



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.

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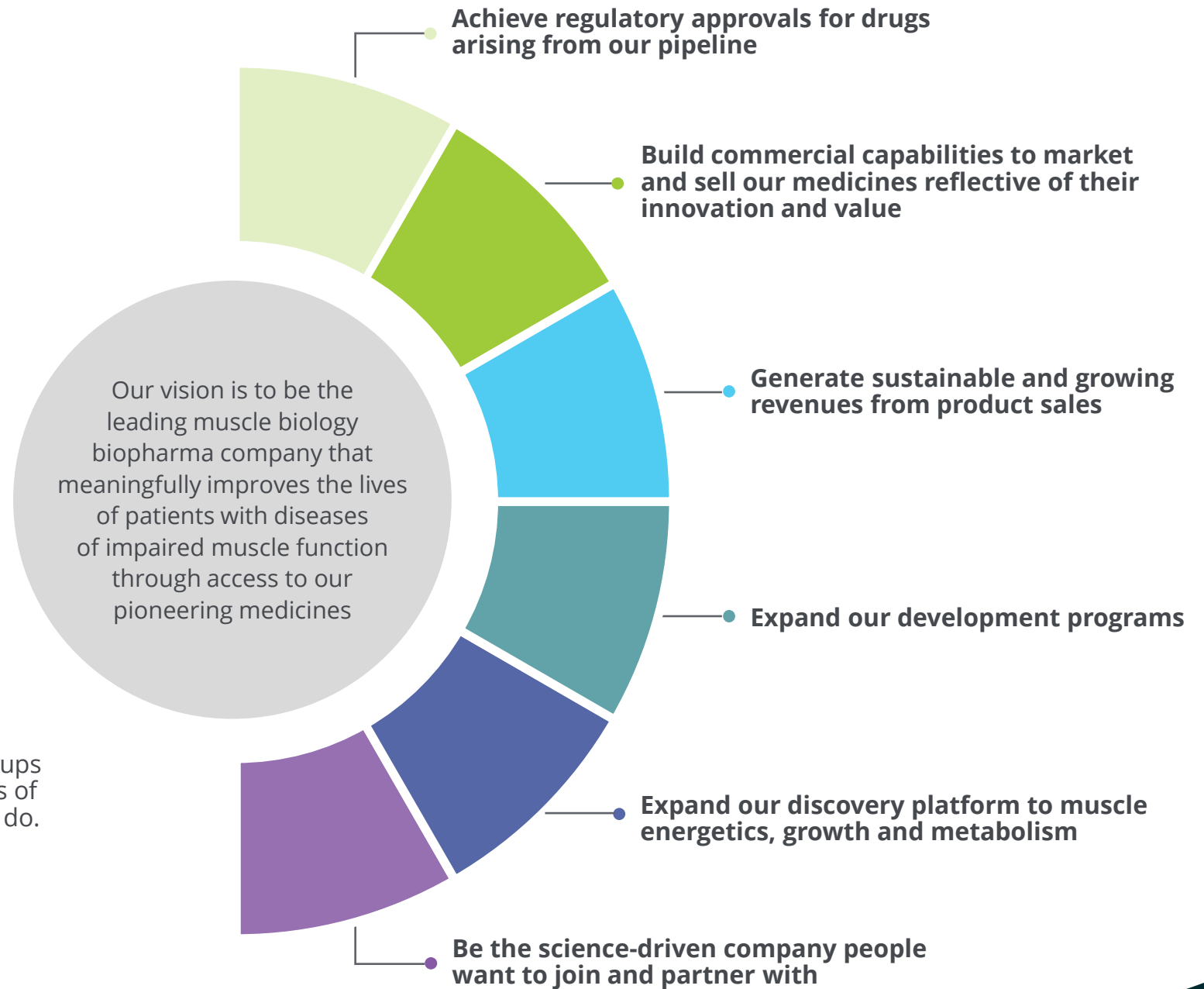
Our Mission

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 Great Place to Work; Uncommon Continuity of Team

VALUES



patients are
our North Star



science is
in our soul



we > me

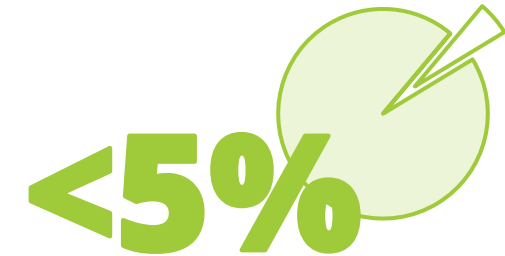


make it
happen

AWARDS



RETENTION



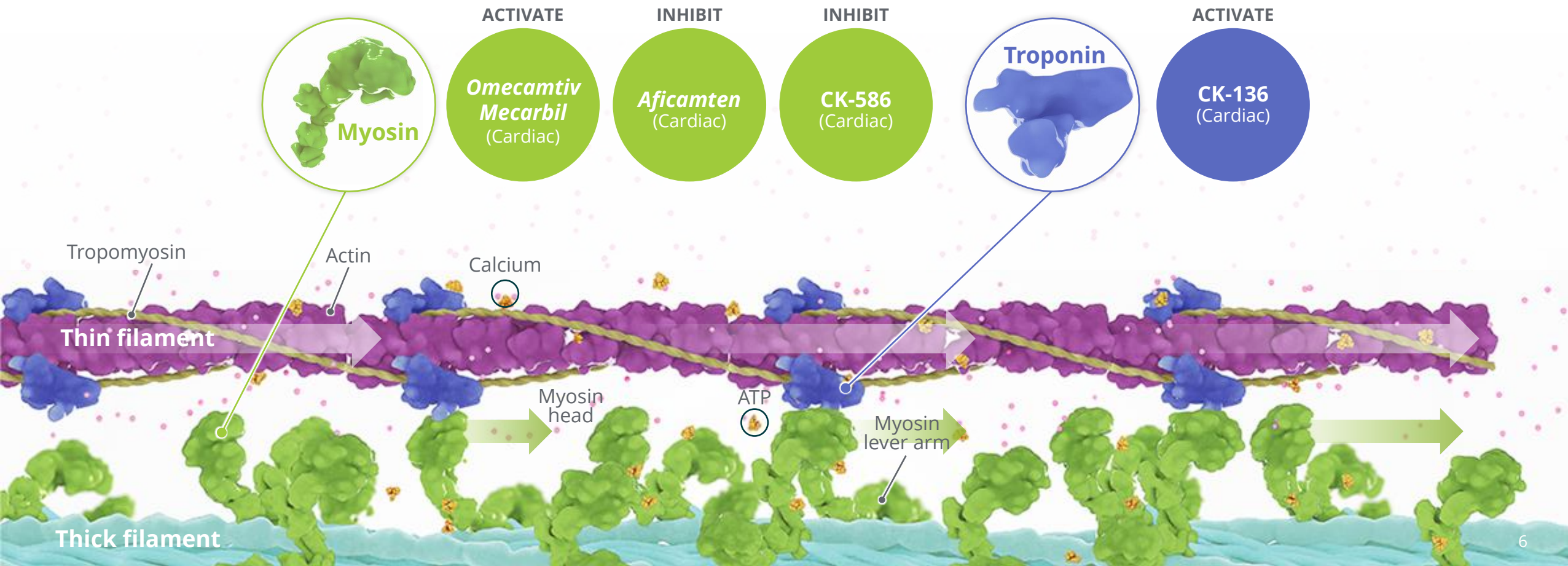
Turnover rate of leadership;
low attrition



Average tenure of leadership;
high continuity

Sarcomere Directed Drug Development

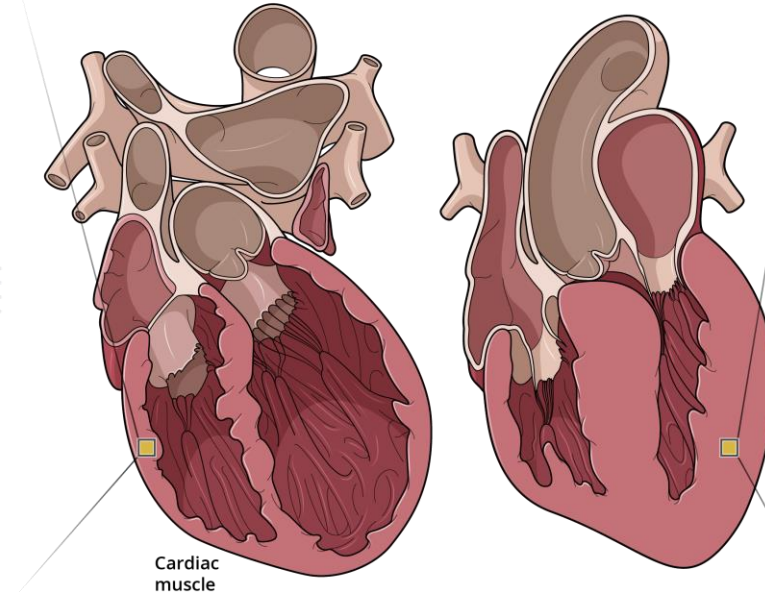
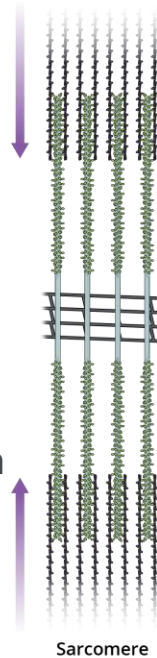
The sarcomere is a molecular structure found in skeletal and cardiac muscle that enables myocytes to contract and generate force



Contractile Dysfunction Underlies Cardiac Diseases

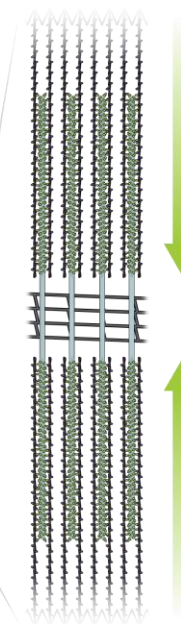
Decreased Cardiac Contractility

- Heart Failure with Reduced Ejection Fraction (HFrEF)
- Genetic Dilated Cardiomyopathy
- Pulmonary Hypertension with Right Ventricular Heart Failure



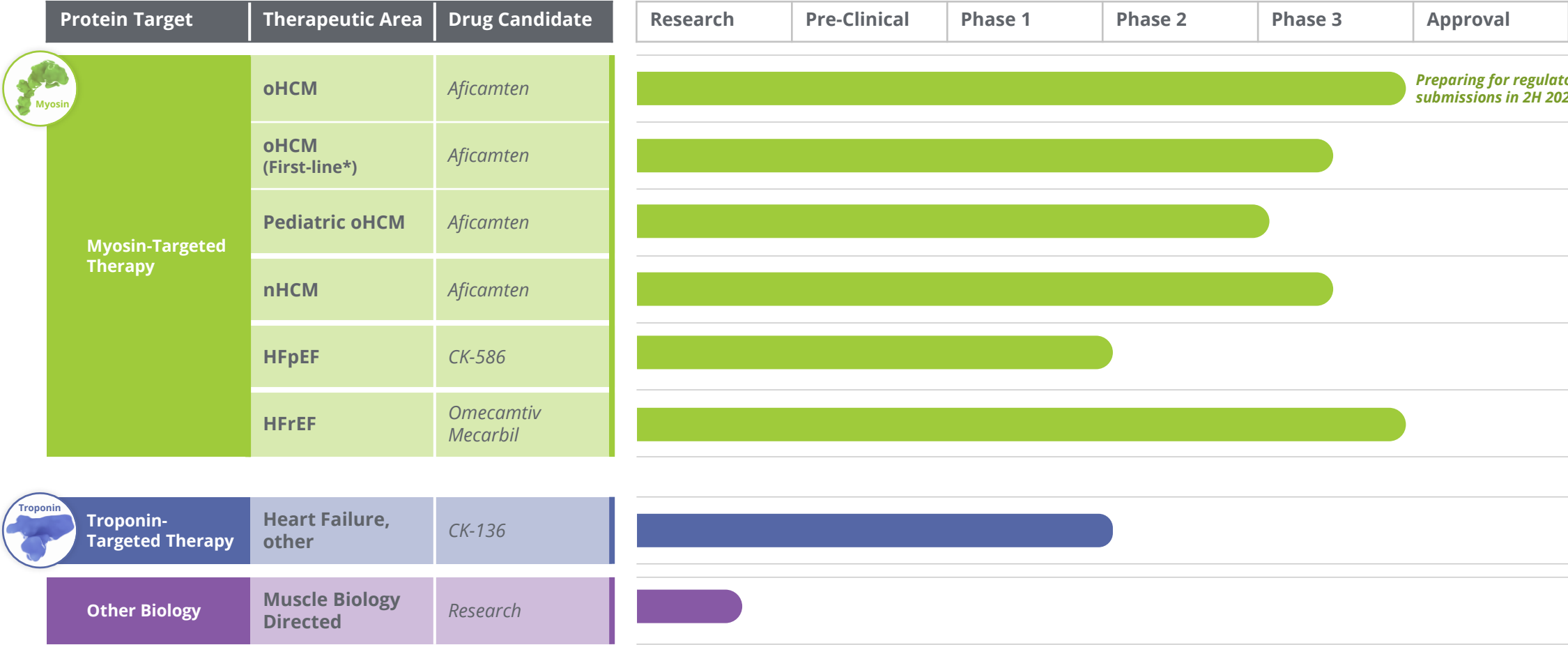
Increased / Preserved Cardiac Contractility

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



A Commitment to Muscle-Directed Cardiac Medicines

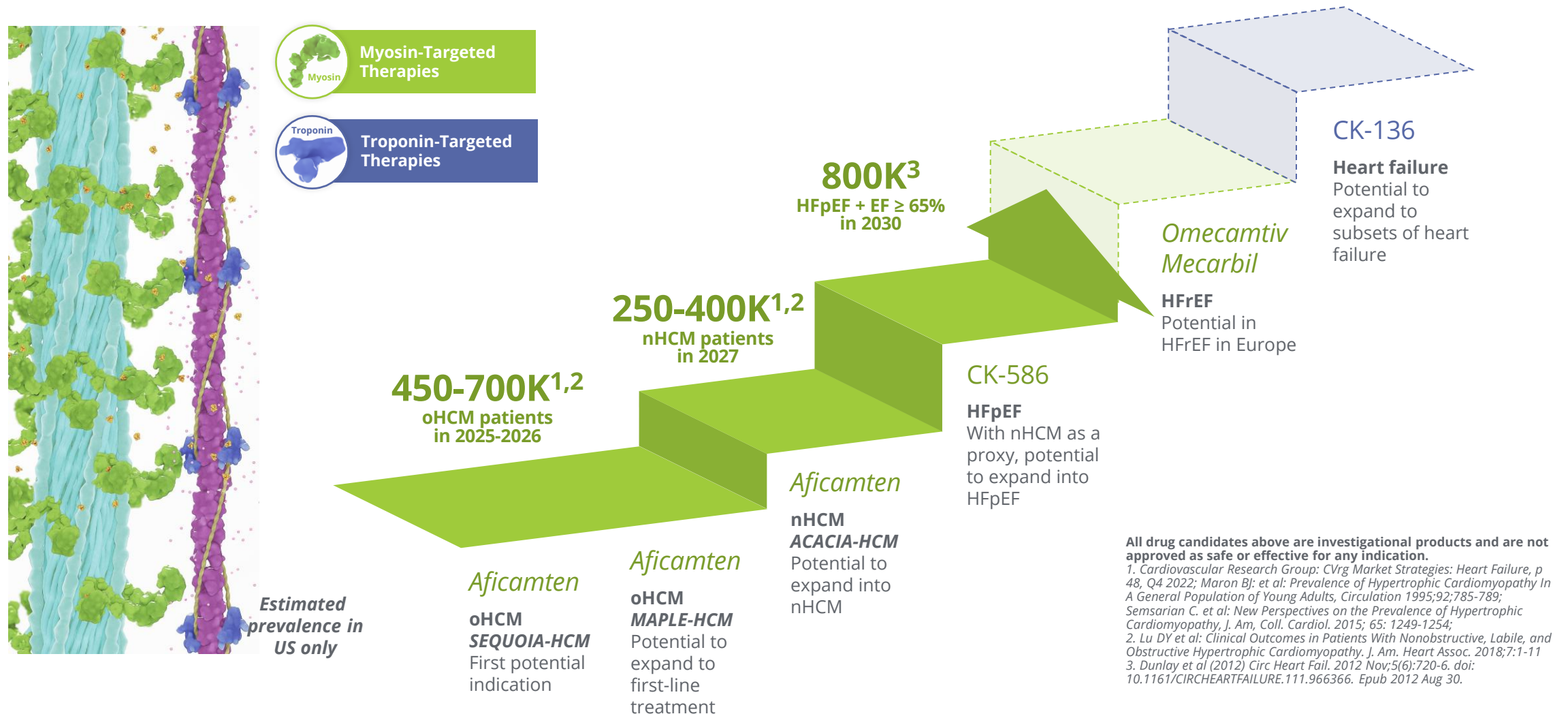
Building a specialty cardiology franchise anchored by *aficamten*



**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.

Building a Specialty Cardiology Franchise Anchored by *Aficamten*

Potential patient market for specialty cardiology franchise strategy

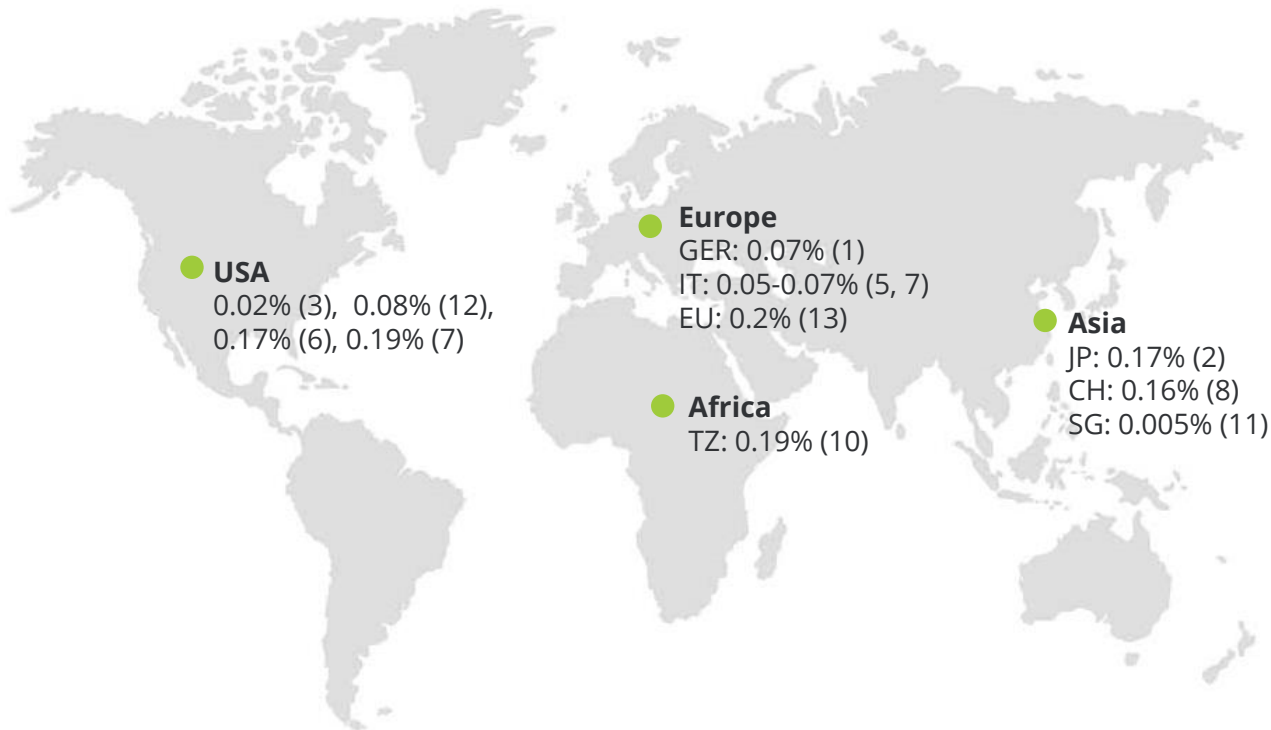


Aficamten

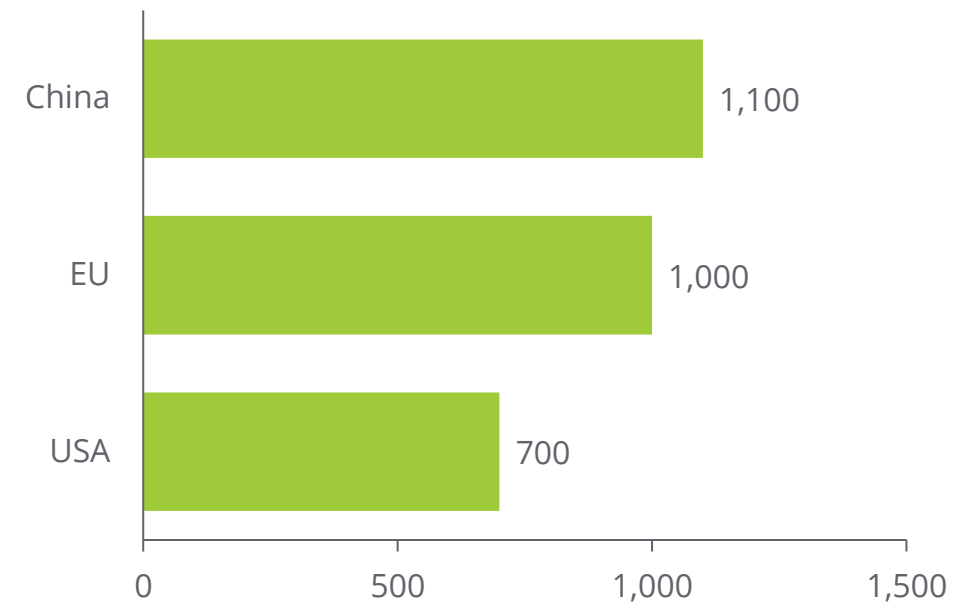
HCM Prevalence: Significant and Growing Globally

