

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 8-K**

**CURRENT REPORT**  
**Pursuant to Section 13 or 15(d)**  
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event Reported): May 22, 2024**

**Cytokinetics, Incorporated**

(Exact Name of Registrant as Specified in Charter)

**Delaware**  
(State or Other Jurisdiction  
of Incorporation)

**000-50633**  
(Commission  
File Number)

**94-3291317**  
(I.R.S. Employer  
Identification Number)

**350 Oyster Point Boulevard, South San Francisco, CA 94080**  
(Address of Principal Executive Offices) (Zip Code)

**(650) 624-3000**  
(Registrant's telephone number, including area code)

**Not Applicable**  
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001	CYTK	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 8.01 Other Events**

On May 22, 2024, Cytokinetics, Incorporated released its current corporate presentation, which is attached hereto as Exhibit 99.1 and is incorporated by reference in this Item 8.01.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

Exhibit No.	Description
99.1	<a href="#">Corporate Presentation.</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**CYTOKINETICS, INCORPORATED**

Date: May 22, 2024.

By: /s/ Robert Blum  
Robert Blum  
Chief Executive Officer



EMPOWERING  
**muscle**  
EMPOWERING  
**lives**



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

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



# Forward-Looking Statements

This presentation contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics, Incorporated ("Cytokinetics" or the "Company") disclaims any intent or obligation to update these forward-looking statements and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements express or implied related to Cytokinetics' research and development 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 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. 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").

## Disclaimer

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.

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.

The trademarks, trade names and service marks appearing in this presentation are the property of their respective owners. Certain information contained in this presentation relate to or are based on studies, publications and other data obtained from third-party sources as well as our own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources.

# Structured Financing Transaction with Royalty Pharma

## Four Separate Components Providing \$250M upon Closing; up to \$575M Total



Royalty Pharma R&D Partnership, Royalty Monetization, Long-term Debt and Equity Investment

Diversifies access to capital to support potential commercial launch and monetize/advance myosin focused pipeline

### **Aficamten: Potential Commercial Launch Capital**

Cytokinetics to receive **\$50M upfront capital**

Cytokinetics eligible to draw additional **\$175M**

within 12 months of FDA approval for oHCM

Capital repayable over 10 years in quarterly installments (totaling 1.9x)

### **Omecamtiv Mecarbil: R&D Funding**

Cytokinetics to receive **\$100M** in upfront capital to fund confirmatory Phase 3 clinical trial

If new Phase 3 clinical trial is positive and FDA approval is received within specified time frames, Royalty Pharma will receive 1.0x milestone payment and incremental 2.0% royalty on global net sales and/or fixed quarterly payments

Otherwise Cytokinetics required to repay loan in fixed quarterly payments (totaling 2.275x – 2.375x) over either 18 or 22 quarters

### **CK-586: R&D Funding**

Cytokinetics to receive **\$50M upfront** in exchange for 1.0% royalty on net sales of CK-586

Royalty Pharma will have option to invest up to additional \$150M for **Phase 3 development**

If Royalty Pharma opts in to Phase 3 funding, it will be eligible to receive up to 0.75x milestone upon certain regulatory approvals and 4.5% royalty on global net sales

If Royalty Pharma does not opt in to Phase 3 funding, eligible for 1% royalty on global net sales

Royalty Pharma's royalty on *aficamten* was restructured so that Royalty Pharma will now receive 4.5% up to \$5.0 billion of annual net sales of *aficamten* and 1% above \$5.0 billion of annual net sales compared to the prior 4.5% up to \$1.0 billion of annual net sales and 3.5% above \$1.0 billion of annual net sales

Royalty Pharma to purchase \$50M of Cytokinetics' common stock, at Cytokinetics' option, subject to certain conditions

