a Narrow, Sicker Patient Population

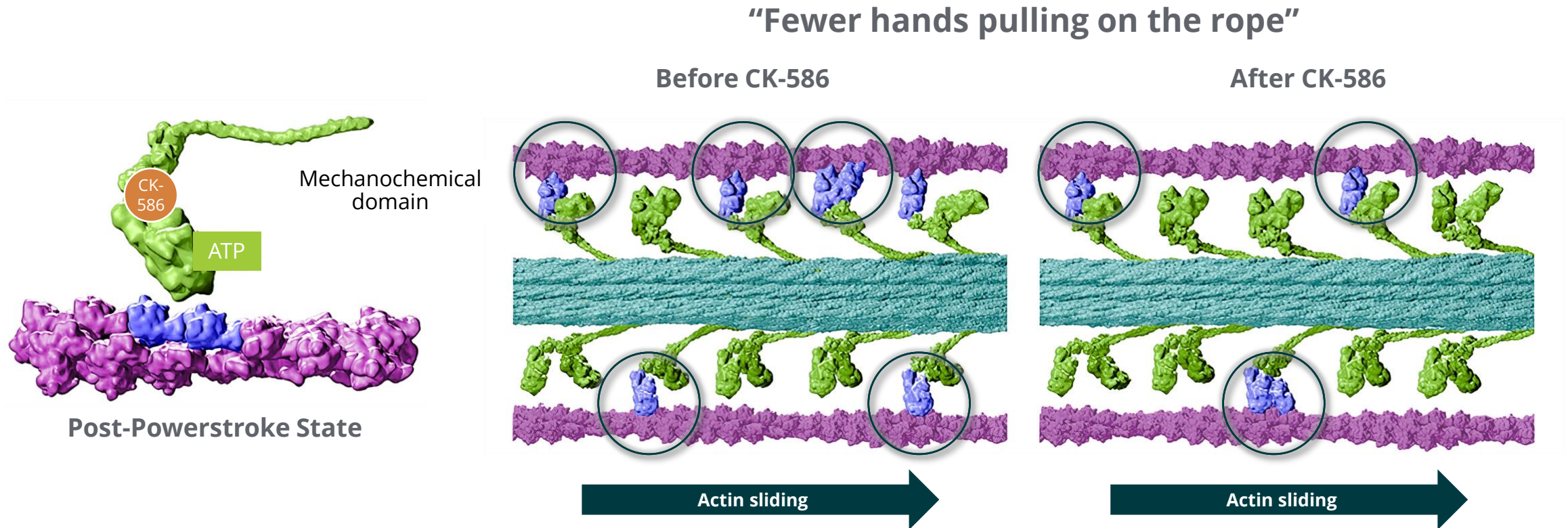
Significant clinical need and lack of treatments drives higher price potential

		"Original Potential Label" (GALACTIC-HF)	"Severely Reduced EF"
US Price Potential		Parity to market	Premium to market
Market Insights	Disease Severity	Worsening HF LVEF ≤ 35	Severe HF LVEF < 30
	Payer Positioning	2M+ patients In addition to GDMT	1M+ patients Post tolerated GDMT
	Therapeutic Choices	Limited treatment options	Limited to no treatment options

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CK-586

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



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Heart Failure with Preserved Ejection Fraction (HFpEF)

Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor¹



8.5 million

Americans will have
heart failure by
2030²



~50%

HF patients have
HFpEF³ &
prevalence of HFpEF
is increasing^{2,4}



~75%

HFpEF patients will
die within five
years of initial
hospitalization²



~84%

HFpEF patients will
be rehospitalized²

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.