HCM prevalence estimates vary across geography and over time

Estimated HCM Prevalence Rates

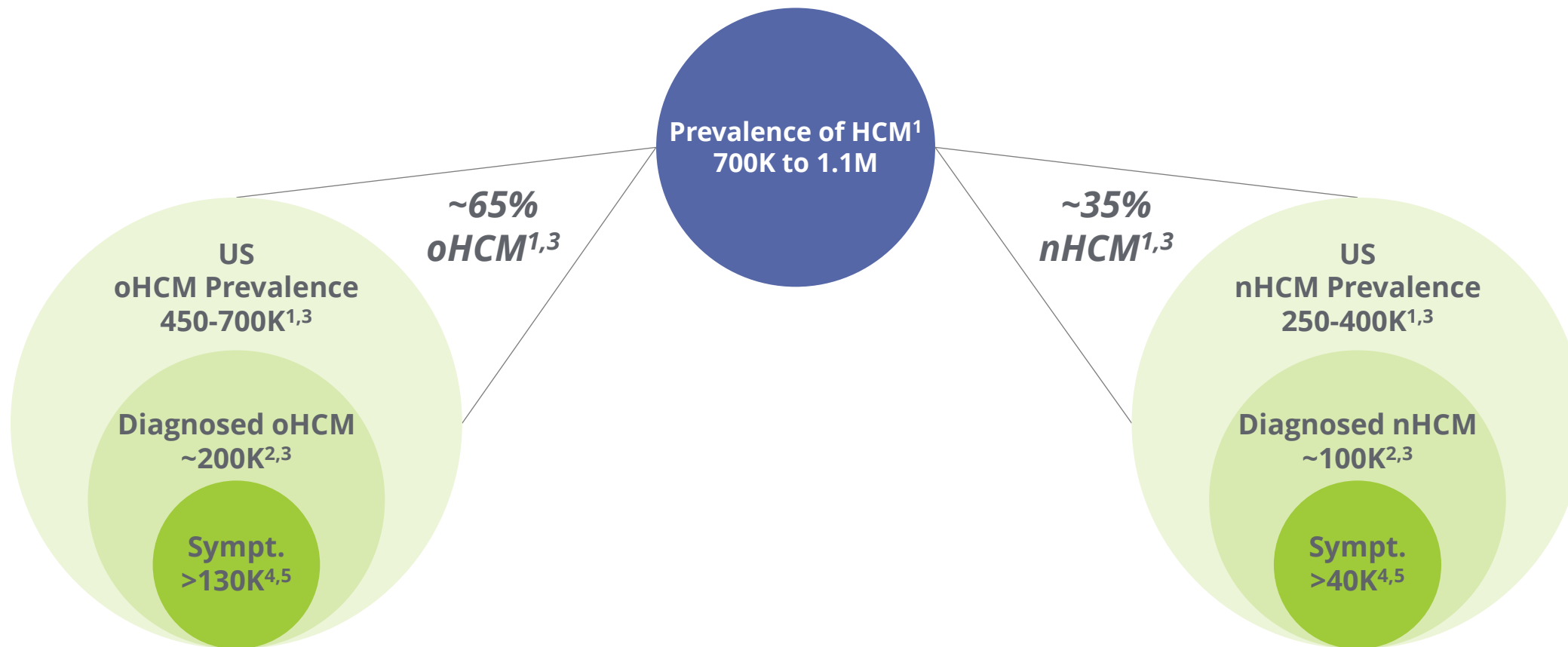


HCM True Patient Prevalence (Est. 2021)



Sources: 1. Husser et al 2018 doi.org/10.1371/journal.pone.0196612; 2. Hada et al [10.1016/s0002-9149\(87\)80107-8](https://doi.org/10.1016/s0002-9149(87)80107-8); 3. Codd 1989 [10.1161/01.cir.80.3.564](https://doi.org/10.1161/01.cir.80.3.564); 4. Maron et al 1995 [10.1161/01.cir.92.4.785](https://doi.org/10.1161/01.cir.92.4.785); 5. Corrado et al 1998 [10.1056/NEJM199808063390602](https://doi.org/10.1056/NEJM199808063390602); 6. Maron et al 1999 [10.1001/jama.281.7.650](https://doi.org/10.1001/jama.281.7.650); 7. Nistri et al 2003 [10.1016/s0002-9149\(03\)00132-2](https://doi.org/10.1016/s0002-9149(03)00132-2); 8. Zou et al 2004 [10.1093/aje/kwh090](https://doi.org/10.1093/aje/kwh090); 9. Maron 2004 <https://doi.org/10.1016/j.amjmed.2003.10.012>; 10. Maro 2006 [10.1258/004947506778604904](https://doi.org/10.1258/004947506778604904); 11. Ng et al 2011 [10.1093/europace/eur051](https://doi.org/10.1093/europace/eur051); 12. Butzner et al 2021 [10.1016/j.amjcard.2021.08.024](https://doi.org/10.1016/j.amjcard.2021.08.024); 13. Cardim et al 2011 [10.1016/j.repc.2011.09.005](https://doi.org/10.1016/j.repc.2011.09.005)

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

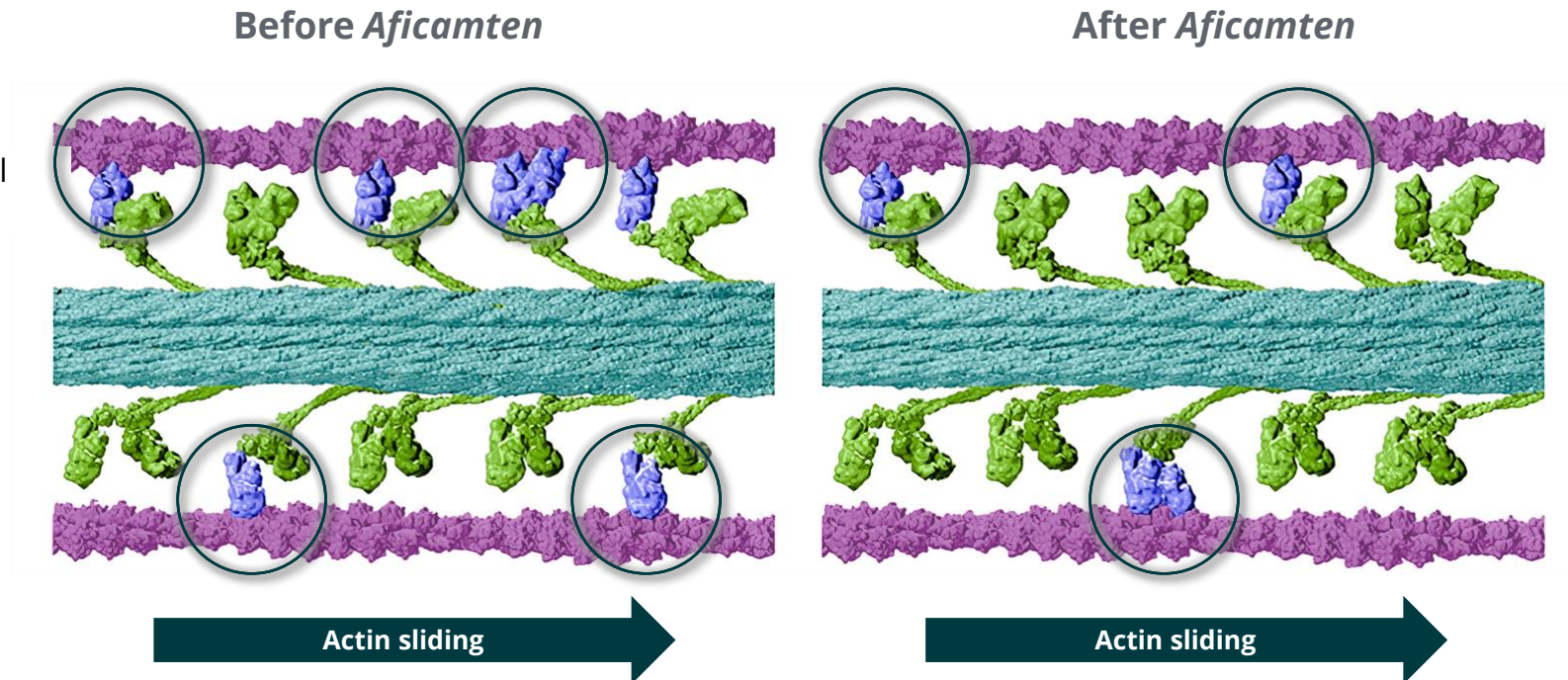
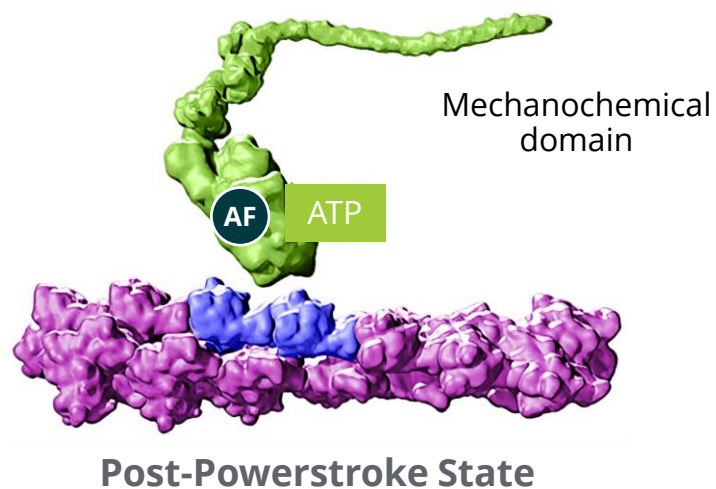
4. DoF: SHA Symphony PTD (Patient Transaction Data) includes any patients with symptoms in the last 2 years: angina, dyspnea, fatigue, palpitations, syncope, tachycardia; and/or treatments in the past 2 years: bb, ccb, dyso, ralo, Camzyos;

5. DoF Primary market research: 443 HCPs treating HCM - % of nHCM patients not considered under control with current SOC.

Aficamten: Mechanism of Action

Aficamten stabilized myosin in the released post-powerstroke state unable to hydrolyze ATP

“Fewer hands pulling on the rope”



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

Aficamten: Aspirational Target Profile

Potential next-in-class cardiac myosin inhibitor



**Rapid
onset**



**Rapid
reversibility**



**Speed to
optimal dose**



**Predictable
dose response**



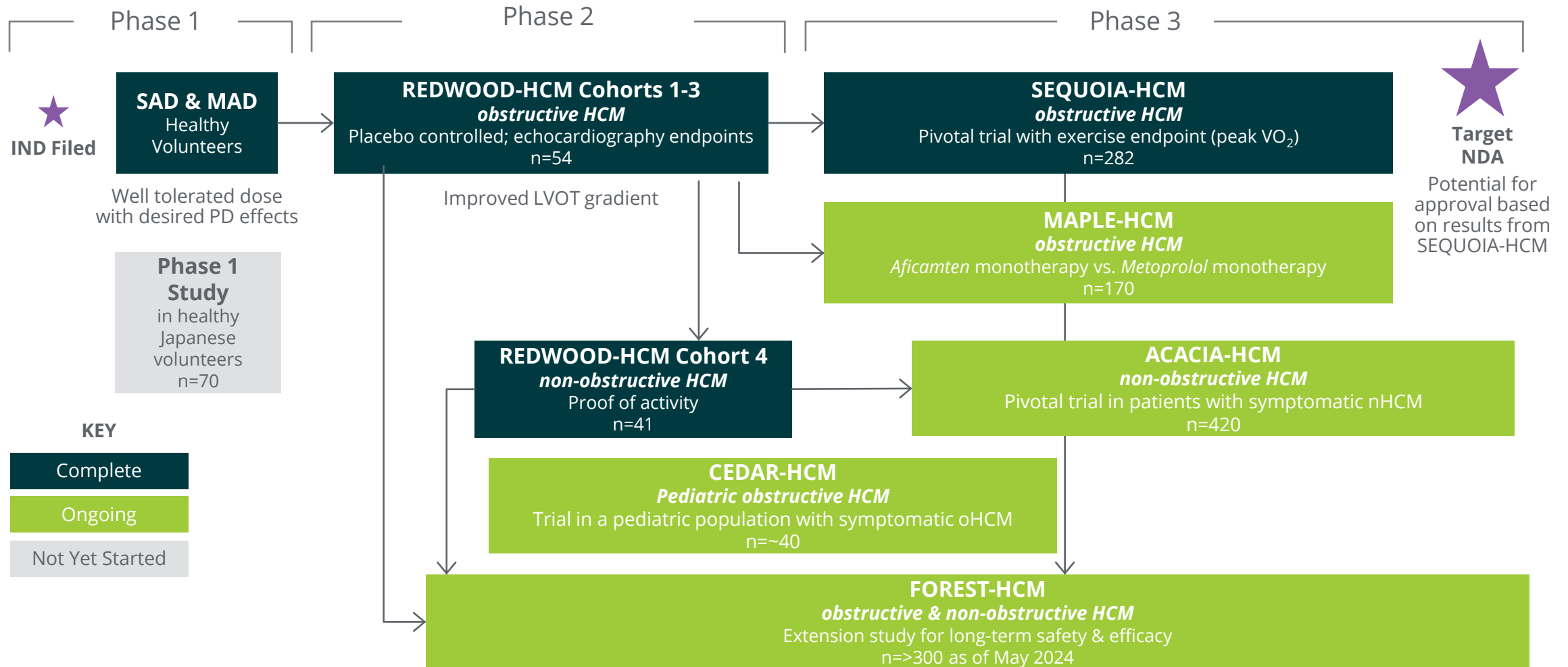
**No
teratogenicity**



**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.

Aficamten: Clinical Development Plan for HCM



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



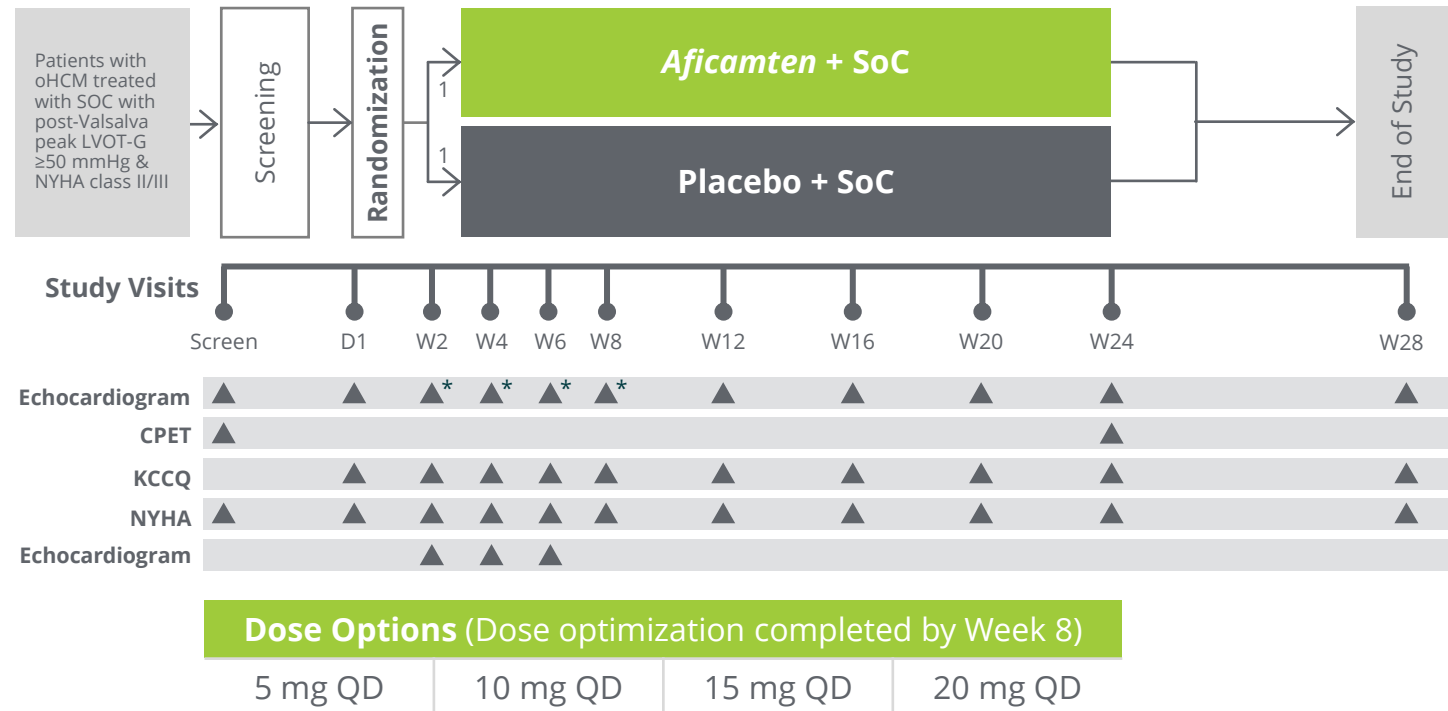
Primary endpoint: **Change in pVO₂ by CPET from baseline to Week 24**

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.