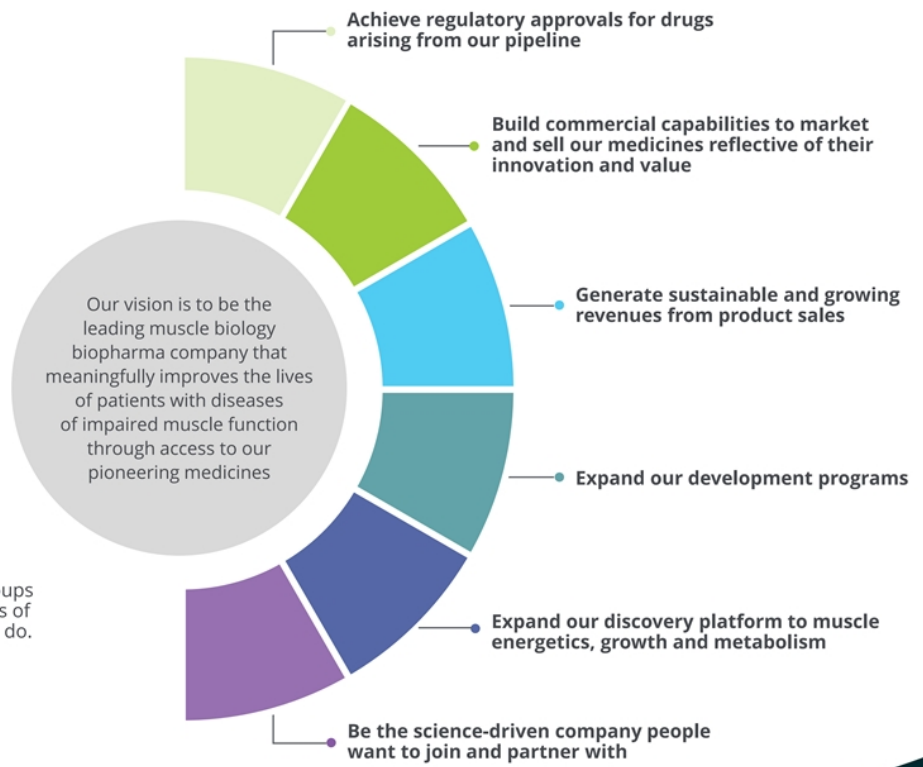


Cytokinetics

# VISION 2025

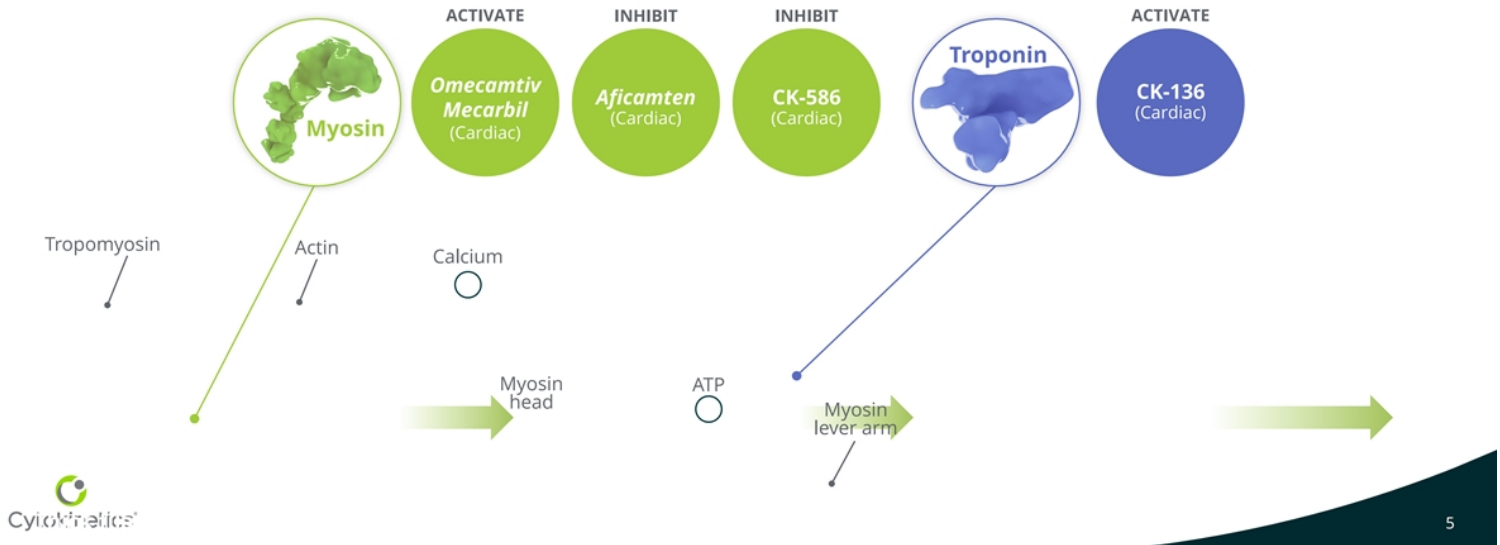
Leading with Science,  
Delivering for Patients

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.



# Sarcomere Directed Drug Development

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



# A Commitment to Muscle-Directed Cardiac Medicines

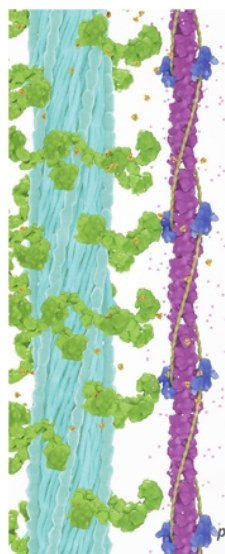
## Building a specialty cardiology franchise anchored by *aficamten*