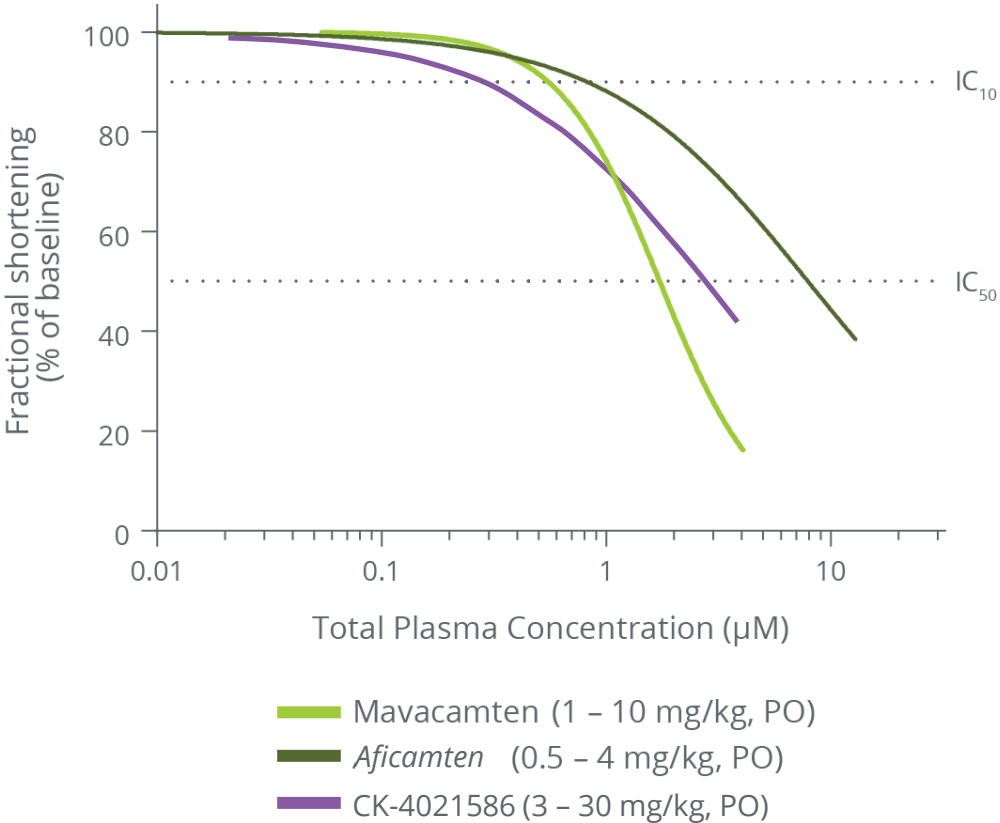
2. Bozkurt B, Ahmad T, Alexander KM, Baker WL, Bosak K, Breathett K, Fonarow GC, Heidenreich P, Ho JE, Hsieh E, Ibrahim NE, Jones LM, Khan SS, Khazanie P, Koelling T, Krumholz HM, Khush KK, Lee C, Morris AA, Page RL 2nd, Pandey A, Piano MR, Stehlik J, Stevenson LW, Teerlink JR, Vaduganathan M, Ziaeian 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.

CK-586: Shallow In Vivo Concentration-Response

CK-586 will have a shorter half-life in humans 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

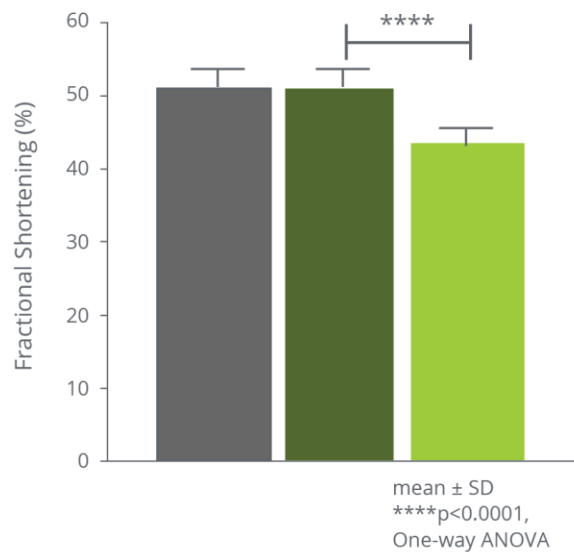
CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

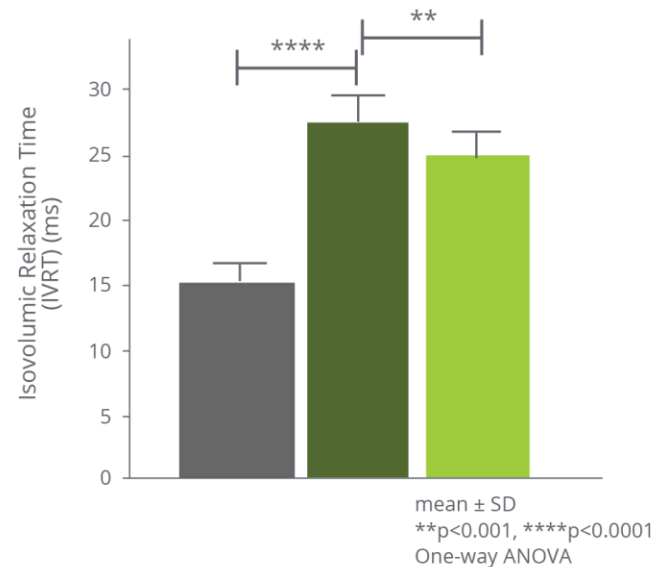
Model is representative of hypertensive, diabetic, metabolic aspects of HFpEF