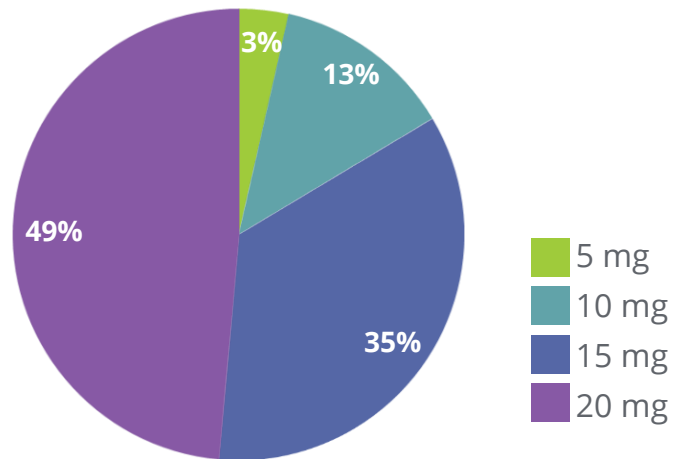
	Aficamten n=142	Placebo n=140
Background HCM therapy, n (%)		
Beta-blocker	86 (60.6)	87 (62.1)
Calcium channel blocker	45 (31.7)	36 (25.7)
Disopyramide	16 (11.3)	20 (14.3)
None	19 (13.4)	22 (15.7)
KCCQ-CSS	76 ± 18	74 ± 18
NYHA FC, n (%)		
II	108 (76.1)	106 (75.7)
III/IV	34 (23.9)	34 (24.3)
Median NT-proBNP (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: Dosing



**Aficamten dose at Week 8
(end of titration)**



There were no differences in age, sex, ethnicity, body mass index, or comorbidities (diabetes, hypertension or AF) between dose groups

Mean ± SD, n (%), or median (IQR)	Placebo n=140	5 mg n=5	10 mg n=18	15 mg n=49	20 mg n=68
% per treatment group	100%	3.5%	12.7%	34.5%	47.9%
Background HCM therapy					
Beta-blocker	87 (62.1)	5 (100.0)	10 (55.6)	31 (63.3)	40 (58.8)
Calcium channel blocker	36 (25.7)	1 (20.0)	3 (16.7)	17 (34.7)	24 (35.3)
Disopyramide	20 (14.3)	1 (20.0)	5 (27.8)	3 (6.1)	7 (10.3)
Baseline study assessments					
KCCQ-CSS	74 ± 18	68 ± 26	75 ± 19	77 ± 20	75 ± 17
NYHA class II	106 (75.7)	3 (60.0)	16 (88.9)	33 (67.3)	54 (79.4)
NT-proBNP, pg/mL	692 (335, 1795)	1133 (992, 1475)	338 (283, 674)	871 (428, 1505)	962 (511, 2085)
hs-cTnI, ng/L	12 (8, 25)	12 (6, 234)	10 (5, 17)	13 (7, 24)	16 (8, 38)
pVO ₂ , mL/kg/min	18.6 ± 4.5	18.7 ± 2.9	18.6 ± 3.9	18.2 ± 4.1	18.3 ± 4.9
Echocardiographic parameters (core laboratory)					
LVEF at baseline, %	75 ± 6	71 ± 12	76 ± 5	75 ± 5	75 ± 5
Peak LVOT-G at rest	55 ± 32	29 ± 13	45 ± 21	56 ± 24	58 ± 30
Peak LVOT-G post-Valsalva	83 ± 33	51 ± 24	71 ± 29	84 ± 26	88 ± 35
Left ventricular MWT, cm	2.10 ± 0.30	2.42 ± 0.74	1.94 ± 0.22	2.04 ± 0.26	2.11 ± 0.28

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hs-cTnI, high-sensitive cardiac troponin; IQR, interquartile range; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary score; MWT, maximal wall thickness; NT-proBNP, N-terminal pro b-type natriuretic peptide; NYHA, New York Heart Association. Coats CJ. "Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.

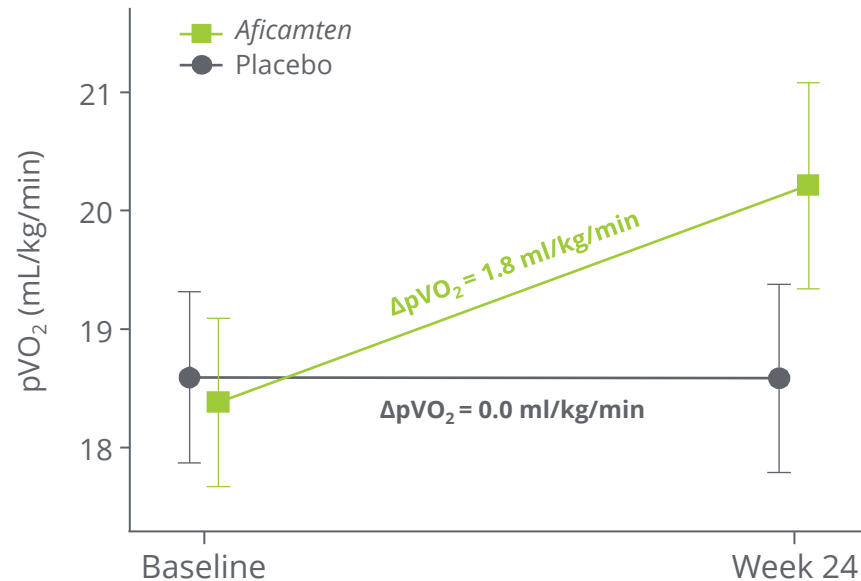
SEQUOIA-HCM: Primary Endpoint

Significant improvement in exercise capacity compared to placebo

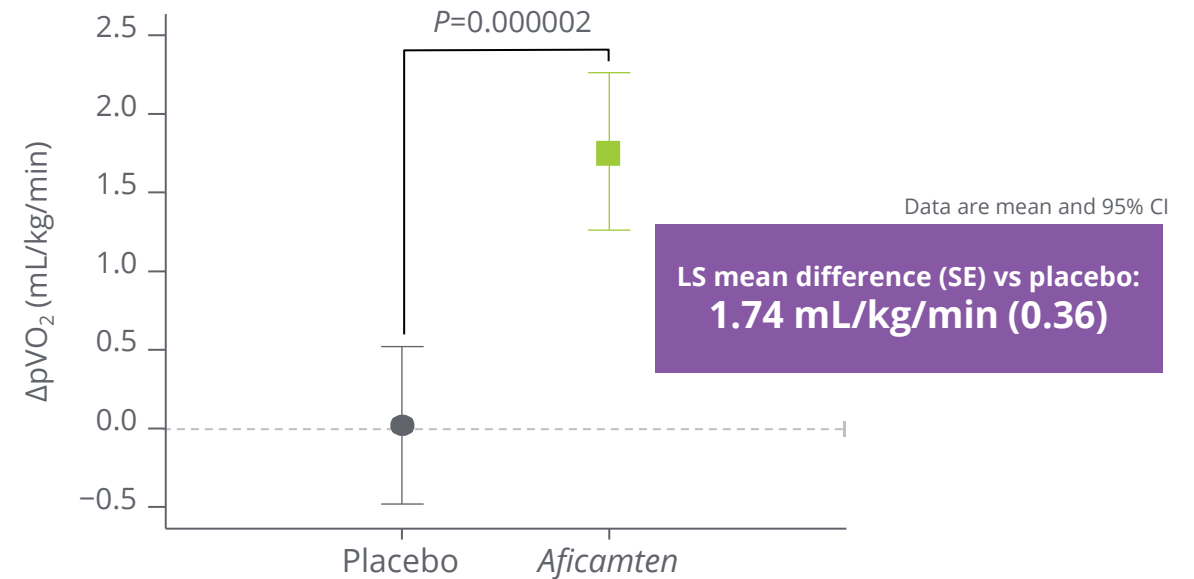


Results presented at Heart Failure 2024 and published in *NEJM*

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

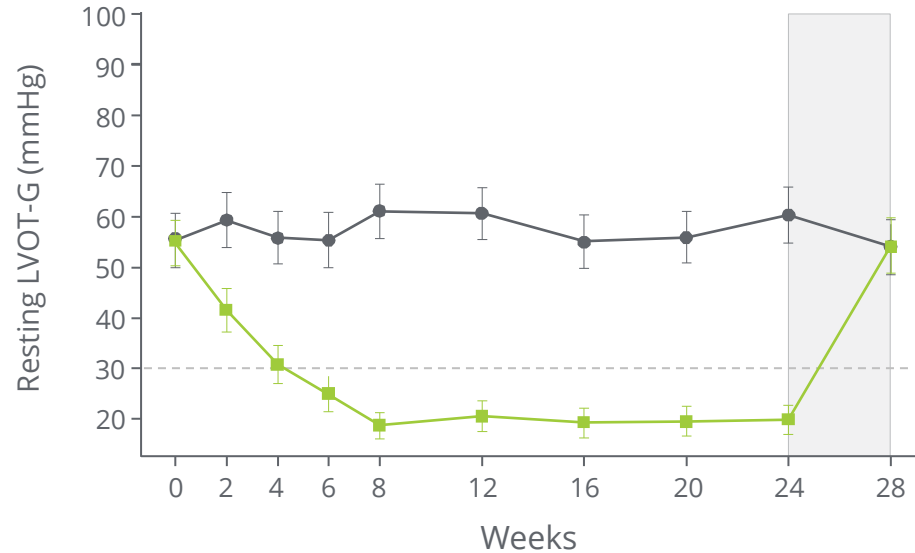
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SEQUOIA-HCM: Secondary & Exploratory Endpoints

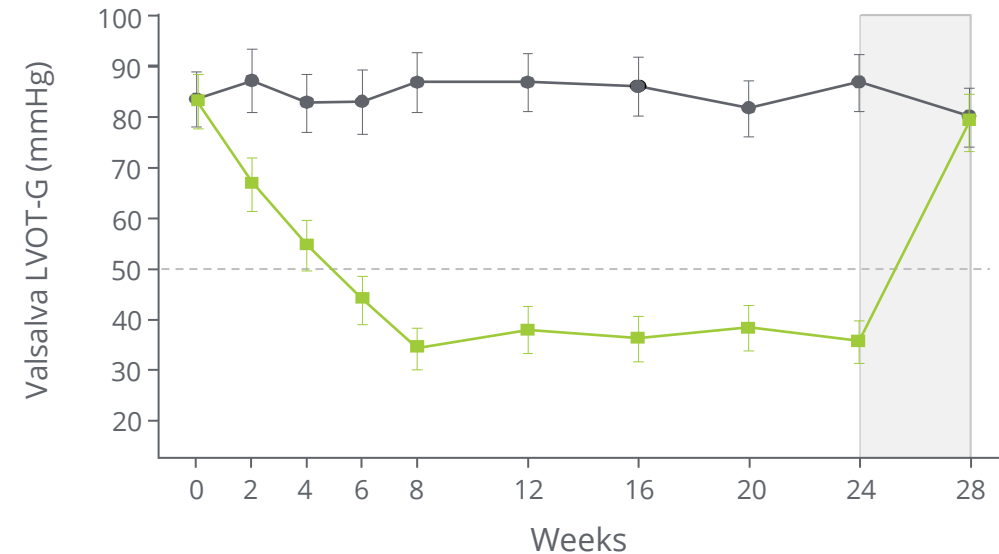


Significant improvement in post-Valsalva left ventricular outflow tract gradient (LVOT-G)

Resting LVOT-G



Valsalva LVOT-G



LS mean difference:
- 50 mmHg

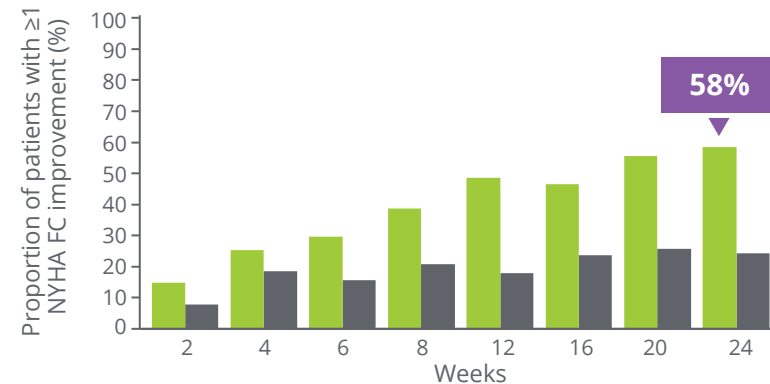
■ Aficamten
● Placebo
■ Washout

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.

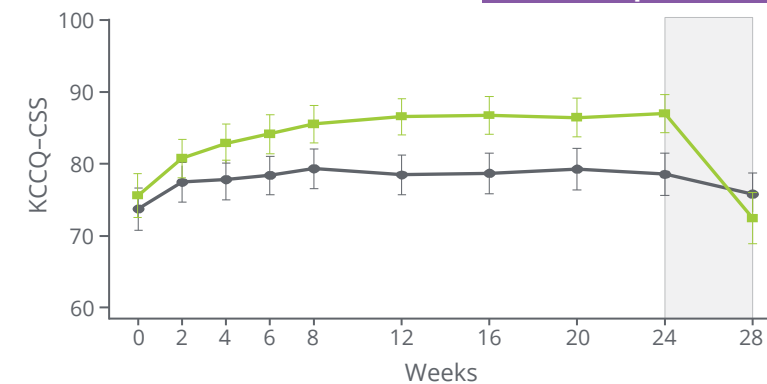
SEQUOIA-HCM: Secondary & Exploratory Endpoints



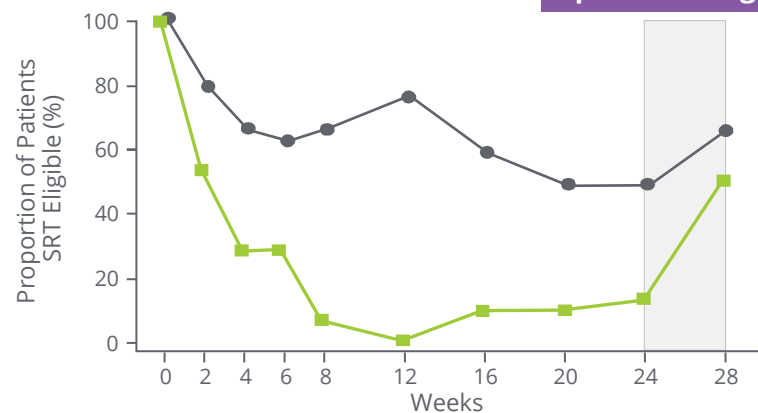
≥1 NYHA FC Improvement



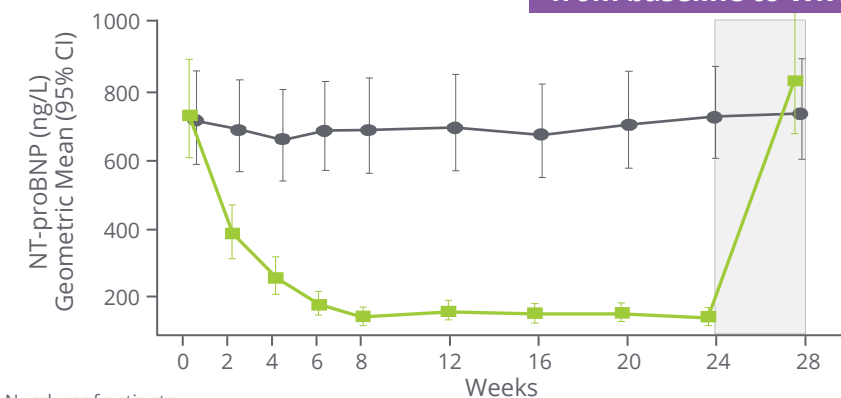
KCCQ-CSS



Guideline Eligibility for SRT



NT-proBNP



■ 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.

Number of patients

	0	2	4	6	8	12	16	20	24	28
Aficamten	139	141	141	139	139	139	137	139	136	135
Placebo	138	138	139	136	137	135	135	137	134	135

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 pVO ₂ and ≥ 1 NYHA FC improvement <i>or</i> ≥ 3.0 mL/kg/min increase in pVO ₂ 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)
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)

AEs with ≥5% incidence

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

^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.

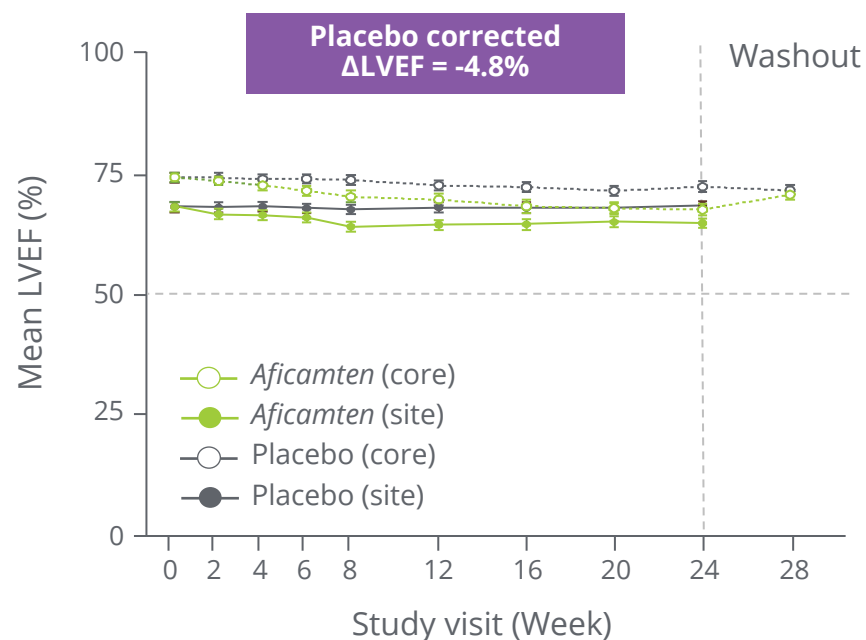
Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

SEQUOIA-HCM: Change in LVEF

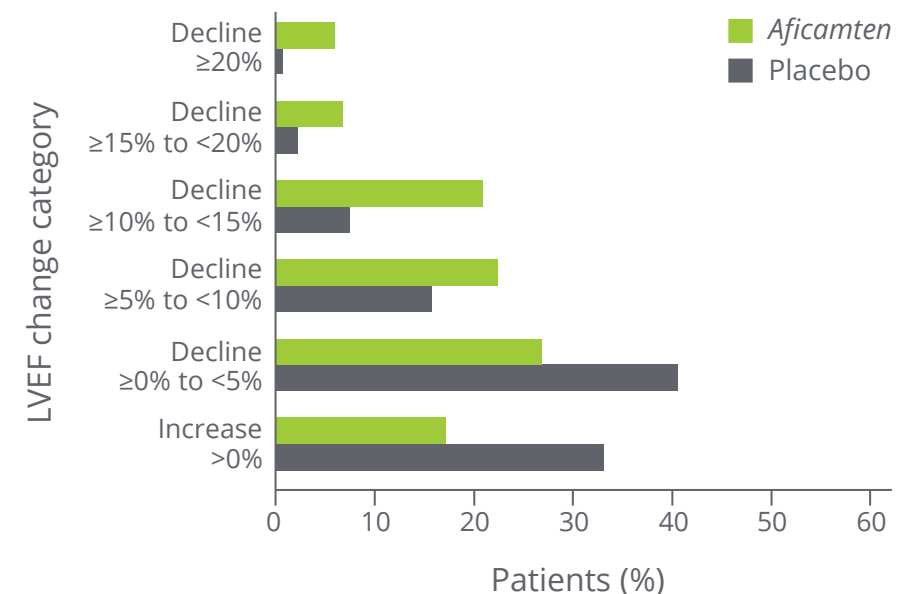


Modest reduction in LVEF in patients on *aficamten* resulted in large reductions in LVOT-G

Mean Change in Core Laboratory LVEF Over 24 Weeks



Distribution of Categorical Changes in Core Laboratory LVEF from Baseline to Week 24

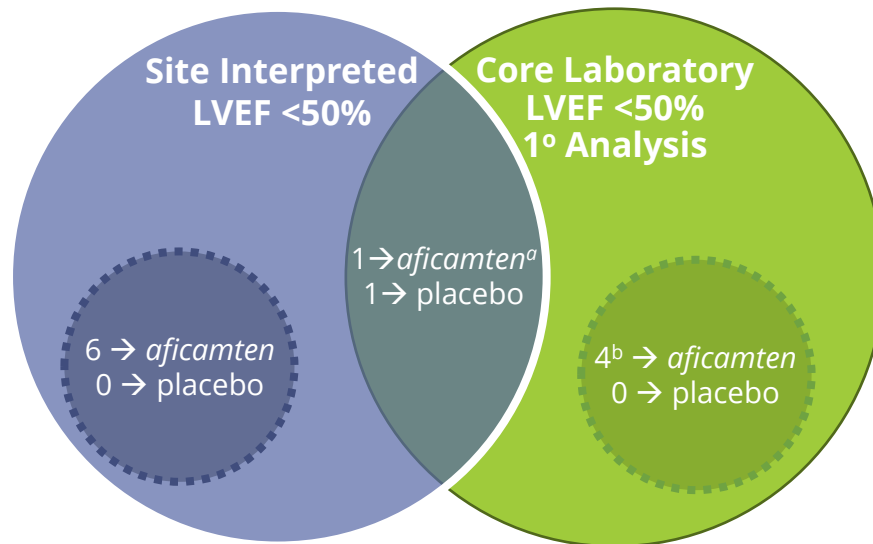


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Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

SEQUOIA-HCM: Low Incidence of LVEF <50%



5 (3.5%) of patients on *aficamten* had LVEF <50% determined by the core laboratory



^a COVID-19 infection preceded LVEF <50% based on both core and site laboratory assessments.