Protein Target	Therapeutic Area	Drug Candidate	Research	Pre-Clinical	Phase 1	Phase 2	Phase 3	Approval
 Myosin-Targeted Therapy	oHCM	<i>Aficamten</i>	 <span style="float: right;">Preparing for regulatory submissions in 2H 2024</span>					
	oHCM (First-line*)	<i>Aficamten</i>						
	Pediatric oHCM	<i>Aficamten</i>						
	nHCM	<i>Aficamten</i>						
	HFpEF	CK-586						
	HFrfEF	<i>Omecamtiv Mecarbil</i>						
 Troponin-Targeted Therapy	Heart Failure, other	CK-136						
Other Biology	Muscle Biology Directed	Research						

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

# Building a Specialty Cardiology Franchise Anchored by *Aficamten*

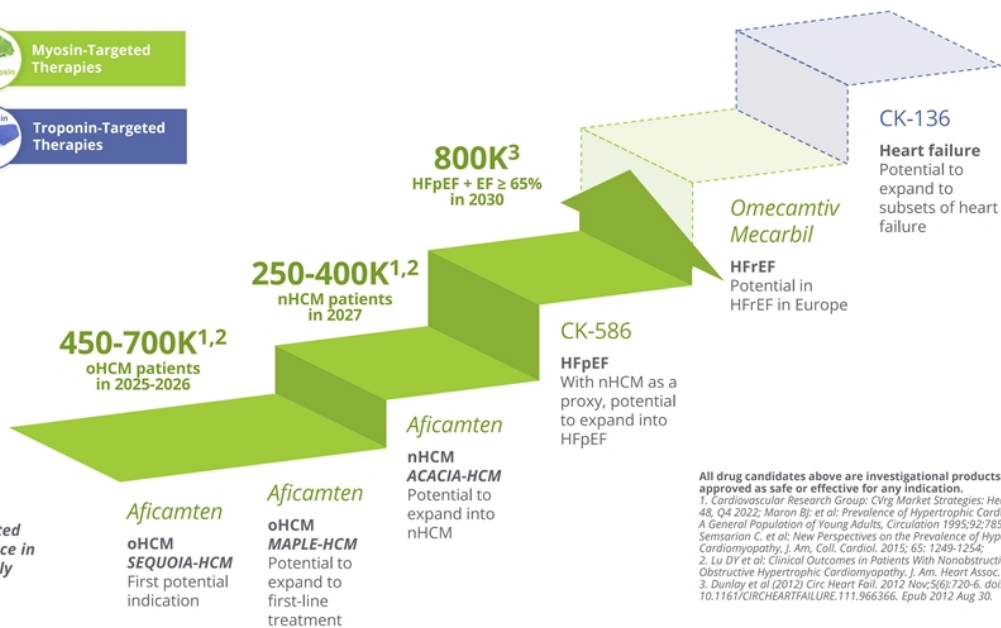
## Potential patient market for specialty cardiology franchise strategy



**Myosin-Targeted Therapies**

**Troponin-Targeted Therapies**

Estimated prevalence in US only



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

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

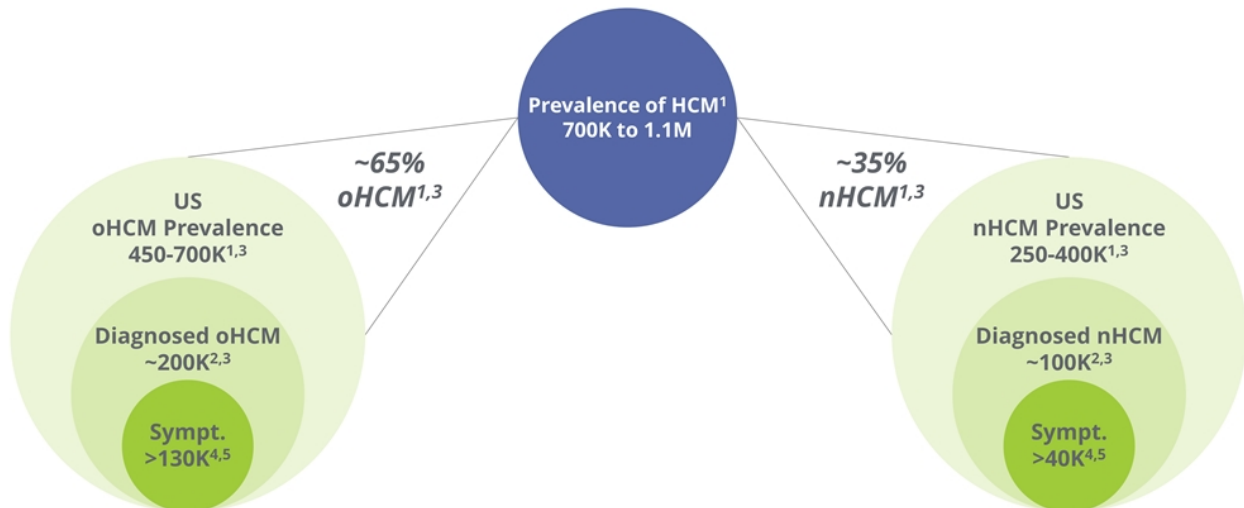
3. Dunlay et al (2012) *Circ Heart Fail.* 2012 Nov;5(6):720-6. doi: 10.1161/CIRCHEARTFAILURE.111.966366. Epub 2012 Aug 30.