10 weeks of treatment improved diastolic function and reduced cardiac fibrosis

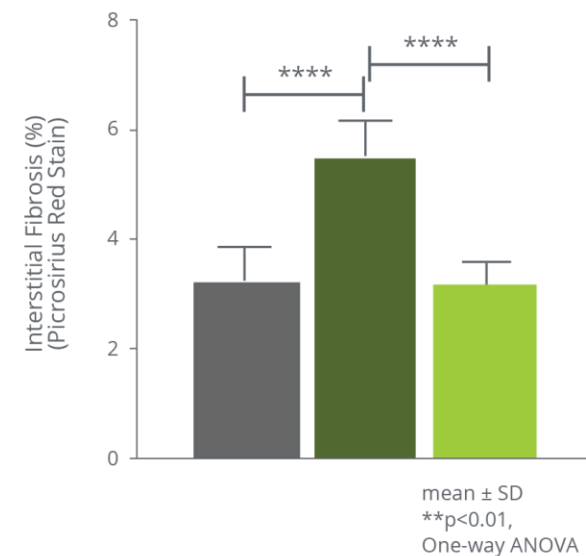
Reduced Fractional Shortening



Improved Diastolic Function



Reduced Fibrosis



■ ZSF1 Lean + Vehicle ■ ZSF1 Obese + Vehicle ■ ZSF1 Obese + CK-586 (10 mg/kg, PO QD)

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Phase 1 Data Support Advancement to Phase 2 Clinical Trial

Full data to be presented at a medical congress in 2H 2024

Phase 2a dose-finding trial in HFpEF expected to start by year-end 2024

Phase 1 Design

- **7 SAD cohorts** (10 mg to 600 mg) comprised of 10 participants each
- **2 MAD cohorts** (100 and 200 mg once daily) comprised of 10 participants each

Key Findings

- Pharmacodynamics were evaluated using echocardiography and **consistent with expectations**
- CK-586 was generally **safe and well-tolerated** with **linear PK**
- **No serious adverse events** were observed
- **Stopping criteria were not met**

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

Financials & Milestones

Strong Financial Position

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

Q1 2024 cash and investments	~\$634M	>\$1B
Strengthened balance sheet with recent financings	>\$800M cash received through equity and structured financing transactions executed in May 2024	
Further access to capital through term loans with RP	Secured access to add'l \$175M* in term loan on top of \$175M** already secured with Royalty Pharma (RP); total available term loans \$350M	Add'l \$500M
Potential further funding through RP opt-in	RP, at its option, can invest up to \$150M in a Phase 3 trial of CK-586	

*Tranche 7 Loan: Cytokinetics, at its option, is eligible to draw up to \$175m during the 1-year period following the FDA approval of aficamten for oHCM provided that the NDA is accepted on or prior to December 31, 2025.

**Tranche 4 & 5 Loans: Cytokinetics is eligible to draw up to \$75m by April 30, 2025 from tranche 4. The minimum draw for tranche 4 is \$50m. Cytokinetics, at its option, is eligible to draw up to \$100m during the 1-year period following the acceptance of the NDA filing for aficamten provided that the NDA filing is accepted on or prior to March 31, 2025.

Planned 2024 Milestones

Aficamten

Submit NDA to FDA in Q3 2024 and
MAA to EMA in Q4 2024

Complete enrollment of MAPLE-HCM
in Q3 2024

Continue enrollment of ACACIA-HCM
in 2024

Continue enrollment of CEDAR-HCM
in 2024

Continue Phase 1 study of *aficamten*
in healthy Japanese volunteers
in Q2 2024

Omecamtiv Mecarbil

Start Phase 3 clinical trial of
omecamtiv mecarbil in HFrEF
in Q4 2024

CK-586

Share full data from Phase 1 study
of CK-586 in 2H 2024

Initiate Phase 2 study
of CK-586 in Q4 2024

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



thank
you



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