^b Did not undergo dose adjustment (3.5%)

- **No treatment interruptions** occurred
- **No heart failure** was experienced by any *aficamten*-treated patient with LVEF <50% by either core laboratory or site interpreted
- All *aficamten* patients with LVEF <50% were **reversible**

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

SEQUOIA-HCM: Low Overall Incidence of LVEF <50%

Core lab LVEF was prespecified source for statistical analyses



LVEF <50% assessed at 3.5% by core lab and 4.9% by site

Prespecified Analysis

Core Lab Only LVEF <50%

4 *aficamten* patients

Age, y, Sex	Aficamten Dose, mg/d	BL Core LVEF, %	Study Week With Lowest Core LVEF	Lowest Core LVEF %	Matching Site LVEF %	NYHA Class	KCCQ-CSS	NT-proBNP, Change from BL, ng/dL	Down-Titration, mg	Next Visit LVEF Core	Matching Site LVEF %
30 M	20	65	8	48	62	1	+21	-535	N/A	56	65
57 F	5	56	24	46	60	2	+14	-372	N/A	51	NR
72 F	15	80	20	48	52	1	+5	-403	N/A	52	51
57 F	20	84	16	43	59	1	+12	-921	N/A	72	68

Both Core & Site-Read LVEF <50%

1 *aficamten* patient

1 placebo patient

75 F	Placebo	53	6	48	45	3	+29	-291	N/A	50	51
72 F *	15	63	16	34	49	2	+14	111	15 to 10	55	51

Site-Read Only LVEF <50%

6 *aficamten* patients

Age, y, Sex	Aficamten Dose, mg/d	BL Core LVEF, %	Study Week With Lowest Site LVEF	Lowest Site LVEF %	Matching Core LVEF %	NYHA Class	KCCQ-CSS	NT-proBNP, Change from BL, ng/dL	Down-Titration, mg	Next Visit LVEF Core	Matching Site LVEF %
41 M	20	70	16	47	59	2	+2	-1597	20 to 15	54	50
52 M	20	69	16	46	51	1	+25	-712	20 to 15	60	50
76 F	15	87	16	48	53	3	+22	-44	15 to 10	52	50
59 M	15	77	12	48	70	2	+10	-1482	15 to 10	60	55
54 M	15	76	8	49	72	1	+31	-162	15 to 10	60	54
66 M	20	76	20	45	53	3	+8	-83	20 to 15	61	60

* COVID-19 infection preceded LVEF <50% based on both core and site laboratory assessments.

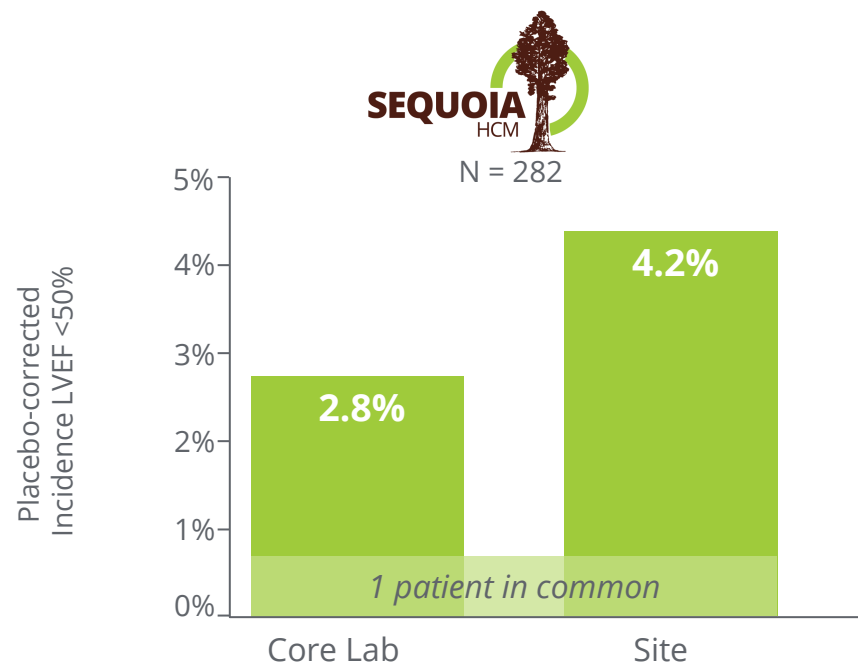
NR = not recorded, site LVEF were not obtained following Week 24 per protocol

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

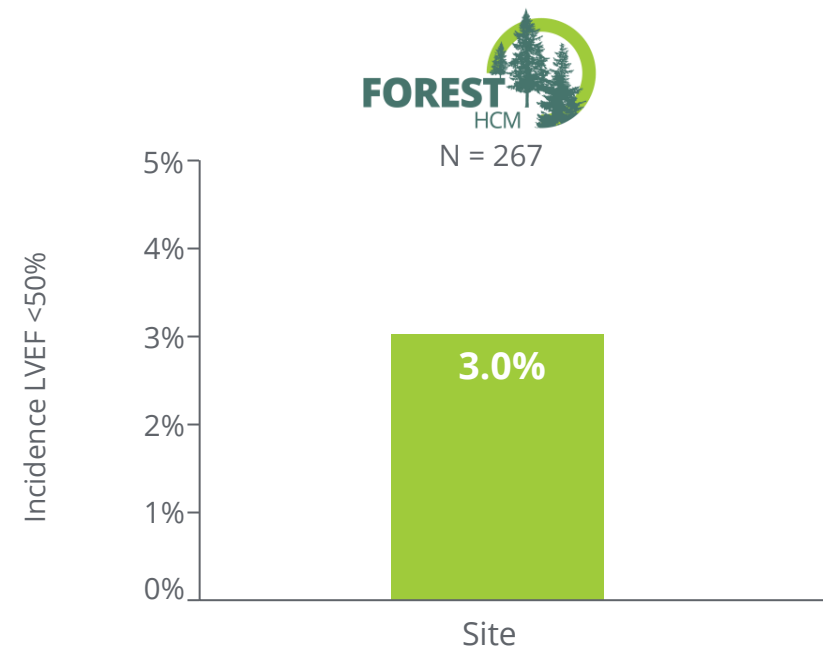
Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

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

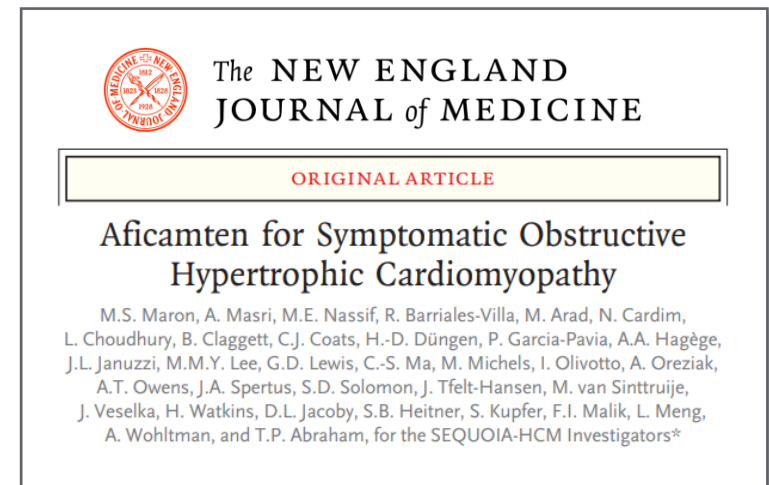
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.
SEQUOIA-HCM Source: Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.
FOREST-HCM Source: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

SEQUOIA-HCM: Conclusions



Trial underscores potential clinical efficacy & safety of *aficamten* in patients with symptomatic oHCM

- Patients treated with *aficamten* observed to have:
 - **Clinically meaningful improvements in exercise capacity (pVO₂), consistent across all prespecified subgroups**
 - **Significant reduction in the burden of limiting symptoms** based on improvement in KCCQ-CSS and NYHA Functional Class
- ***Aficamten* was generally well-tolerated with low frequency of LVEF <50%, all asymptomatic, with no treatment interruptions and no instances of worsening HF**
- **Functional & symptomatic improvements associated with benefits as early as 2 weeks; remained consistent & durable throughout treatment period:**
 - Substantial relief from resting and provokable LVOT obstruction observed
 - Large reductions in cardiac biomarker NT-proBNP observed
 - Considerable reduction in the number of patients eligible for SRT observed
- **Treatment effects were reversible within the 4-week washout period**



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Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy". ESC Heart Failure 2024.
Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.
Lewis G. Enhancing Exercise Response in Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

Preparing for Regulatory Submissions to FDA, EMA



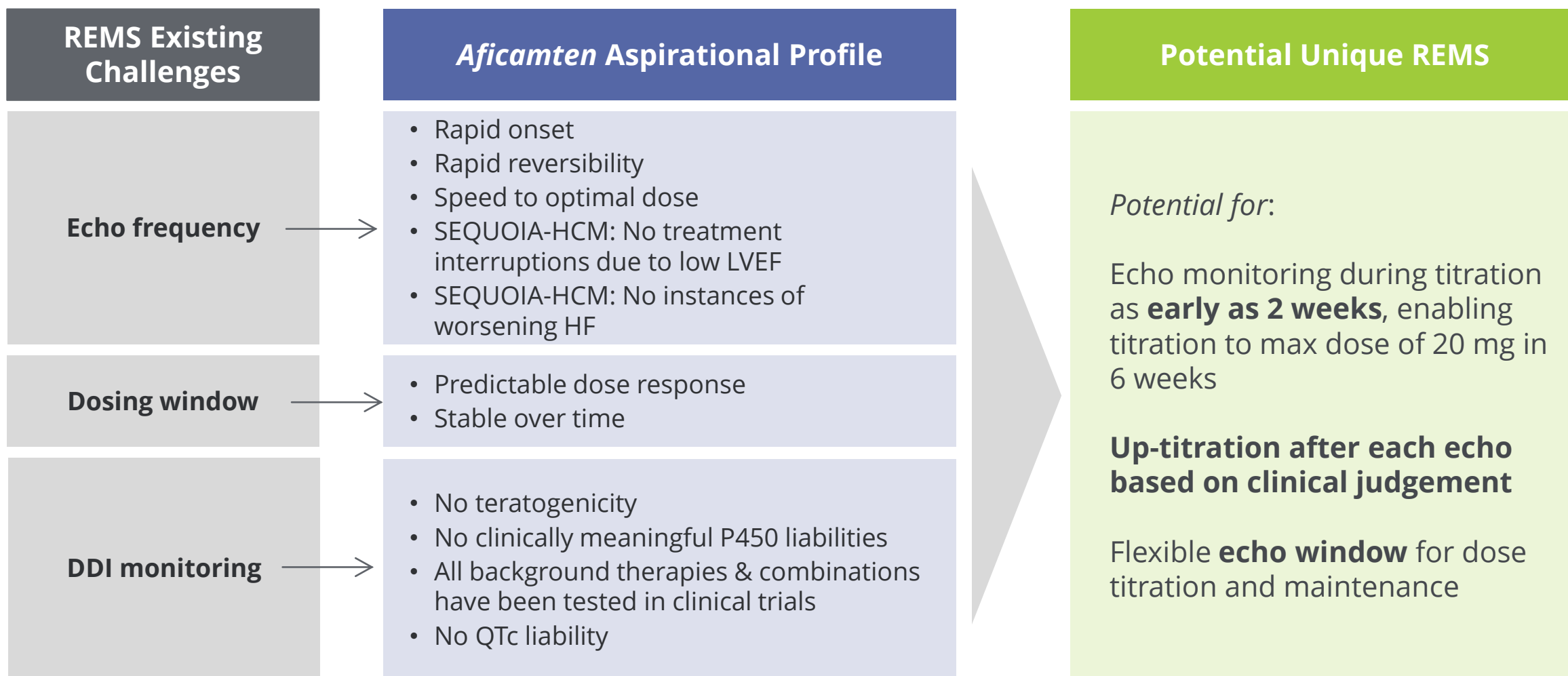
Positive Results from
SEQUOIA-HCM

2024

- Participated in **two meetings with FDA** in Q1 2024
- **Type B meeting with FDA** to occur 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



Few Dose Reductions Occurred During Maintenance

FOREST-HCM data cut as of September 15, 2023



Dose Titration Phase

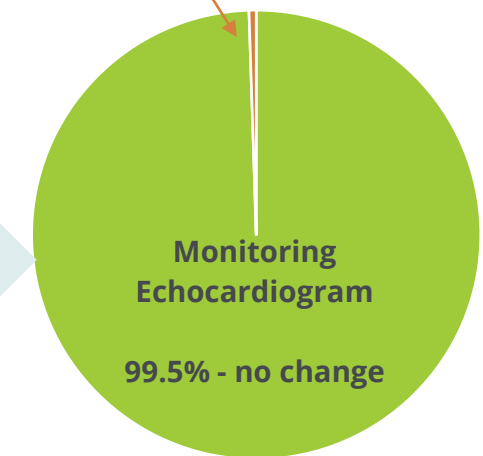
- No treatment-related LVEF <50% during the titration period
- Of the 94 patients having completed the titration period, **~2/3 are receiving 15 and 20 mg qd**
- Approximately 30% of patients have **reduced doses or discontinued background therapy** at the discretion of the treating physician and/or request from the patient

Maintenance Phase

- 579 monitoring echocardiograms completed* in oHCM patients
- **None with LVEF <40%** requiring treatment interruption
- 3 patients (0.5%) with LVEF <50%
 - Two asymptomatic patients (LVEF of 47% and 49%) resulting in per-protocol dose reduction
 - One patient with atrial fibrillation (unrelated) and LVEF of 47%
- All 3 patients are currently receiving *aficamten* with apparent relief from obstruction, symptoms & improved biomarkers

Down-titration triggered

0.5%



Target dose defined as achieved if Valsalva LVOT-G \leq 30 mmHg or no dose change for 2 consecutive visits

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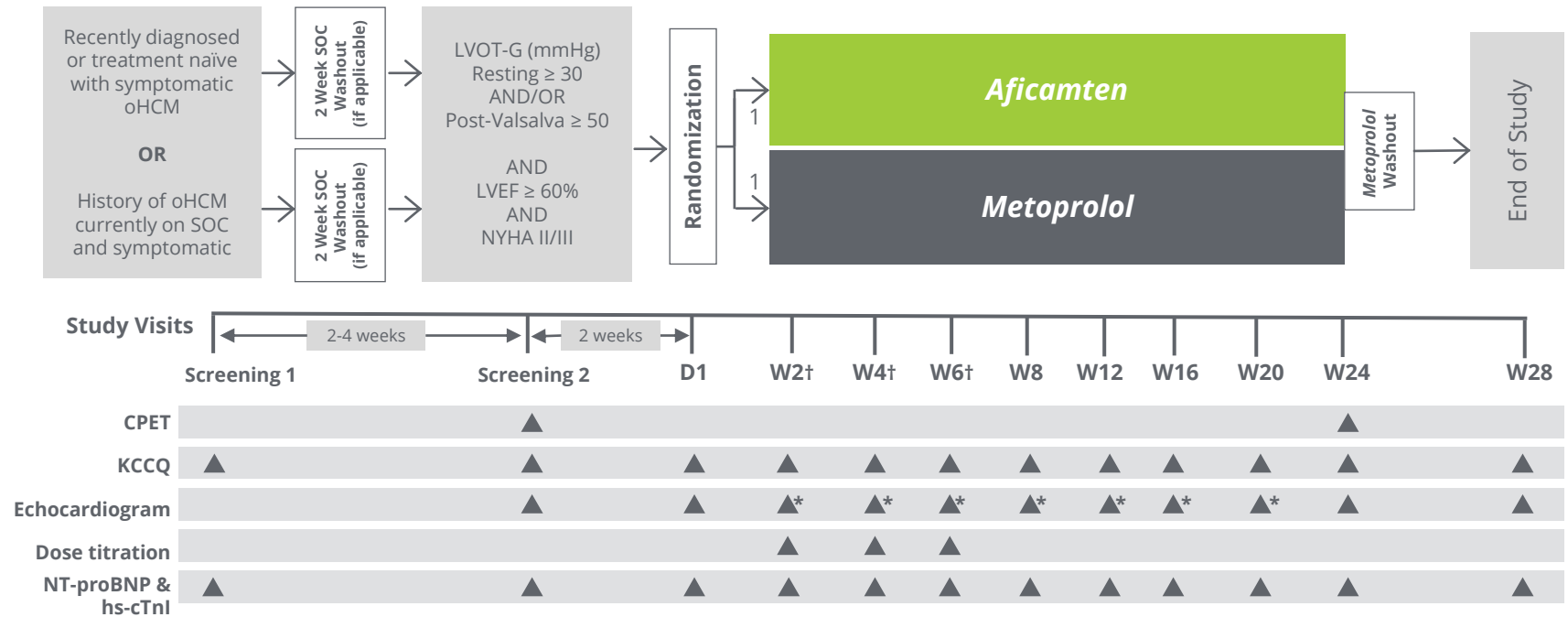
MAPLE-HCM: Phase 3 Monotherapy Trial

Currently enrolling



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

- Trial to enroll approximately **170 patients**
- Primary endpoint: **change in peak VO_2 , assessed by CPET from baseline to Week 24**
- Secondary endpoints: **change in NYHA class, KCCQ, NT-proBNP, and measures of structural remodeling**



SOC: standard of care
*Focused echocardiogram

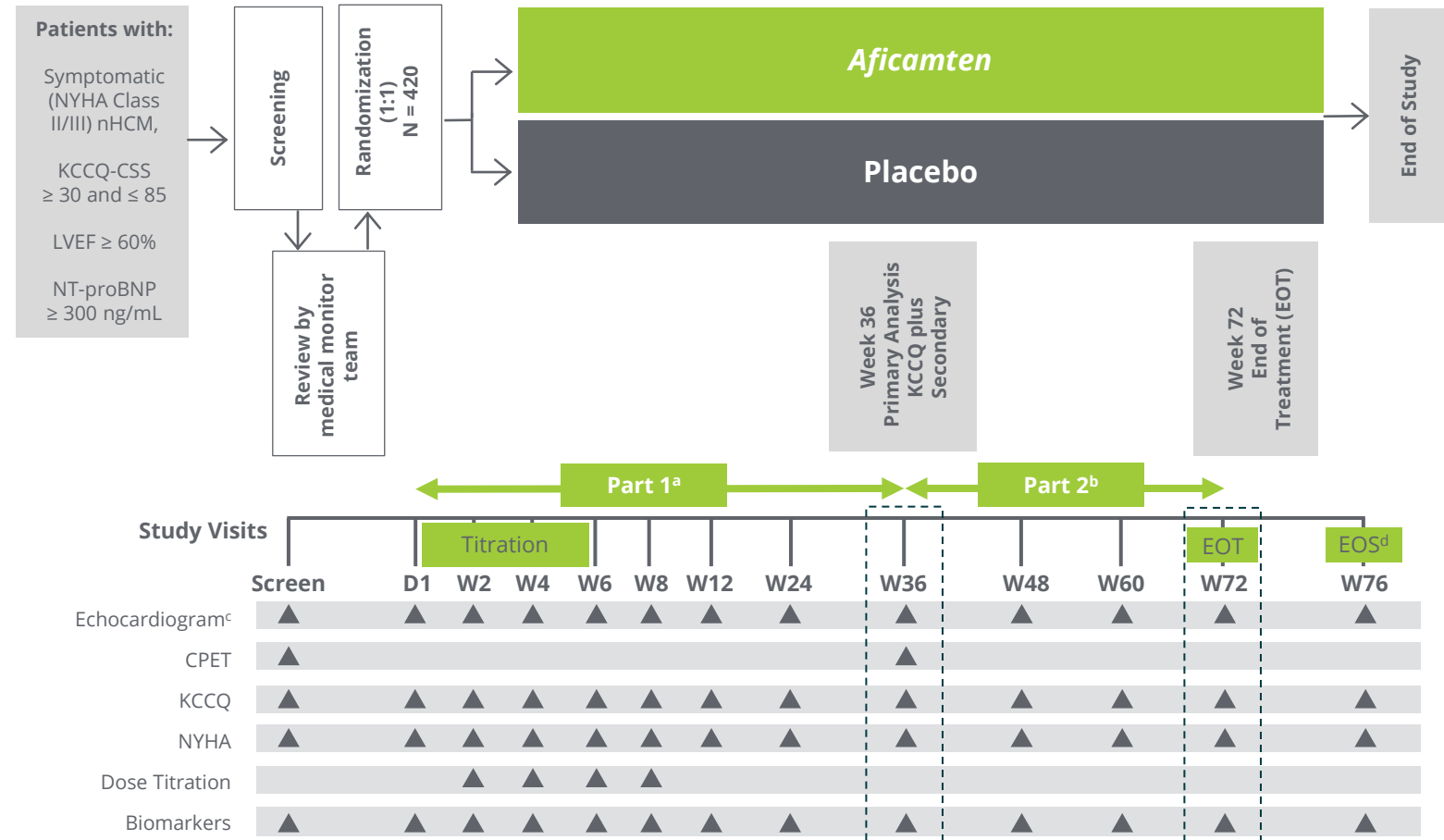
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

ACACIA-HCM: Pivotal Phase 3 Trial in nHCM

Currently enrolling



- Trial to enroll approximately **420 symptomatic nHCM patients**
- Primary endpoint: **change in KCCQ Clinical Summary Score** from baseline to Week 36
- **5-20 mg doses**; 6-week titration period
- Secondary endpoints:
 - Change in pV_{O_2} , Ve/VCO_2 ,
 - Left atrial volume index (LAVI)
 - NT-proBNP
 - Proportion of patients with ≥ 1 class improvement in NYHA from baseline to Week 36
 - Time to first cardiovascular event



^a Part 1: All participants followed until week 36

^b Part 2: Participants completing Week 36 continue until either Week 72 (followed by EOS at Week 76) OR the last randomized participant in Part 1 completes Week 36.