# Aficamten



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

# Opportunity for CMLs in Diagnosed, Symptomatic HCM Patients



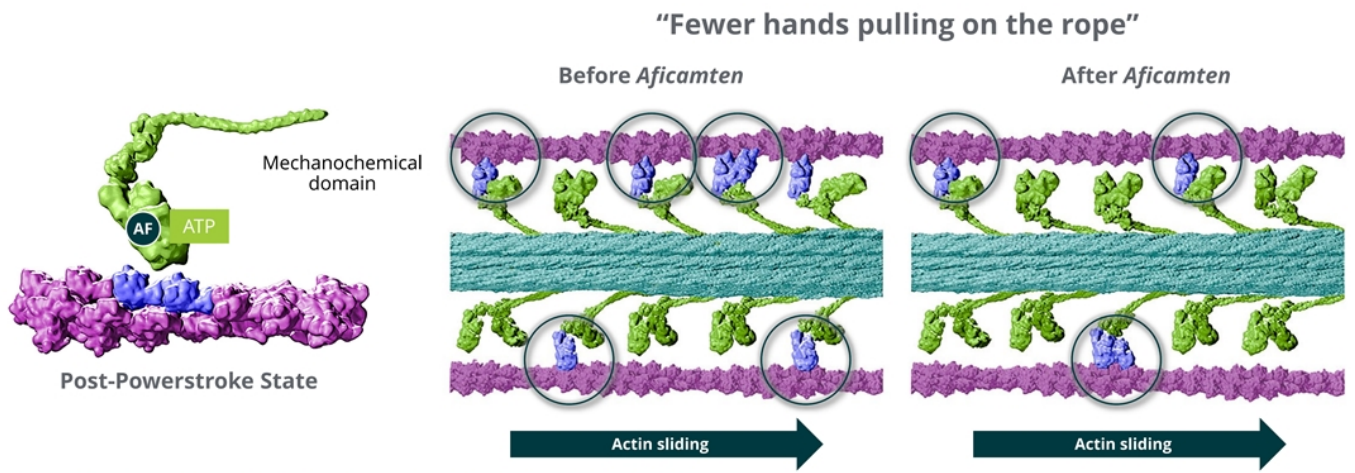
**Projections and forecasts for illustration.**

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; Semnarion 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, ral, Comzyos;
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**