^c Site-read focused echocardiogram for titration visit (sole criterion). *Aficamten* dose range 5-20 mg.

^d 4-week follow up after last dose

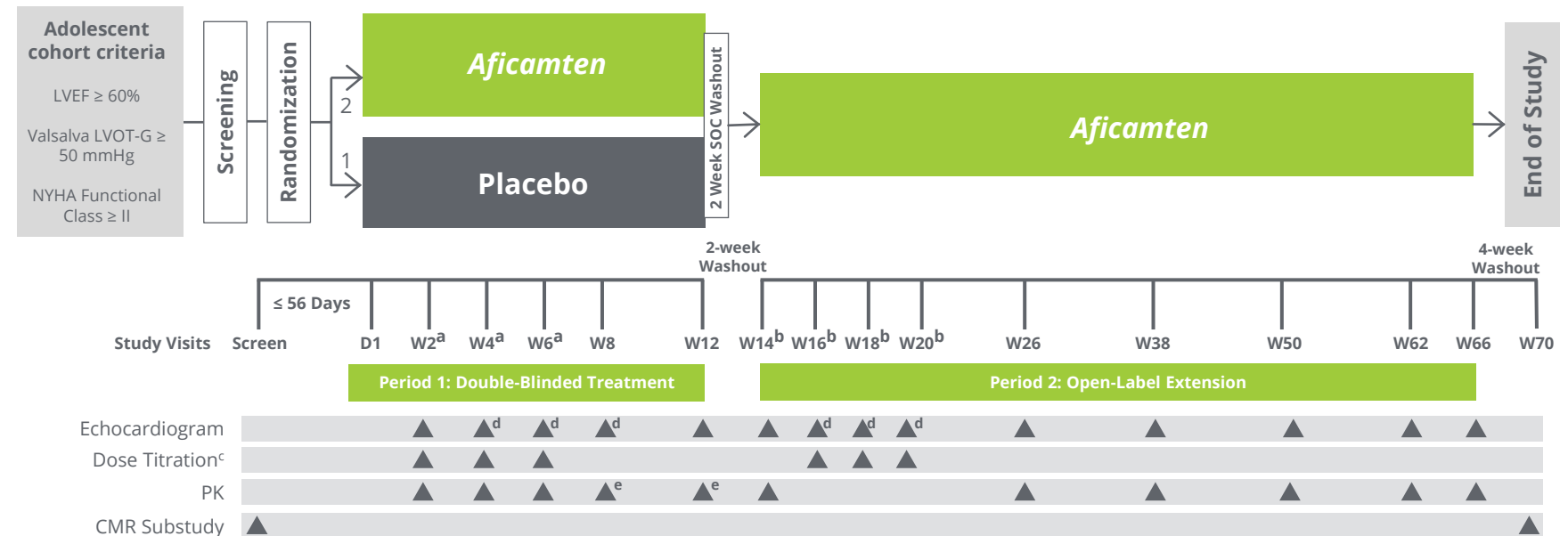
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

CEDAR-HCM: Clinical Trial in Pediatric Population

Currently enrolling



- Expected to enroll initial cohort of **~40 adolescent patients aged 12 to 17**
- Data from adolescent patients will support decision to enroll **cohort of ~8 to 10 patients aged 6 to 11**
- 5-20 mg doses; 6-week titration period**
- Primary endpoint: **change in LVOT-G** from baseline to Week 12
- Secondary endpoints: **change in resting LVOT-G, NYHA Functional Class, pharmacokinetics & cardiac biomarkers**



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^a Up-titration to the next dose in Period 1 will be managed by the IRT system and will only occur if Valsalva LVOT-G is ≥ 30 mmHg and biplane LVEF is $\geq 55\%$

^b In Period 2, participants will start dosing with aficamten at the lowest dose (5 mg) and up-titration to the next dose (10, 15, or 20 mg) will be managed by the Principal Investigator or designee if Valsalva LVOT-G is ≥ 30 mmHg and biplane LVEF is $\geq 55\%$. Up-titrations may occur no more frequently than every 2 weeks

^c Additional ad hoc titrations after Week 20 may occur at ad hoc titration visits (at least 2 weeks apart) or during a planned visit (ie, Weeks 26, 38, 50, or 62). A titration follow-up visit is required 2 weeks after any titration occurring after Week 20

^d Focused echocardiogram (LVOT-G and LVEF only)

^e Intensive PK substudy may occur at Week 8 or Week 12

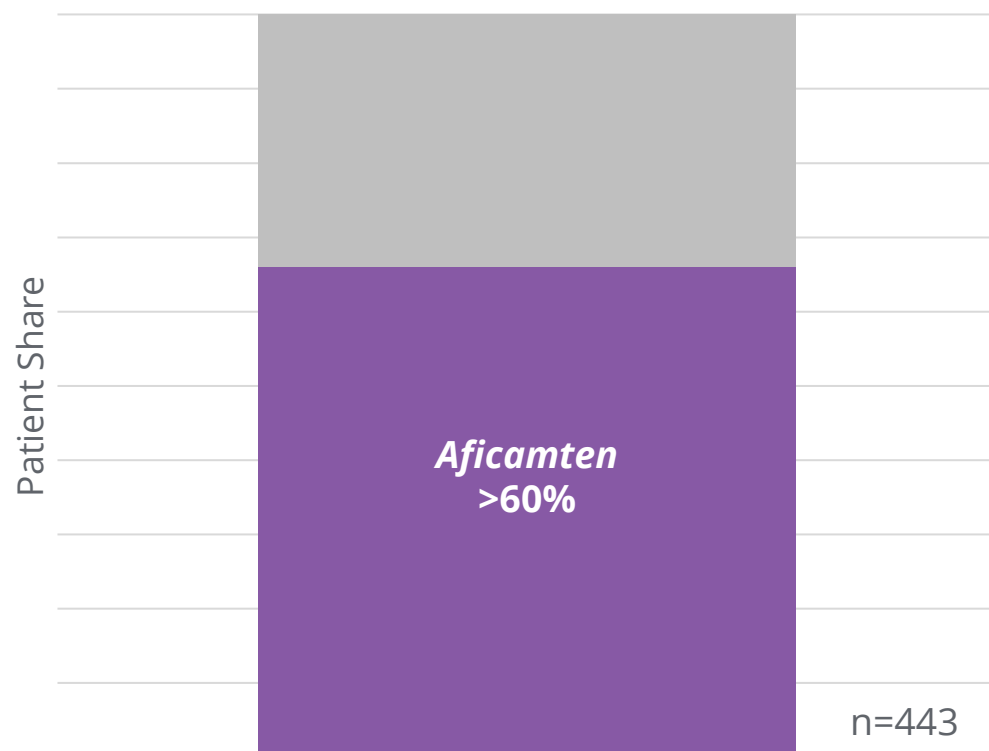
Cytokinetics Poised to Compete in the Specialty Cardiology Business

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

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.

- 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

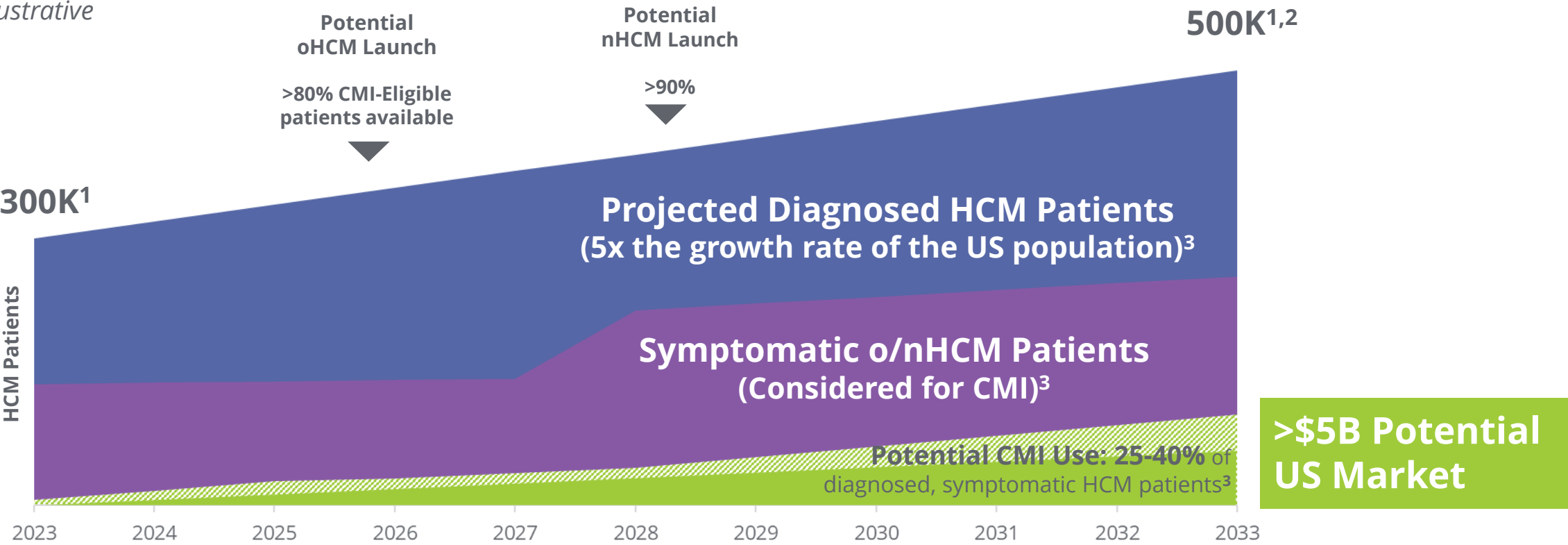
Source: *Aficamten* Impact of Product Attributes on Product Preference Share n=443 cardiologists, Quantitative research including conjoint - Cogent
Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

US HCM Patients (in '000)

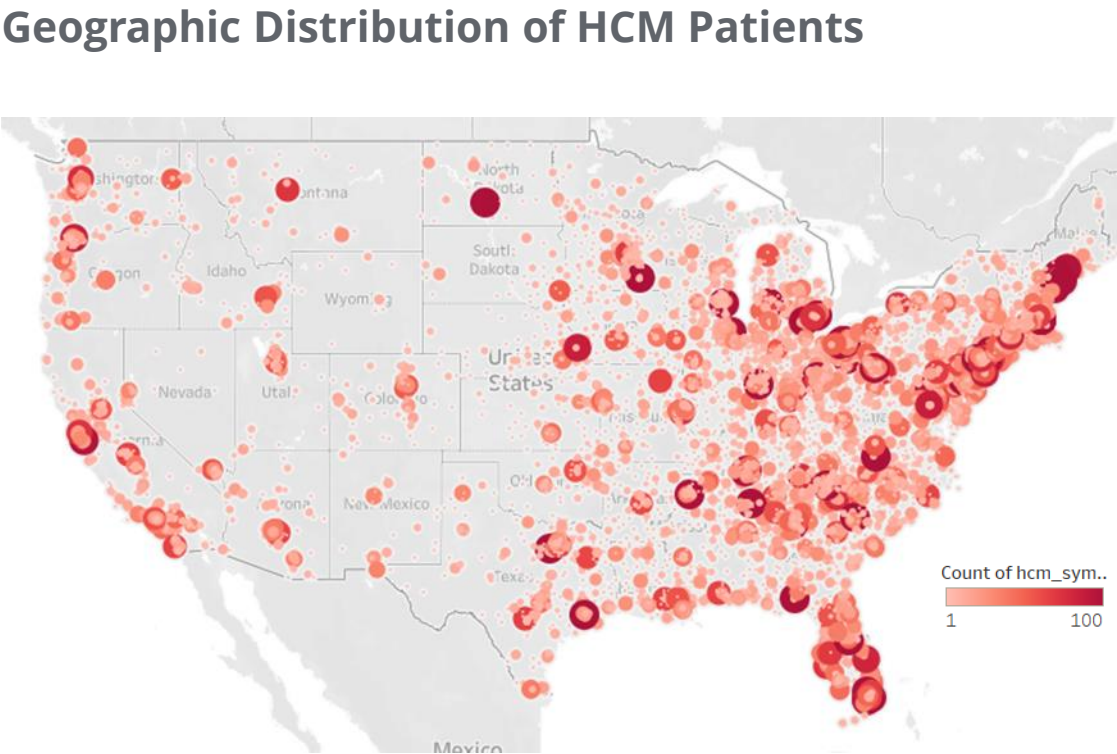
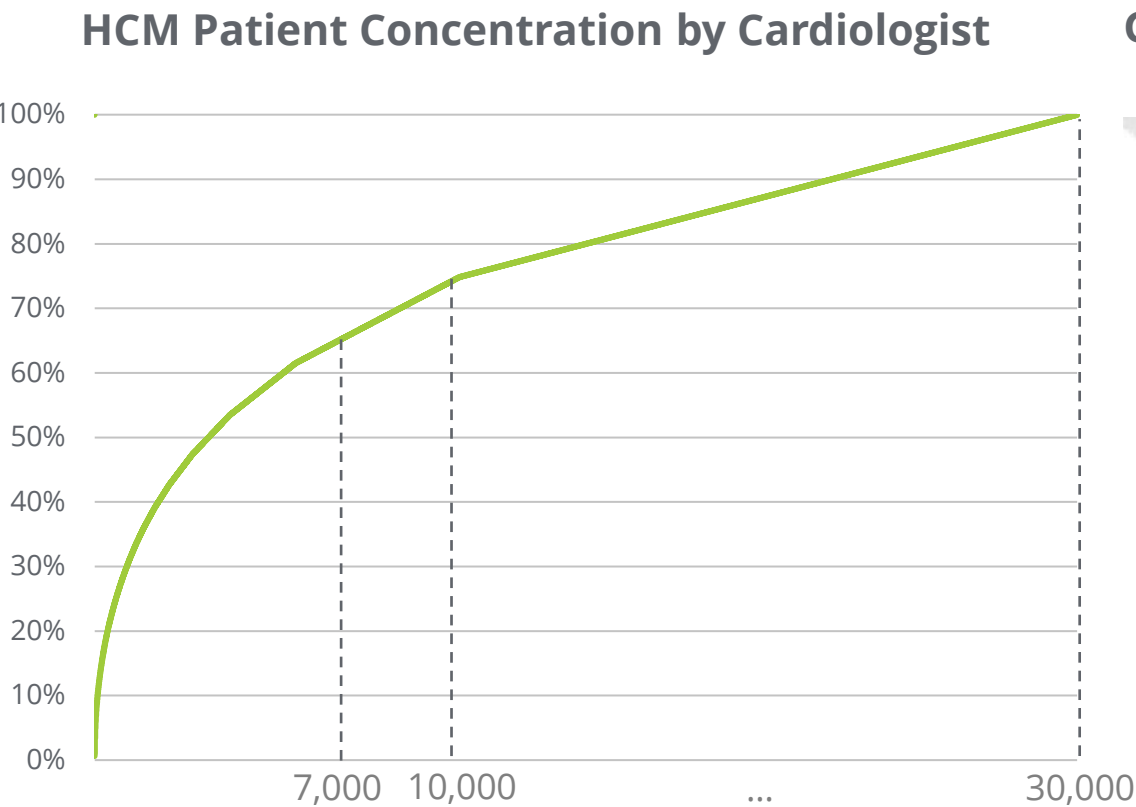
Illustrative



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;
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

Cardiologists Located in Concentrated Geographic Clusters Across the US

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

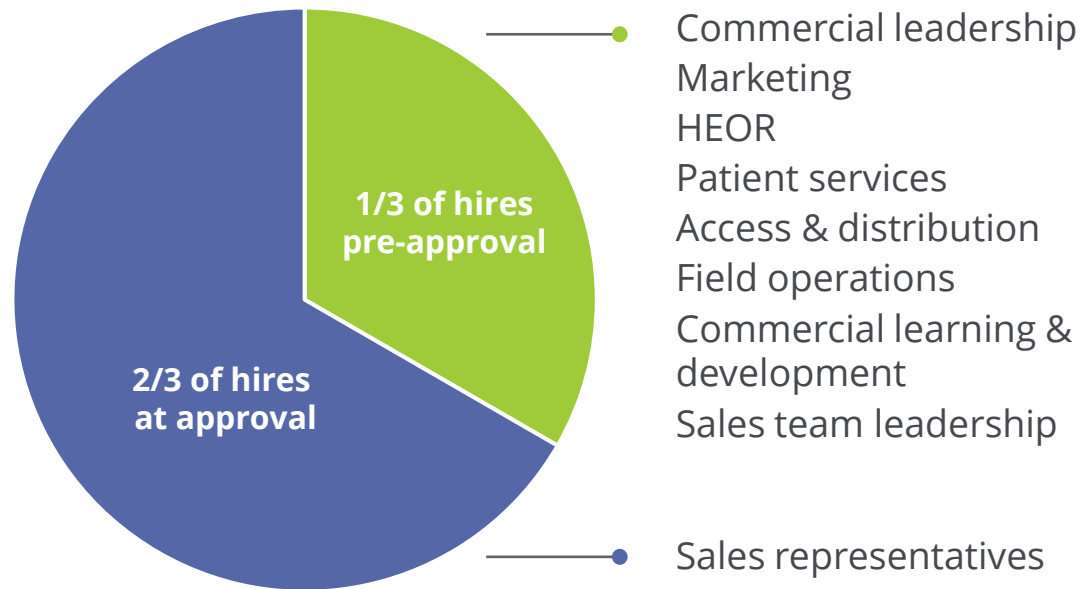


Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients
Source: Symphony PTD (Patient Transaction Data); mapping of HCPs to HCOs using Definitive Healthcare Data 2023 and 7/2023 mapping; Patient volume by dominant Cardiologist Location 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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US Commercial Readiness Milestones for *Aficamten*

2024-2025

	2024	2025
Launch Planning	<div>Final GTM Strategy</div> <div>Launch Tactical Plan</div>	<div>Launch Ready</div>
Marketing	<div>Final Positioning</div> <div>Market Development</div> <div>Full Campaign Development</div>	<div>Digital / Omnichannel</div> <div>HCP Branded Messages & Campaign Finalized</div> <div>Patient Campaign Finalized</div>
Value & Access	<div>Pricing Research</div> <div>Distribution Model Finalized</div> <div>Value Proposition & Payer Deck</div> <div>Patient Support Strategy</div>	<div>Value Dossier</div> <div>Final Market Price</div>
Sales	<div>Field Roles & Responsibilities</div> <div>Target Accounts & Territory Alignments</div>	<div>Sales Representative Recruiting</div>
Medical Affairs	<div>Investigator Spon. Studies Launch</div> <div>CME Launch</div> <div>Clinical Value Payer Deck</div> <div>Publish Primary & Key Secondary SEQUOIA-HCM Results</div>	<div>Medical Contact Center</div> <div>AMCP Dossier</div>