*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



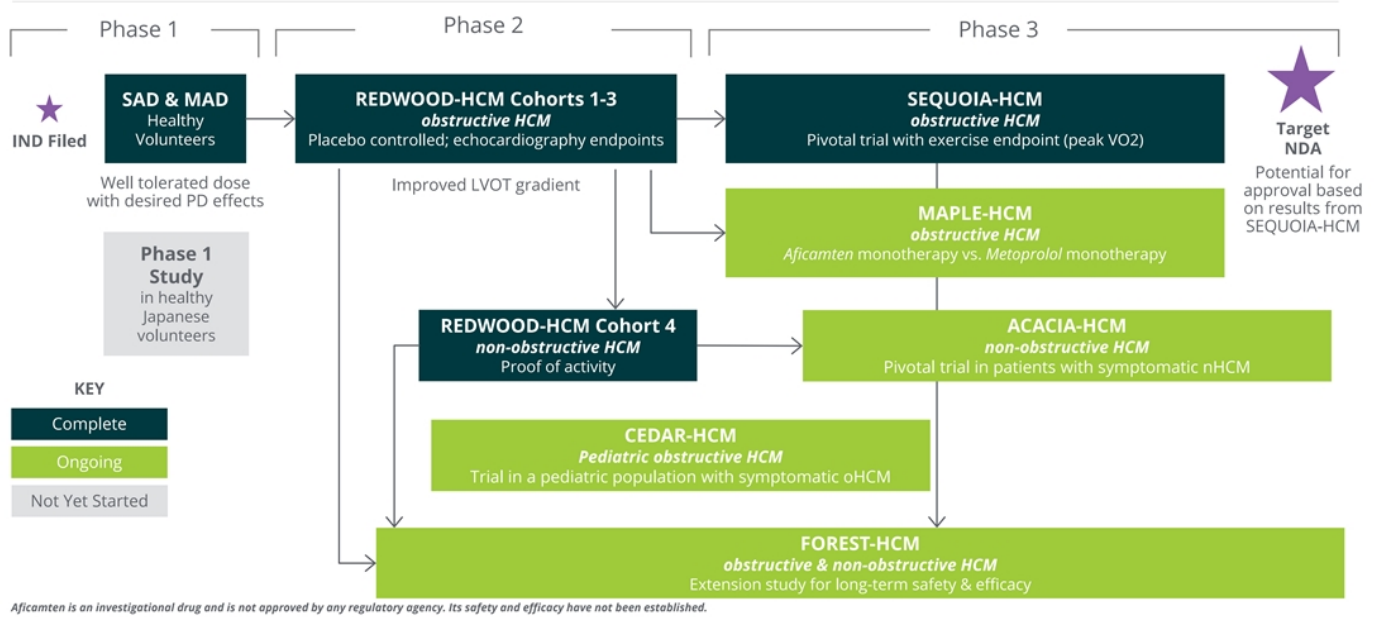
No teratogenicity



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



# SEQUOIA-HCM: Phase 3 Trial



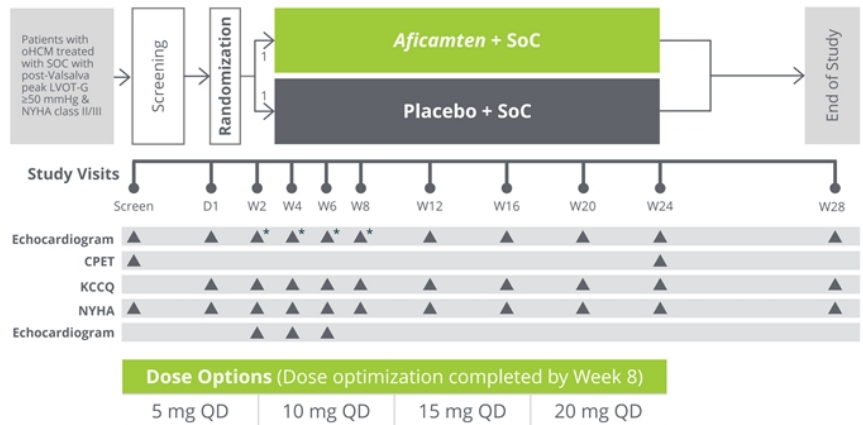
Primary endpoint: **Change in pVO<sub>2</sub> by CPET from baseline to Week 24**

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

Individualized dose up-titration based on echocardiography: LVEF  $\geq 55\%$ , post-Valsalva LVOT-G  $\geq 30$  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		Aficamten n=142	Placebo n=140
<b>Age, y</b>	59.2 ± 12.6	59.0 ± 13.4	<b>Background HCM therapy, n (%)</b>		
<b>Female sex, n (%)</b>	56 (39.4)	59 (42.1)	<b>Beta-blocker</b>	86 (60.6)	87 (62.1)
<b>Race, n (%)</b>			<b>Calcium channel blocker</b>	45 (31.7)	36 (25.7)
<b>White</b>	108 (76.1)	115 (82.1)	<b>Disopyramide</b>	16 (11.3)	20 (14.3)
<b>Geographic region, n (%)</b>			<b>None</b>	19 (13.4)	22 (15.7)
<b>North America</b>	49 (34.5)	45 (32.1)	<b>KCCQ-CSS</b>	76 ± 18	74 ± 18
<b>China</b>	24 (16.9)	22 (15.7)	<b>NYHA FC, n (%)</b>		
<b>Europe and Israel</b>	69 (48.6)	73 (52.1)	<b>II</b>	108 (76.1)	106 (75.7)
<b>Medical history, n (%)</b>			<b>III/IV</b>	34 (23.9)	34 (24.3)
<b>Hypertension</b>	75 (52.8)	70 (50.0)	<b>Median NT-proBNP (IQR), pg/mL</b>	818 (377–1630)	692 (335–1795)
<b>Paroxysmal atrial fibrillation</b>	21 (14.8)	20 (14.3)	<b>Median hs-cTnI (IQR), ng/L</b>	12.9 (7.6–33.6)	11.5 (7.7–25.0)
<b>Permanent atrial fibrillation</b>	2 (1.4)	1 (0.7)	<b>Echocardiographic parameters</b>		
<b>CPET</b>			<b>Valsalva LVOT-G, mmHg</b>	82.9 ± 32	83.3 ± 33
<b>pVO<sub>2</sub> (mL/kg/min)</b>	18.5 (4.5)	18.6 (4.5)	<b>Resting LVOT-G, mmHg</b>	54.8 ± 27	55.3 ± 32
<b>Percent of predicted pVO<sub>2</sub>(%)</b>	58 (13)	57 (12)	<b>LVEF, %</b>	74.8 ± 5.5	74.8 ± 6.3
			<b>Maximal LV wall thickness, mm</b>	20.7 ± 3.0	21.0 ± 3.0

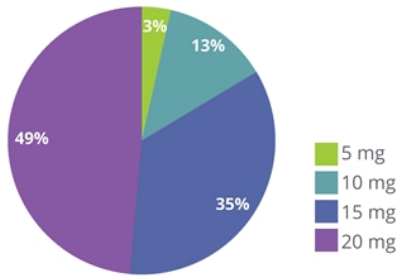
Values are the mean ± SD unless otherwise indicated.

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
<b>% per treatment group</b>	100%	3.5%	12.7%	34.5%	47.9%
<b>Background HCM therapy</b>					
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)
<b>Baseline study assessments</b>					
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 <sub>2</sub> , mL/kg/min	18.6 ± 4.5	18.7 ± 2.9	18.6 ± 3.9	18.2 ± 4.1	18.3 ± 4.9
<b>Echocardiographic parameters (core laboratory)</b>					
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

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

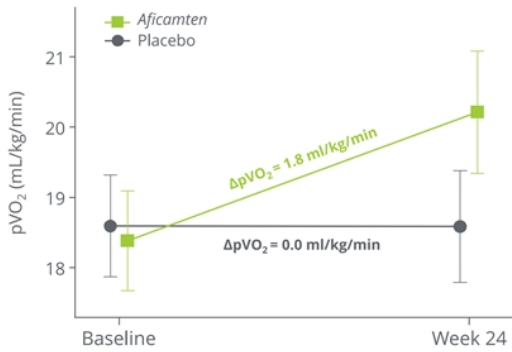
# SEQUOIA-HCM: Primary Endpoint

## Significant improvement in exercise capacity compared to placebo

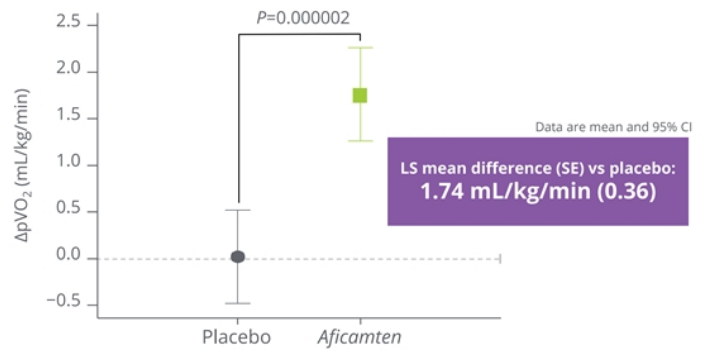


Results presented at Heart Failure 2024 and published in *NEJM*

Absolute Change from Baseline to Week 24



LS mean Change from Baseline to Week 24



*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: Subgroup Analysis



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

	n (Afi/Pib)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)		n (Afi/Pib)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)	
<b>Age</b>										
<65 y	85/84	2.4	0.4	2.0 (1.1, 2.8)						
≥65 y	57/56	0.9	-0.5	1.4 (0.3, 2.5)						
<b>Sex</b>										
Male	86/81	2.5	0.7	1.8 (0.9, 2.7)						
Female	56/59	0.6	-0.8	1.4 (0.4, 2.5)						
<b>Baseline BMI</b>										
<30 kg/m <sup>2</sup>	97/94	1.9	0.1	1.8 (1.0, 2.7)						
≥30 kg/m <sup>2</sup>	45/46	1.4	-0.2	1.6 (0.3, 2.8)						
<b>Baseline Median LVEF</b>										
≤75.6%	73/68	1.9	0.0	1.8 (0.8, 2.8)						
>75.6%	69/72	1.7	0.0	1.6 (0.6, 2.6)						
<b>Baseline NYHA FC</b>										
Class II	108/106	2.0	0.3	1.7 (0.9, 2.5)						
Class III /IV	34/34	1.0	-0.9	1.9 (0.5, 3.3)						
<b>Baseline Median KCCQ-CSS</b>										
≤78.1	67/75	1.7	-0.1	1.8 (0.8, 2.8)						
>78.1	75/65	1.8	0.1	1.7 (0.7, 2.6)						
Interaction P values were >0.05 for all prespecified subgroups										
				Favors Placebo	Favors Treatment				Favors Placebo	Favors Treatment
<b>Baseline NT-proBNP (median)</b>										
≤ 788 pg/mL	66/73	2.2	0.6	1.7 (0.7, 2.7)						
> 788 pg/mL	73/65	1.4	-0.6	2.0 (1.0, 2.9)						
<b>CPET Modality</b>										
Treadmill	78/77	2.5	0.2	2.3 (1.4, 3.2)						
Bicycle	64/63	0.9	-0.1	1.0 (-0.0, 2.1)						
<b>Baseline Median pVO<sub>2</sub></b>										
≤18.4 mL/kg/min	74/67	1.5	-0.1	1.6 (0.6, 2.5)						
>18.4 mL/kg/min	68/73	2.0	0.1	1.9 (1.0, 2.9)						
<b>Baseline Beta-Blocker Use</b>										
Yes	86/87	1.4	-0.2	1.6 (0.7, 2.5)						
No	56/53	2.2	0.2	1.9 (0.8, 3.1)						
<b>Baseline Resting LVOT (median)</b>										
≤51.1 mmHg	72/69	1.8	0.5	1.3 (0.3, 2.3)						
>51.1 mmHg	70/71	1.7	-0.4	2.1 (1.2, 3.1)						
<b>Genotype</b>										
Positive	20/22	1.6	-1.0	2.6 (0.9, 4.2)						
Negative	71/70	1.4	-0.1	1.4 (0.5, 2.3)						