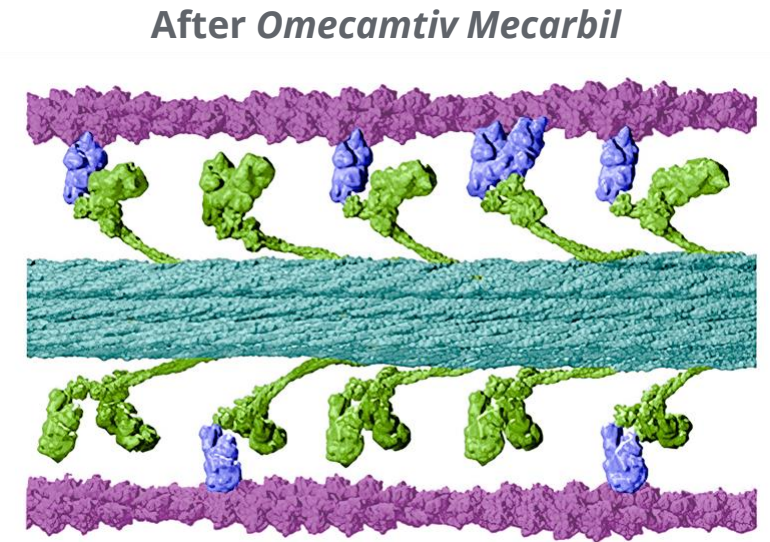
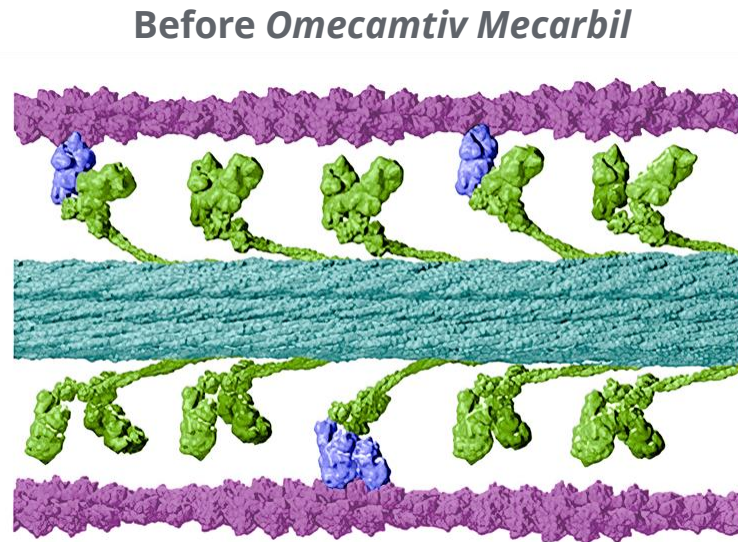
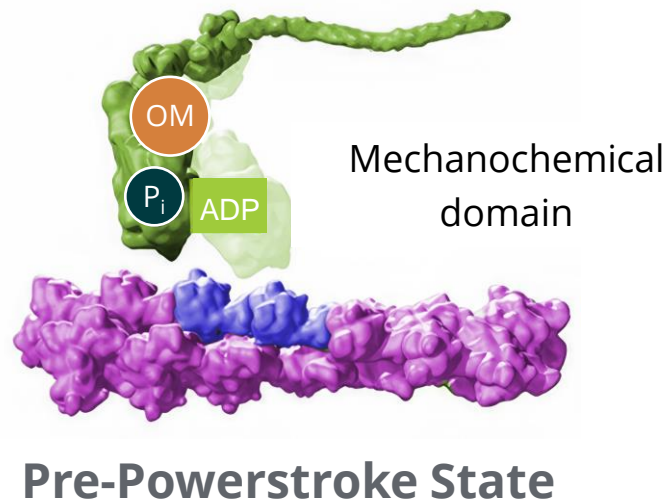
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Omecamtiv Mecarbil

Omecamtiv Mecarbil: Mechanism of Action

Omecamtiv mecarbil shifted equilibrium in favor of the pre-powerstroke state

“More hands pulling on the rope”



Malik, et al. *Science* 2011; 1439-1443
Planelles-Herrero, et al. *Nature Comm* 2017; 1-10
Shen et al, *Circ HF*, July 2010, 522-527
Teerlink, et al. *JACC-HF* 2020; 329-340
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

Advancing efficient, pragmatic Phase 3 clinical trial

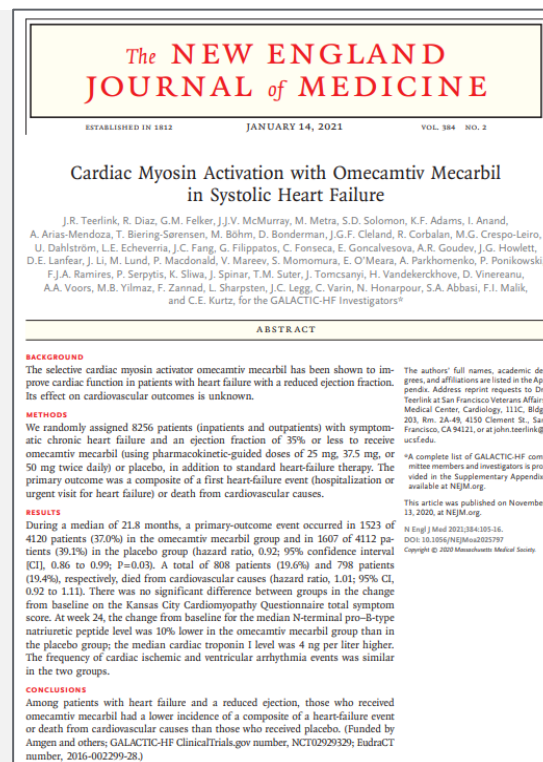
High Unmet Need

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, 2-3 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

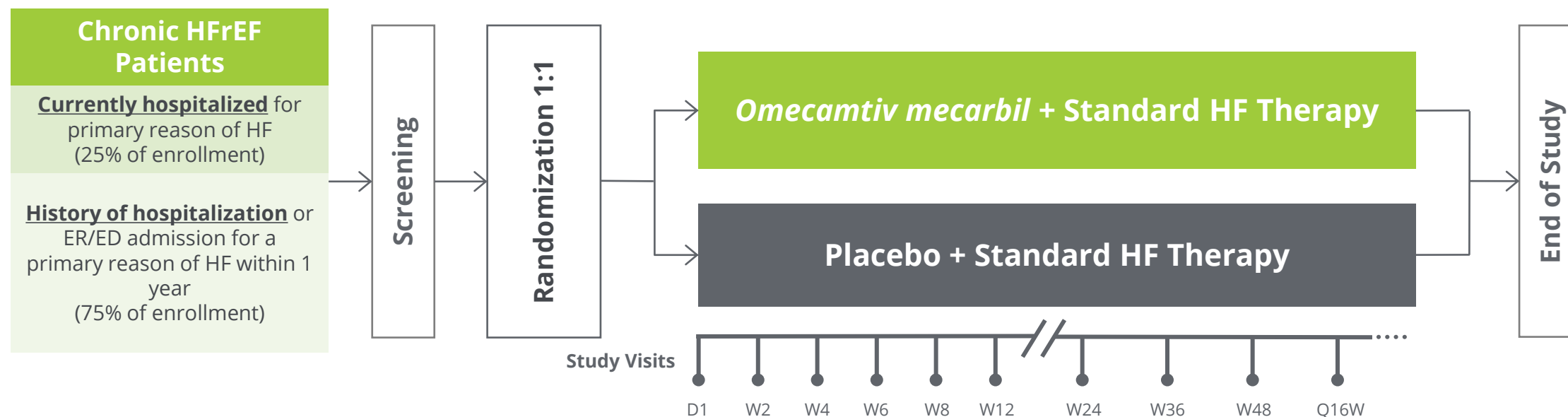
Pragmatic design elements including EHR screening, limited monitoring visits, remove visits, and limited safety labs & AE reporting

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

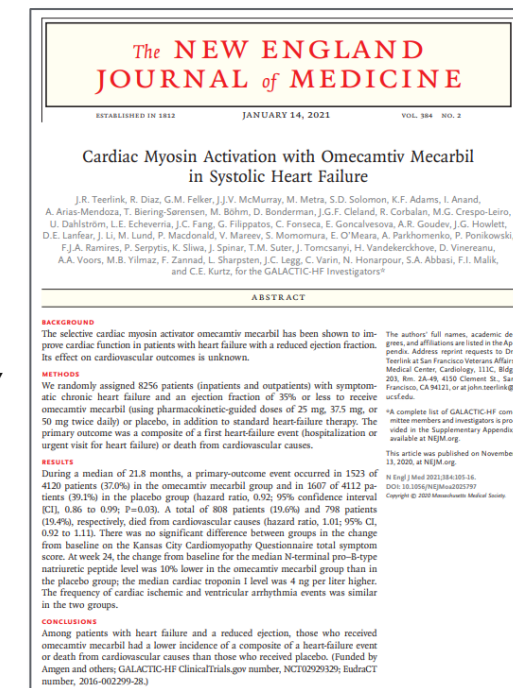
GALACTIC-HF: Clinical Trial Overview

Phase 3 clinical trial

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

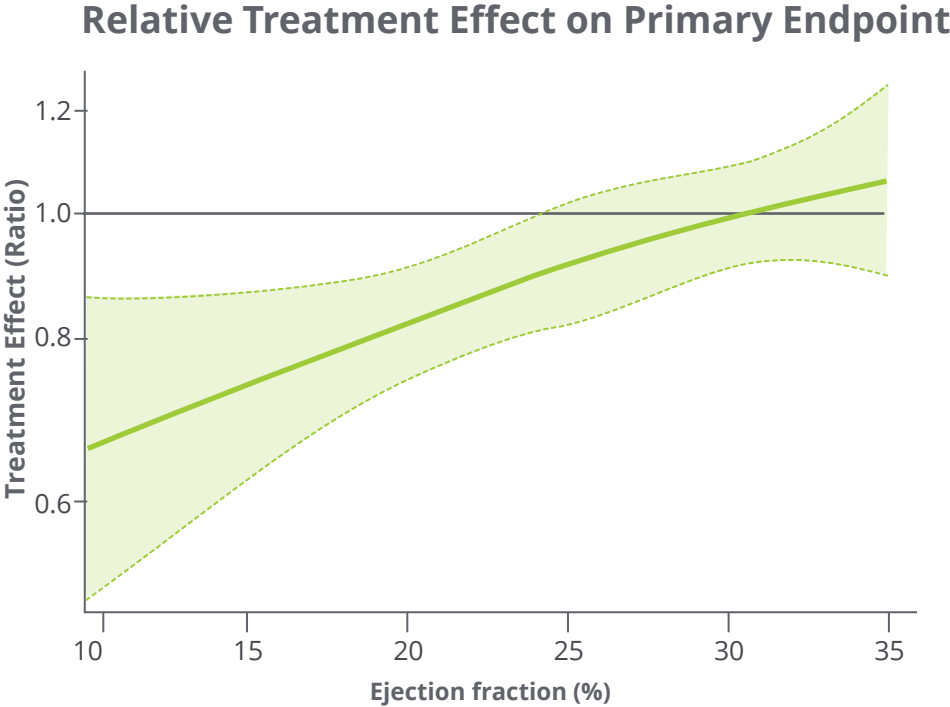
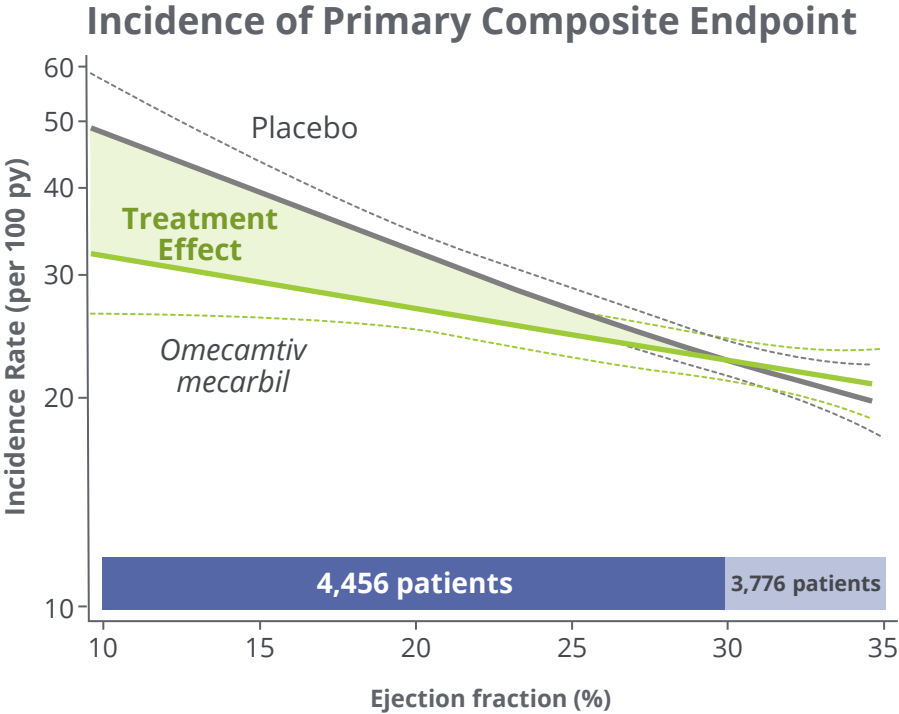


Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.



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



ORIGINAL INVESTIGATIONS

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

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ABSTRACT

BACKGROUND: In GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure) (N = 8,263), the cardiac myosin activator, omecamtiv mecarbil, significantly reduced the primary composite endpoint (PCE) of time to first heart failure event or cardiovascular death in patients with heart failure and reduced ejection fraction (EF) (<35%).

OBJECTIVES: The purpose of this study was to evaluate the influence of baseline EF on the therapeutic effect of omecamtiv mecarbil.

METHODS: Outcomes in patients treated with omecamtiv mecarbil were compared with placebo according to EF.

RESULTS: The risk of the PCE in the placebo group was nearly 1.8-fold greater in the lowest EF (<25%) compared with the highest EF (>35%) quartile. Amongst the pre-specified subgroups, EF was the strongest modifier of the treatment effect of omecamtiv mecarbil on the PCE (interaction as continuous variable, $p = 0.004$). Patients receiving omecamtiv mecarbil had a progressively greater relative and absolute treatment effect as baseline EF decreased, with a 17% relative risk reduction for the PCE in patients with baseline EF <25% ($p = 2.24\%$, hazard ratio 0.83, 95% confidence interval: 0.73 to 0.93) compared with patients with EF >35% ($p = 1.76\%$, hazard ratio 0.99, 95% confidence interval: 0.84 to 1.16; interaction as EF by quartile, $p = 0.010$). The absolute reduction in the PCE increased with decreasing EF (EF <25%: absolute risk reduction, 1.4 events per 100 patient-years; number needed to treat for 3 years = 11.8), compared with no reduction in the highest EF quartile.

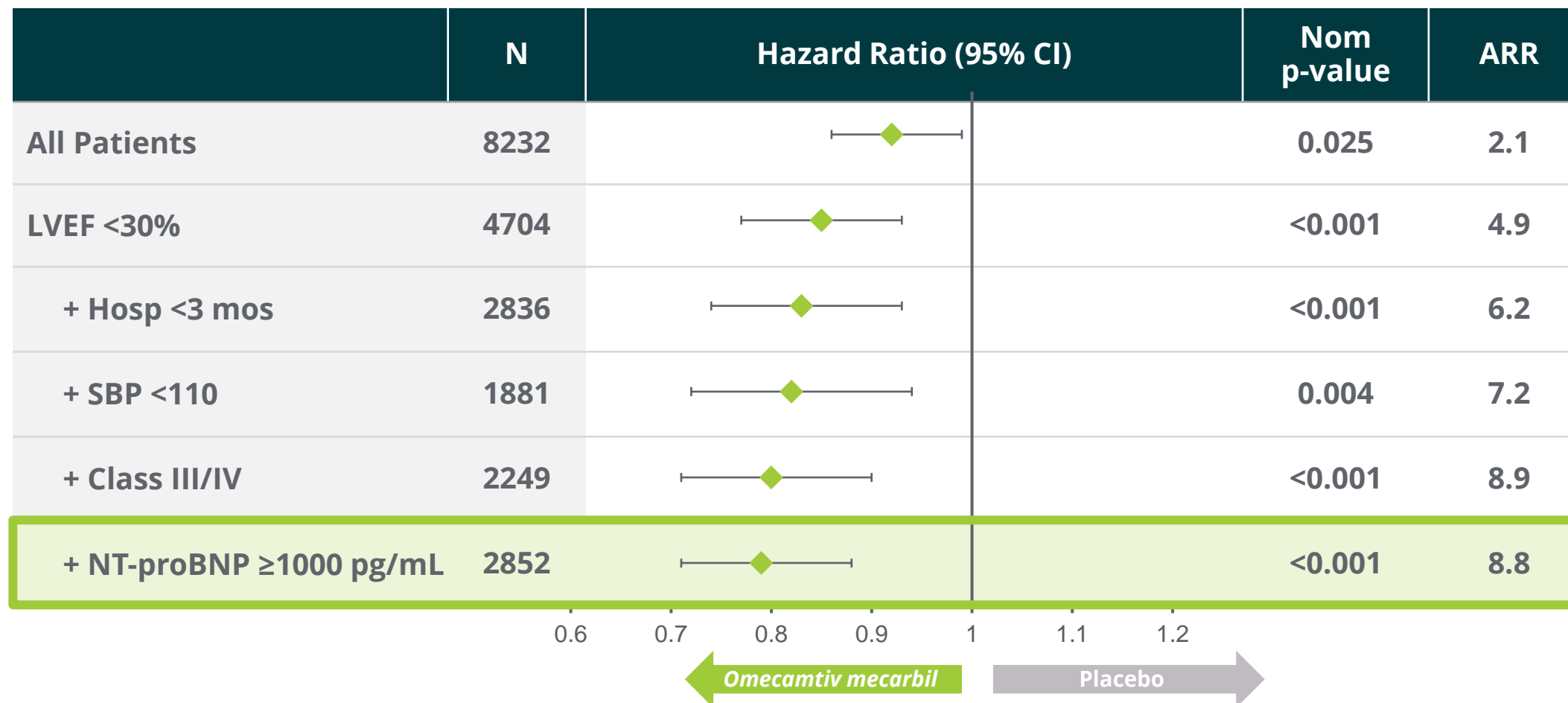
CONCLUSIONS: In heart failure patients with reduced EF, omecamtiv mecarbil produced greater therapeutic benefit as baseline EF decreased. These findings are consistent with the drug's mechanism of selectively improving systolic function and presents an important opportunity to improve the outcomes in a group of patients at greatest risk (Registered Study With Omecamtiv Mecarbil [AMG-423] to Treat Chronic Heart Failure With Reduced Ejection Fraction [GALACTIC-HF], NCT02053209) (J Am Coll Cardiol 2021;78:97-108) Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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

Large Treatment Effect in Easily Defined HF Population



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Treatment Effect in High-Risk Population with LVEF <30%



LVEF < 30% NTproBNP ≥ 1000 pg/mL Hospitalization within <u>12 mo</u>	N	HR (95% CI)	Placebo Event Rate (%)	ARR (/100 p-y)	p-value
<u>Primary Composite Endpoint</u> (CV death, HF event, LVAD/transplant, stroke)	2852	0.78 (0.70, 0.86)	49.4	8.8	p < 0.001
CV Death		0.87 (0.75, 1.01)	25.5	1.8	p = 0.07
First HF Event		0.75 (0.66, 0.85)	38.1	7.5	p < 0.001

LVAD = left ventricular assist device, ARR = absolute risk reduction
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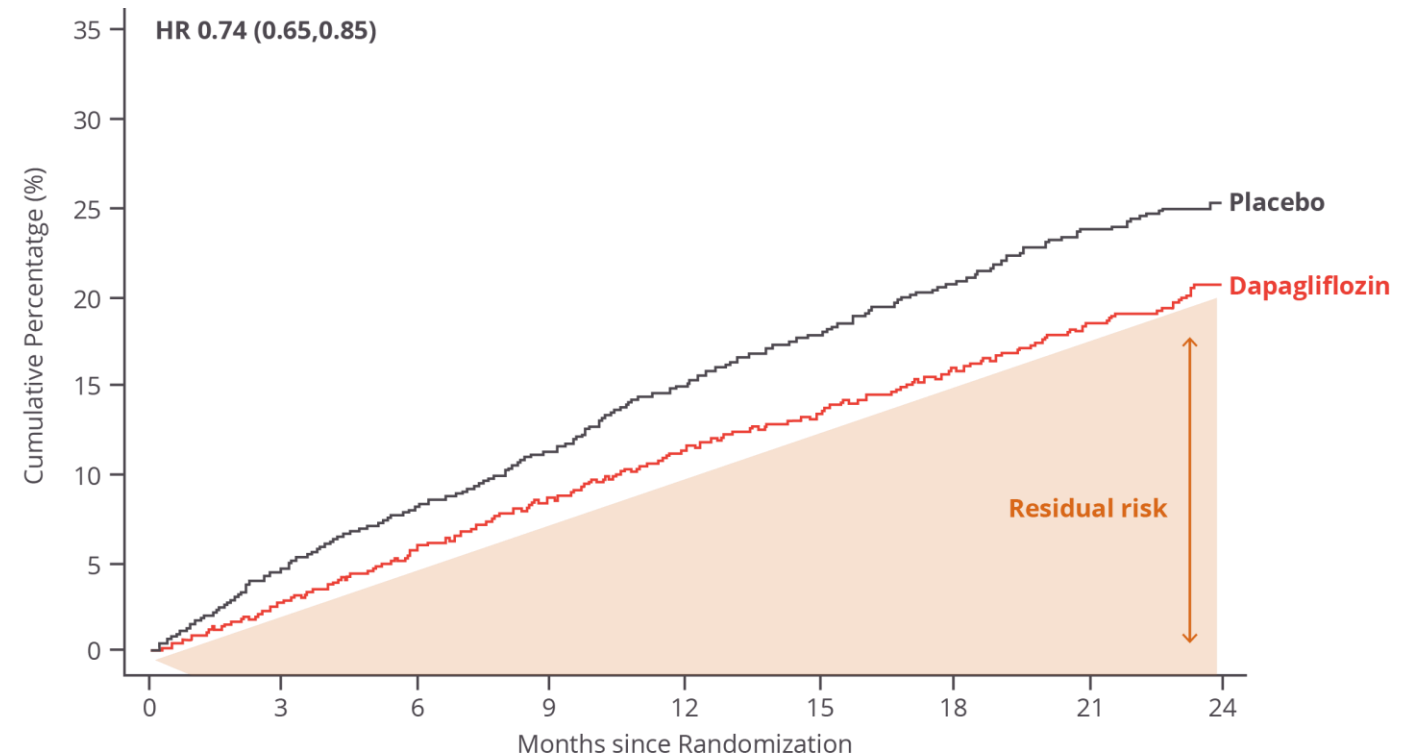
Residual Risk is High Despite Best Therapy

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%**
- 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

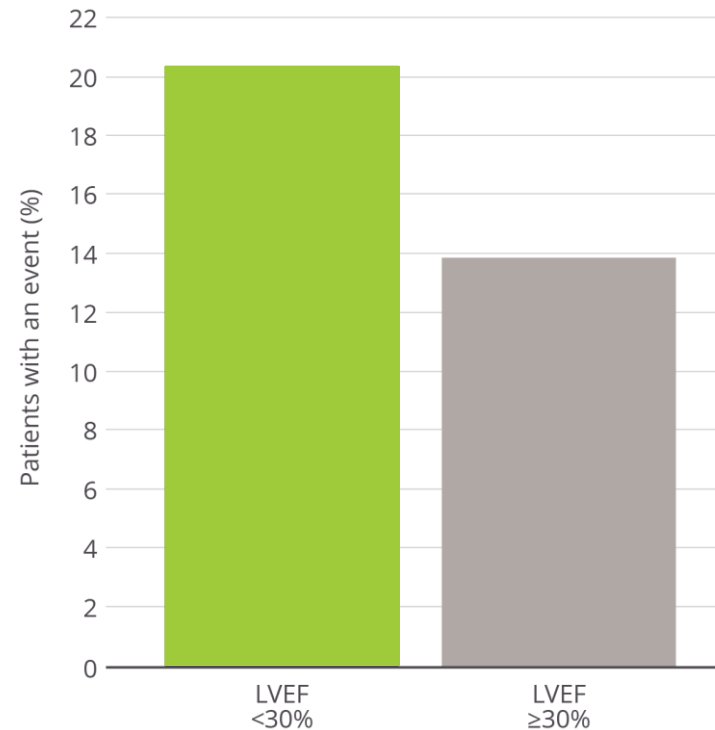
McMurray J et al, N Engl J Med. 2019;381:1995-2008

Residual Risk is High Despite Best Therapy

DAPA-HF trial (dapagliflozin group)

- **2373 patients**
- **Median follow-up 18.2 months**
- Renin-angiotensin system blocker **94%**
- Beta-blocker **96%**
- Mineralocorticoid receptor (aldosterone) antagonist **71%**
- SGLT2 inhibitor **100%**

Event rate according to LVEF (<30% vs. ≥30%)



Safety in Low LVEF Subgroup Consistent with Overall Population



Incidences of SAEs, ventricular arrhythmias, & cardiac ischemic events were similar

Incidence of stroke was lower with *omecamtiv mecarbil*

	Overall Population		LVEF ≤28%	
	<i>Omecamtiv Mecarbil</i> N=4110 %	Placebo N=4101 %	<i>Omecamtiv Mecarbil</i> N=2208 %	Placebo N=2236 %
Serious adverse events	57.7	59.4	58.8	61.9
Adverse events				
Ventricular tachyarrhythmia (narrow SMQ)	7.1	7.4	8.0	8.2
Torsade de pointes/QT prolongation (SMQ)	4.3	4.8	5.2	5.8
Serious adverse ventricular arrhythmia requiring Rx	2.9	3.1	3.4	3.6
Adjudicated major cardiac ischemic event	4.9	4.6	4.6	4.2
Myocardial infarction	3.0	2.9	3.0	2.9
Hospitalized for unstable angina	0.6	0.3	0.4	0.2
Coronary revascularization	2.8	2.9	2.6	2.5
Adjudicated stroke	1.6	2.8	2.1	2.6

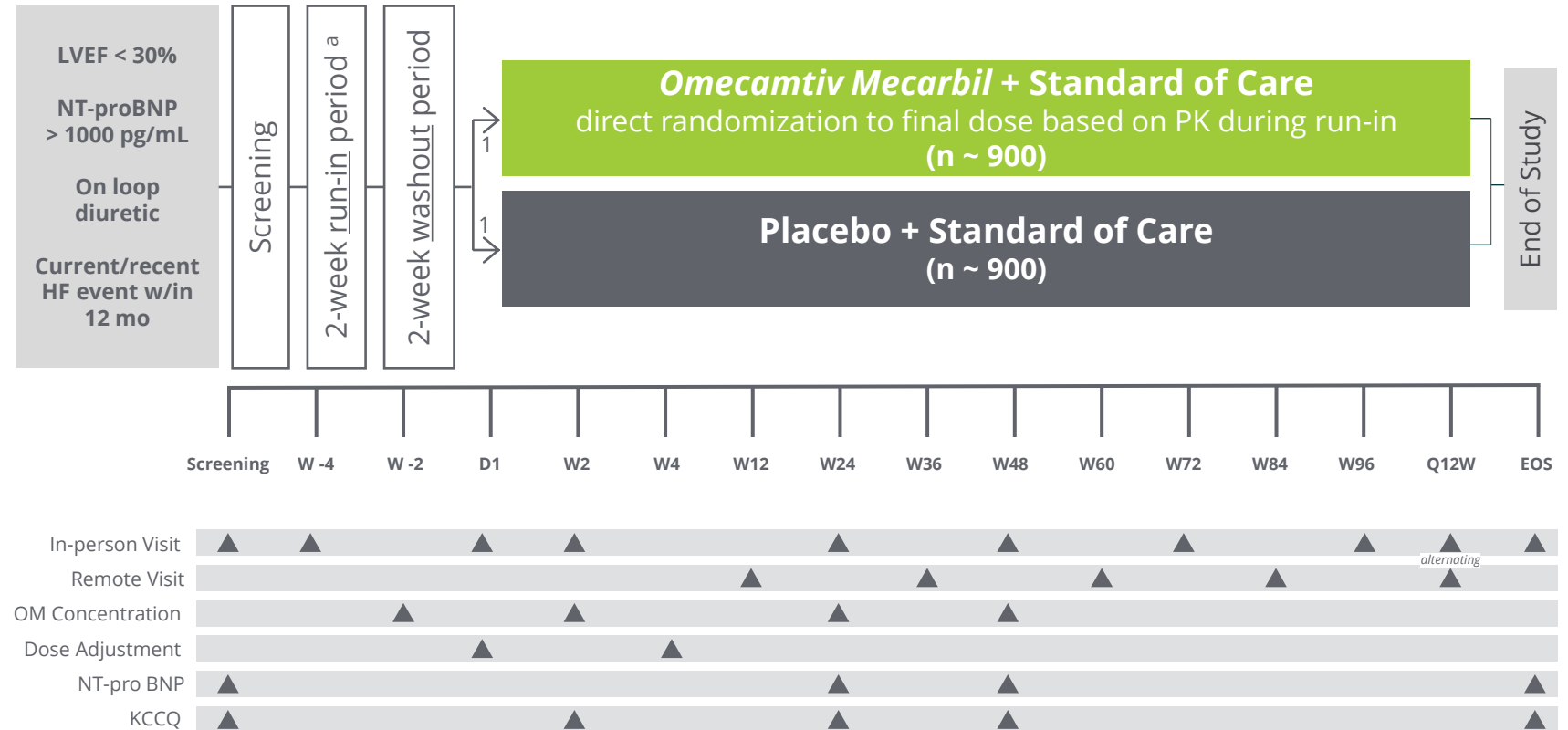
GALACTIC-HF CSR Table 14.3.4.5.27

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

Phase 3 Confirmatory Anticipated Clinical Trial Design

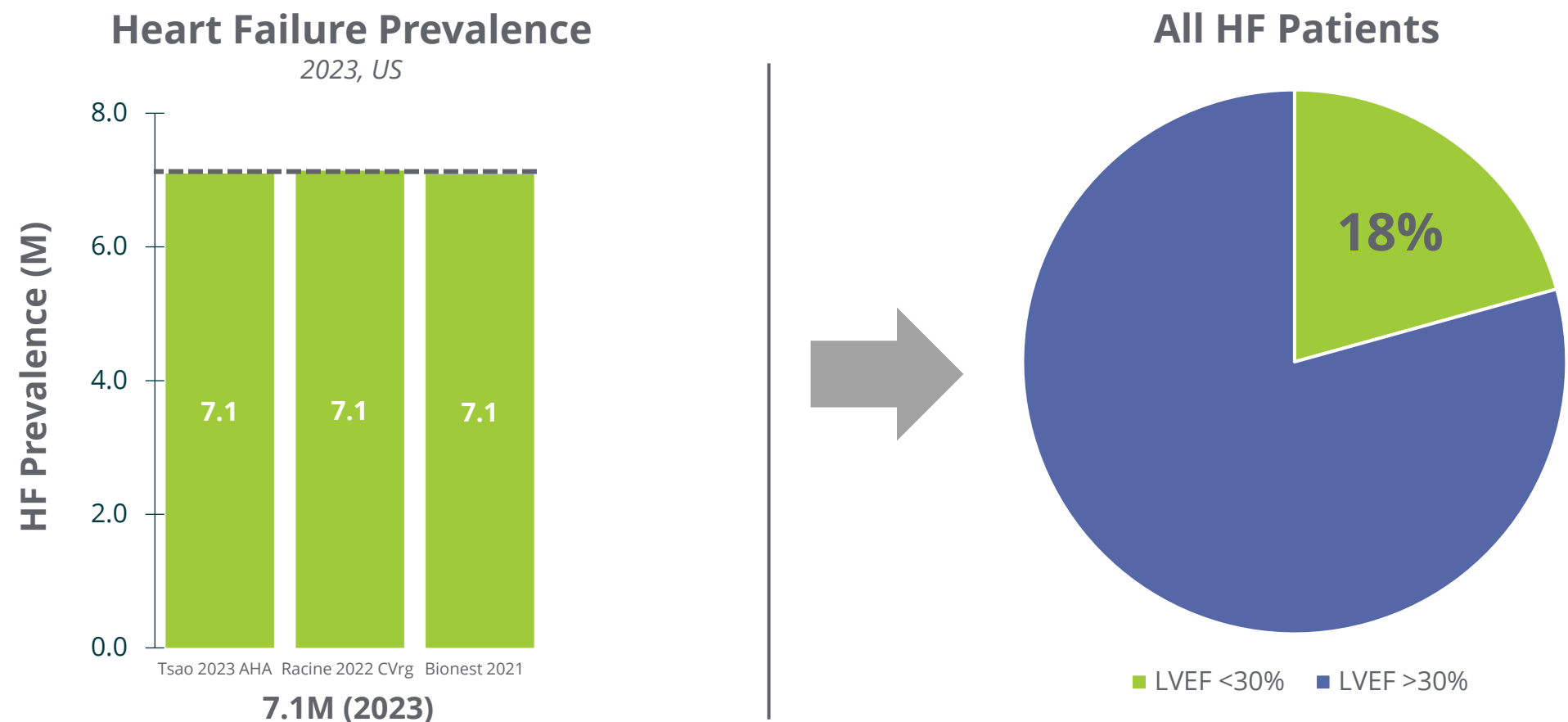
Trial design to be finalized

- 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



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

Omecamtiv Mecarbil: HFrEF Epidemiology



Circ Heart Fail. 2012;5:720-726
REAL HFrEF Study 2021
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

Omecamtiv Mecarbil: SOC Not Addressing Needs of Patients with EF <30%

Physician Experience with HFrEF Treatment

Physicians have many tools in their toolbox –ACEs, ARBs, Entresto and SGLT2s are standard of care

They're balancing maximally tolerated treatment with side effects and safety

They're still looking for something more to treat patients with severely reduced LVEF

Proposed Patient Type for *Omecamtiv Mecarbil*

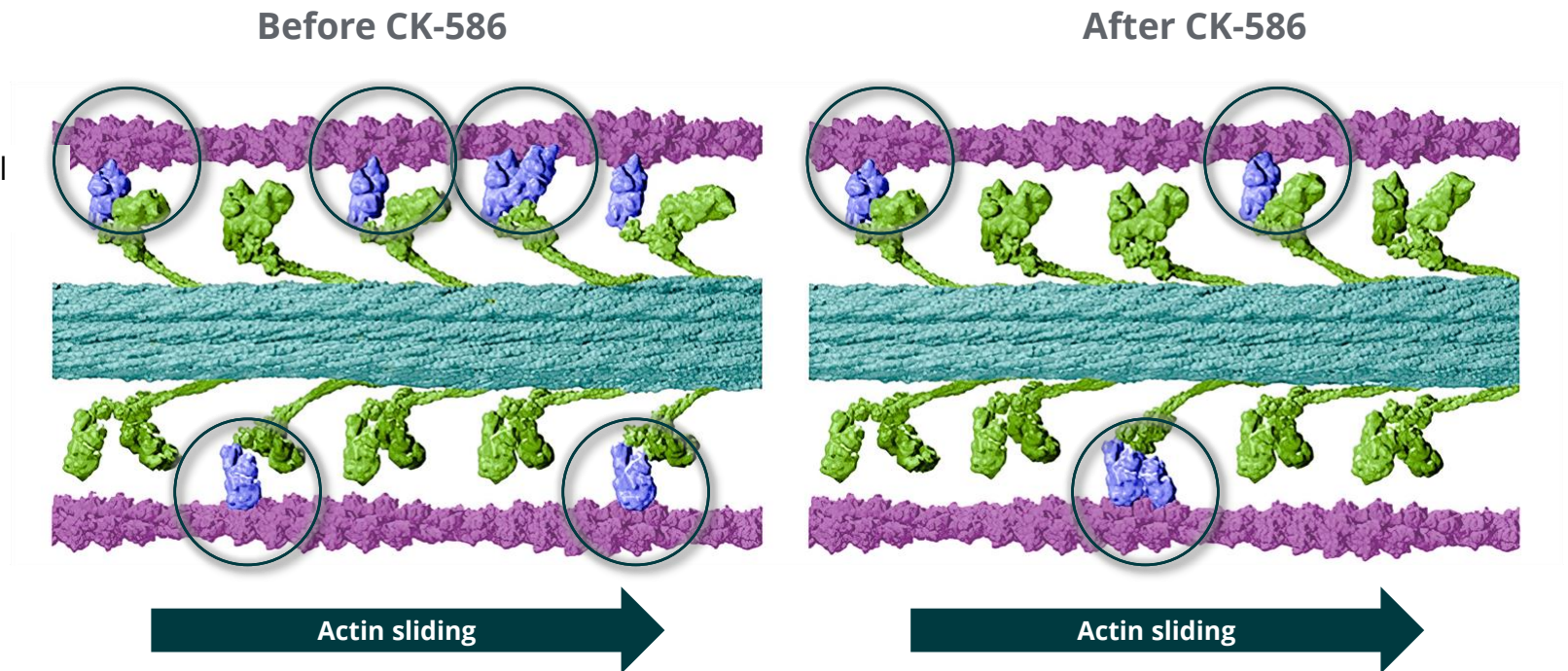
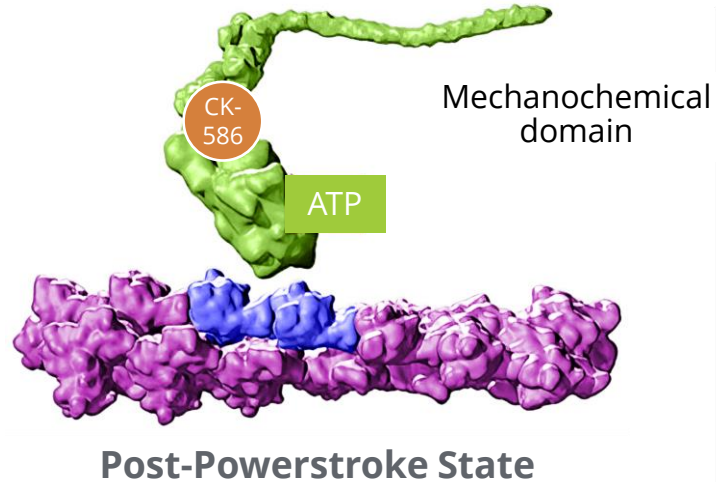
- EF <30%
- Not responding to current treatment options, recently hospitalized
- Patients with renal insufficiency / hypotension / elevated NT-pro BNP
- Have contraindications limiting necessary SoC dose increases, e.g. low BP or renal dysfunction
- Higher NYHA grade

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

CK-586

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

“Fewer hands pulling on the rope”



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

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.