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# SEQUOIA-HCM: Secondary Endpoints



Statistically significant improvements in all 10 pre-specified secondary endpoints

Endpoints	P value
<b>Primary Endpoint</b>	
pVO <sub>2</sub> change from baseline to Week 24	<0.0001
<b>Secondary Endpoints</b>	
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

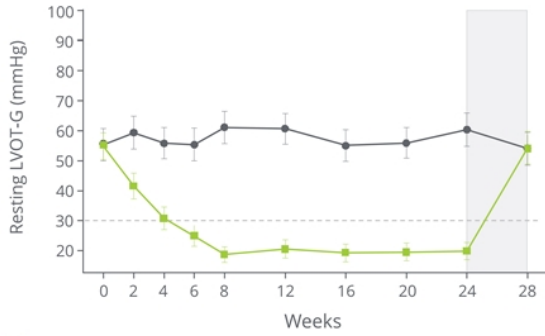
*Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.*  
 Maron M. "Aficamten for the Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy", ESC Heart Failure 2024.

# SEQUOIA-HCM: Secondary & Exploratory Endpoints

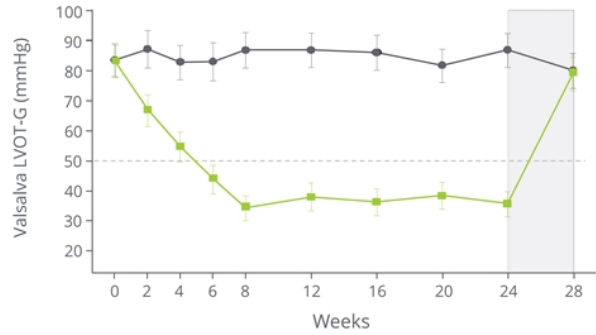


Significant improvement in post-Valsalva left ventricular outflow tract gradient (LVOT-G)

Resting LVOT-G



Valsalva LVOT-G



LS mean difference:  
- 50 mmHg

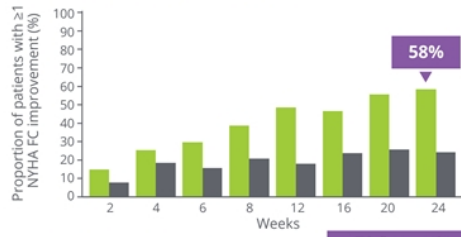
- Aficamten
- Placebo
- Washout

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.

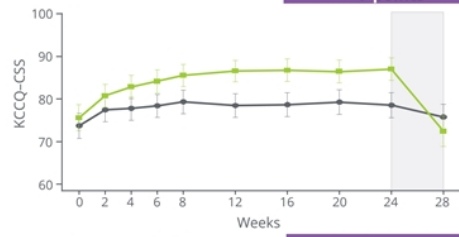
# SEQUOIA-HCM: Secondary & Exploratory Endpoints



## ≥1 NYHA FC Improvement



## KCCQ-CSS



## 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.

# SEQUOIA-HCM: Responder Analysis



Significant improvement in exercise capacity and symptoms in composite responder endpoint

	Aficamten n=142	Placebo n=140
<b>≥1.5 mL/kg/min increase in pVO<sub>2</sub> and ≥1 NYHA FC improvement or ≥3.0 mL/kg/min increase in pVO<sub>2</sub> and no worsening of NYHA FC, n (%)</b>	60 (42)	19 (14)
≥1.5 mL/kg/min increase in pVO <sub>2</sub> and ≥1 NYHA class improvement	44 (31)	9 (6)
≥3.0 mL/kg/min increase in pVO <sub>2</sub> and no worsening of NYHA class	37 (26)	13 (9)
Both ≥3.0 mL/kg/min increase in pVO <sub>2</sub> and ≥1 NYHA class improvement	21 (15)	3 (2)
<b>Common rate difference vs placebo (95% CI) P value</b>	<b>28.7</b> (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)	Aficamten (n=142)
Overall AEs	99 (70.7)	105 (73.9)
<b>Headache</b>	10 (7.1)	11 (7.7)
<b>Hypertension</b>	3 (2.1)	11 (7.7)
<b>Palpitations</b>	4 (2.9)	10 (7.0)
<b>Upper respiratory infection</b>	12 (8.6)	9 (6.3)
<b>COVID-19</b>	9 (6.4)	8 (5.6)
<b>Dyspnea</b>	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 <sup>a</sup>	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