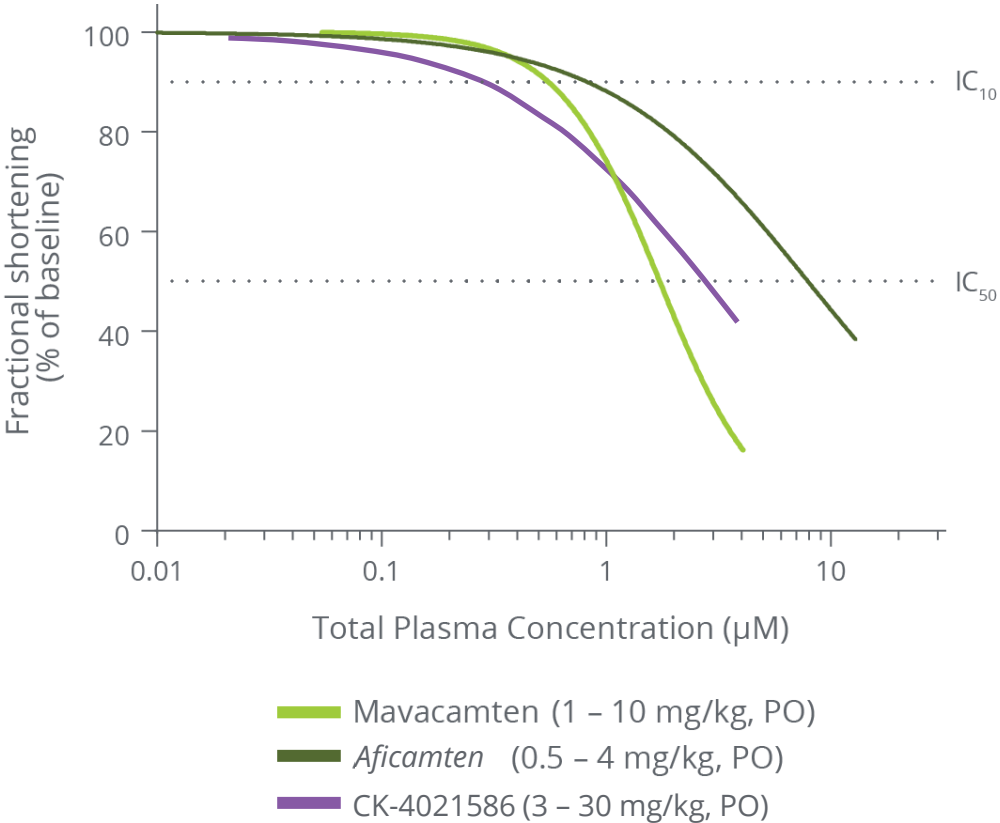
2. Bozkurt B, Ahmad T, Alexander KM, Baker WL, Bosak K, Breathett K, Fonarow GC, Heidenreich P, Ho JE, Hsieh E, Ibrahim NE, Jones LM, Khan SS, Khazanie P, Koelling T, Krumholz HM, Khush KK, Lee C, Morris AA, Page RL 2nd, Pandey A, Piano MR, Stehlik J, Stevenson LW, Teerlink JR, Vaduganathan M, Ziaeian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

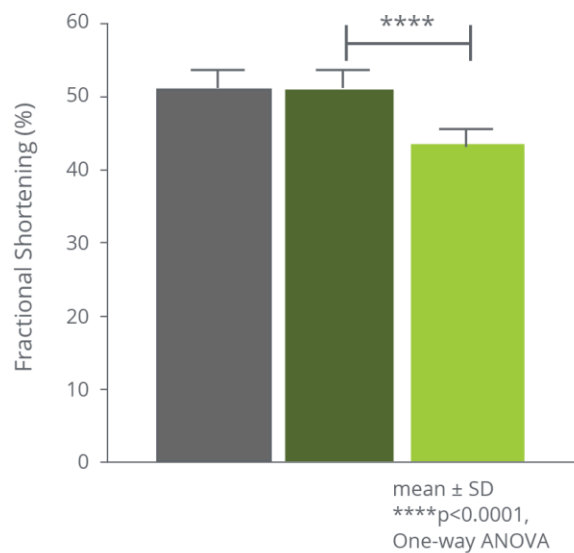
CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

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

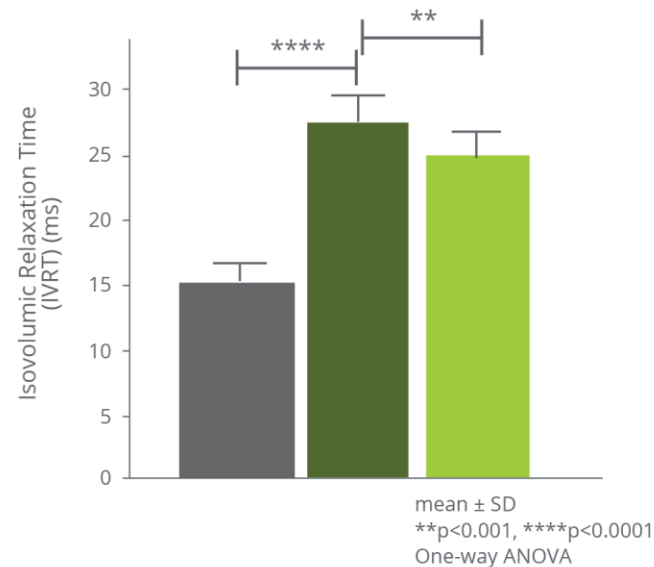
Model is representative of hypertensive, diabetic, metabolic aspects of HFpEF

10 weeks of treatment improved diastolic function and reduced cardiac fibrosis

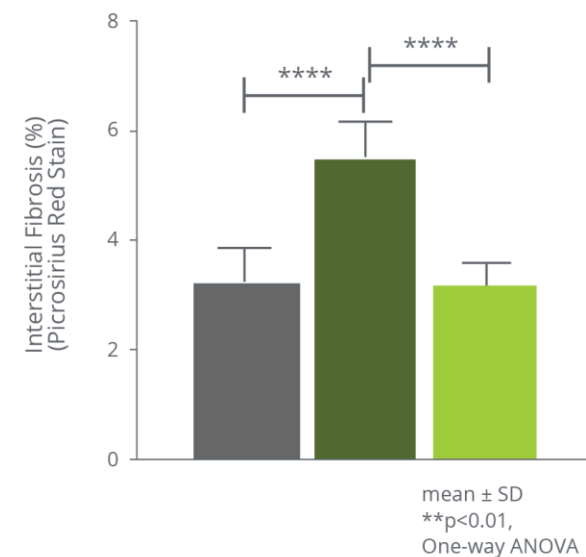
Reduced Fractional Shortening



Improved Diastolic Function



Reduced Fibrosis



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

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

Phase 1 Data Support Advancement to Phase 2 Clinical Trial

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

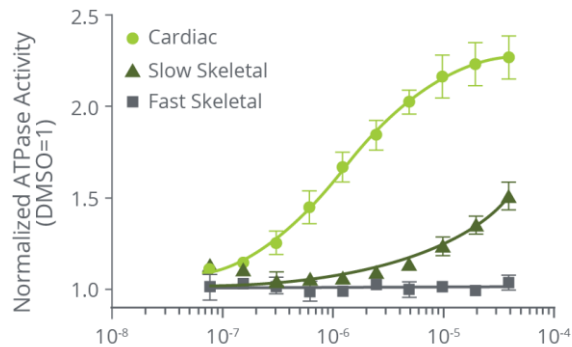
CK-136

CK-136: Mechanism of Action

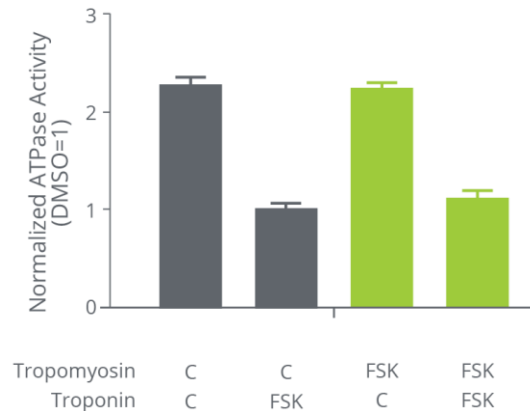
Key biochemical and cellular features

The first selective cardiac troponin activator

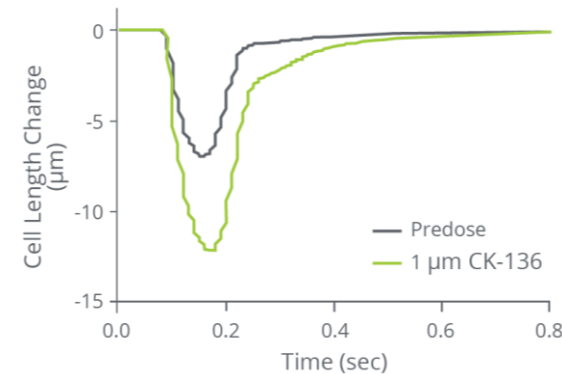
Greater ATPase Activity



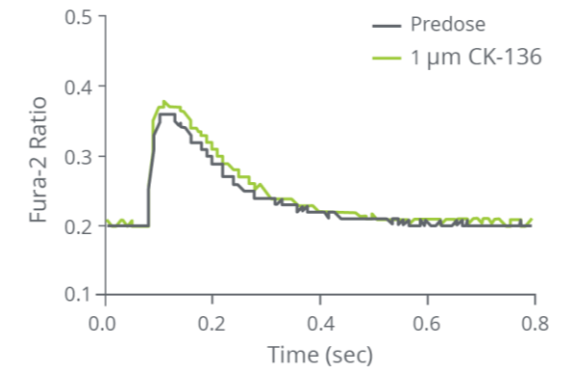
Greater ATPase Activity



Contractability Strongly Activated After Treatment



Calcium Transients Unchanged After Treatment



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

CK-136 is an investigational agent and has not been approved for use by any regulatory agency. Its safety and efficacy have not been established.

CK-136: Exposure Response Relationship

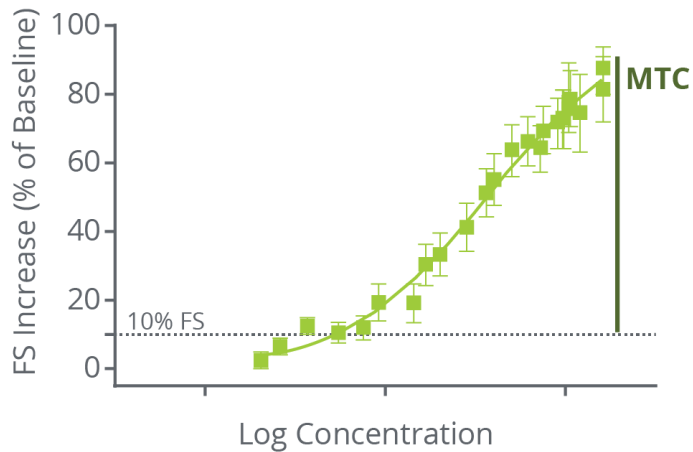
Exposure-response of troponin activator is shallower than myosin activator

Completed Phase 1 study and have begun analyzing data

Animal Models of Cardiac Function

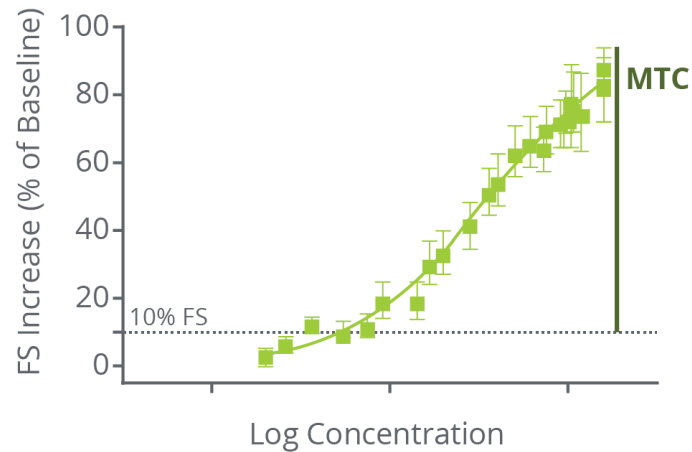
Healthy Rats PD Window¹

≥15X



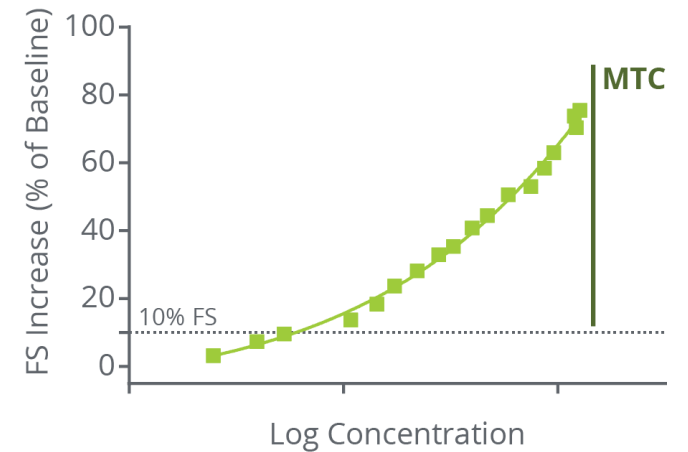
MI Rats PD Window¹

≥15X



Healthy Dogs PD Window¹

≥15X



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

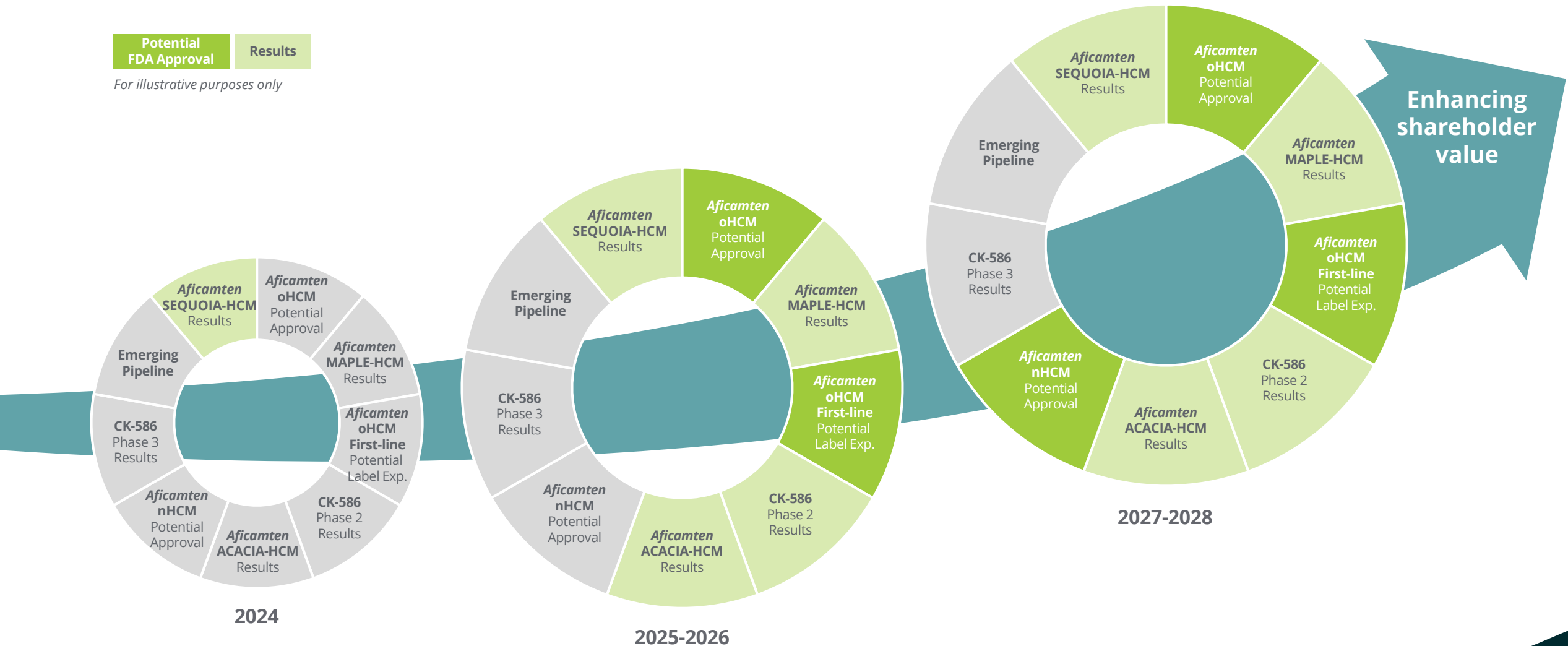
CK-136 is an investigational agent and has not been approved for use by any regulatory agency. Its safety and efficacy have not been established.

Corporate Profile

Myosin Platform Drives Multiple Data Milestones and Potential Approvals

Potential FDA Approval	Results
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For illustrative purposes only



Equity Financing, Royalty Pharma Fundraising

Well funded to enable our strategic priorities

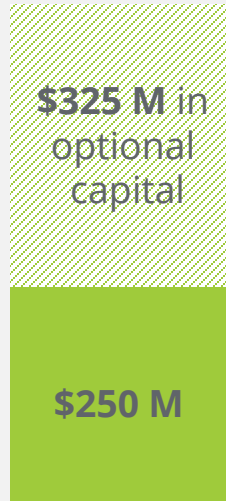
Mix of equity, longer-term debt, and revenue sharing secured over **\$1 billion** in capital, with **~\$740 million** in immediate cash

~ \$500 M



Equity Financing

\$325 M in
optional
capital



\$250 M

Royalty Pharma Deal

Strategic
Priorities

Aficamten



Global commercial launch of *aficamten* upon regulatory approvals



Conduct additional label-expanding *aficamten* trials worldwide

Research & Development



Advance our pipeline, including:



- Confirmatory Phase 3 trial of *omecamtiv mecarbil*



- Phase 2 proof-of-concept trial of CK-586

- Potential Phase 3 registrational trial of CK-586

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

Structured Financing Transaction with Royalty Pharma

Revenue sharing, royalty monetization, longer-term debt & equity investment



Four separate components providing \$250M upon closing; up to \$575M total

Broadens capital access to support prospective commercial launch and monetize myosin pipeline

Aficamten \$50M Upfront Capital for Future Commercial Launch <ul style="list-style-type: none">Eligible for additional \$175M within 12 months of FDA approval for oHCMCapital repayable over 10 years in quarterly installments (totaling 1.9x)	Aficamten Royalty <ul style="list-style-type: none">Restructured to 4.5% up to \$5B of annual net sales and 1% above \$5B, compared to prior 4.5% up to \$1B and 3.5% above \$1B	Omecamtiv Mecarbil \$100M Upfront Capital to Fund Ph 3 Trial <ul style="list-style-type: none">Positive Ph 3 and timely FDA approval yield RP a 1.0x milestone payment and 2% royalty on global salesOtherwise, Cytokinetics repays loan quarterly (2.275x-2.375x) over 18 or 22 quarters starting in 2028 or 2030	CK-586 Phase 2 Trial Funding <ul style="list-style-type: none">\$50M Upfront Capital to Fund Ph 2 PoC trialIn exchange for 1.0% royalty on net sales of CK-586	CK-586 Phase 3 Trial Funding <ul style="list-style-type: none">Option to invest up to an additional \$150M for Ph 3 developmentIf RP opts into Ph 3, it may receive up to 0.75x milestone and 4.5% royalty on global salesIf RP opts out of Ph 3 funding, it gets a 1% royalty on global net sales
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Royalty Pharma purchased \$50M of Cytokinetics' stock

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Royalty Pharma Agreement: Efficient Fundraising for Next Wave of Innovation

Omecamtiv Mecarbil

Cytokinetics received **\$100M** at a market-rate competitive cost of capital (low double-digit interest rate)

- **Cost effective Ph 3 trial:** \$100M covers costs
- Clinical trial designed to confirm results from pre-specified sub-group in GALACTIC-HF
- Expected to start in Q4 2024

>\$700m

Estimated peak sales in U.S. market

at least 8

Years of market opportunity in U.S. estimated



Highly Synergistic

Can leverage commercial infrastructure for *aficamten*

CK-586 Investment

Cytokinetics received **\$50M** up-front and is eligible to receive an additional **\$150M**



High Conviction

- RP made investment after having only seen Ph 1 data
- Initial investment covers entire Ph 2 POC trial
- RP has opt-in right to fund Ph 3 costs up to \$150M



Shareholder Value

- RP entitled to 1% royalty on future net sales
- If opt-in is exercised, royalty rate increases to 4.5%
- RP receives 0.75x milestone upon approval

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Balance Sheet & Financial Guidance

Approximately 2 years of cash runway based on 2024 guidance*

2024 Condensed Balance Sheet

As of 3/31/2024

in millions

	Total
Cash and investments	\$634.3
Accounts receivable	\$0.8
PPE	\$68.0
Leased assets	\$78.2
Other assets	\$26.8
Total Assets	\$808.1
Convertible Debt, net	\$549.8
Liability related to sale of future royalties	\$390.2
Lease liability	\$136.8
Other liabilities	\$127.4
Total Liabilities	\$1,204.2
Working capital	\$549.8
Accumulated deficit	(\$2,247.9)
Stockholders' deficit	(\$396.2)
Wtd Avg Basic Shares Outstanding (million)	101.9

2024 Financial Guidance

- **GAAP Operating (R&D and G&A) Expense:**  \$535 to \$555 million
- **Non-cash expenses included in GAAP Operating Expense**:**  \$115 to \$105 million
- **Operating Expense (R&D and G&A) excluding non-cash expenses**  \$420 to \$450 million
- **Expected Net Cash Utilization***:**  \$390 to \$420 million

* Including up to \$175M we expect to be available to us under our loan agreement with Royalty Pharma, upon satisfaction of conditions.

**Non-cash expenses included in GAAP Operating Expenses are comprised of stock-based compensation and depreciation. Non-cash expense is a non-GAAP financial measure that should be considered as supplemental information regarding our operations and should not be considered without also considering our results prepared in accordance with U.S. GAAP. It should not be considered as a substitute for, or superior to, our U.S. GAAP results. We believe non-cash expenses is a relevant and useful operational measure as our management uses it to budget and plan for the business and also useful to investors because similar measures are used by securities analysts, investors and others in their evaluation of companies in similar industries. Non-cash expense as we present it may not be comparable with similarly titled operational measures used by other companies. Our expectations regarding non-cash expenses are based on information currently available to us, but are forward-looking statements subject to change.

***We define "Net Cash Utilization" as change in cash, cash equivalents and investments year over year.

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 in ACACIA-HCM
in 2024

Continue enrollment of CEDAR-HCM
in 2024

Begin Phase 1 study of *aficamten* in
healthy Japanese volunteers
in Q2 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

Pre-Clinical Development & Ongoing Research

Initiate clinical development with
another muscle-directed
compound in 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