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

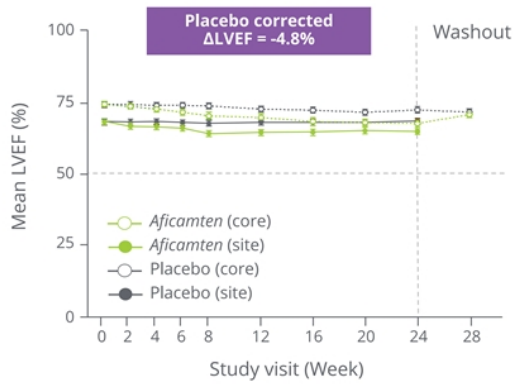
*Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.*  
 AE, adverse event; SAE, serious adverse event.  
 Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart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

# SEQUOIA-HCM: Change in LVEF

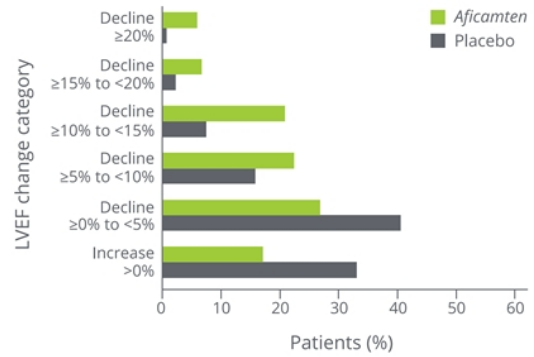


Modest reduction in LVEF in patients on *aficamten* resulted in large reductions in LVOT-G

Mean Change in Core Laboratory LVEF Over 24 Weeks



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

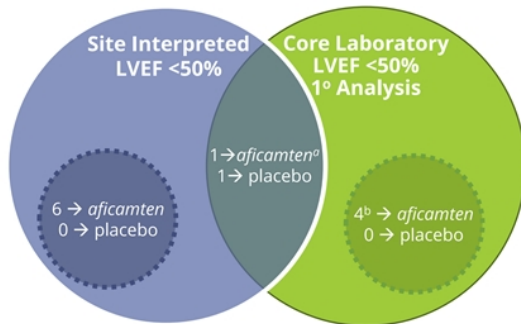


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 Coats CJ. Dosing and Safety Profile of Aficamten in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.

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



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



<sup>a</sup> COVID-19 infection preceded LVEF <50% based on both core and site laboratory assessments.  
<sup>b</sup> 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**

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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

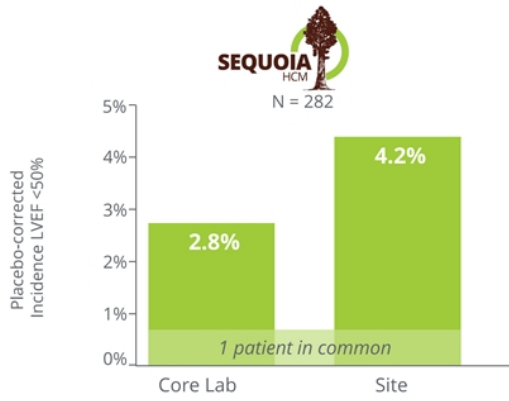
Prespecified Analysis												
Age, y, Sex	Aficamten Dose, mg/d	BL Core LVEF, %	Study Week With Lowest Core LVEF	Lowest Core LVEF %	Matching Site LVEF %	NYHA Class	KCCQ-CSS	NT-proBNP, Change from BL, ng/dL	Down-Titration, mg	Next Visit LVEF Core	Matching Site LVEF %	
<b>Core Lab Only LVEF &lt;50%</b> 4 aficamten patients												
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	
<b>Both Core &amp; Site-Read LVEF &lt;50%</b> 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	
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 %	
<b>Site-Read Only LVEF &lt;50%</b> 6 aficamten patients												
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.

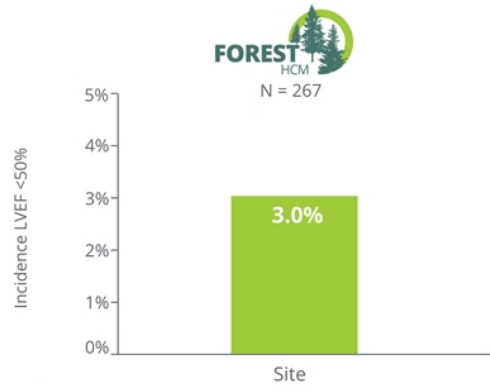


# Implementation of Dosing in Real-World Setting (FOREST-HCM)

## 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

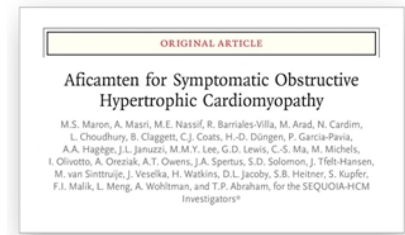
*Aficamten is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.*  
 SEQUOIA-HCM Source: Coats CJ. Dosing and Safety Profile of *Aficamten* in Symptomatic Obstructive Hypertrophic Cardiomyopathy. ESC Heart Failure 2024.  
 FOREST-HCM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

## 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 (pVO<sub>2</sub>), 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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*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.  
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

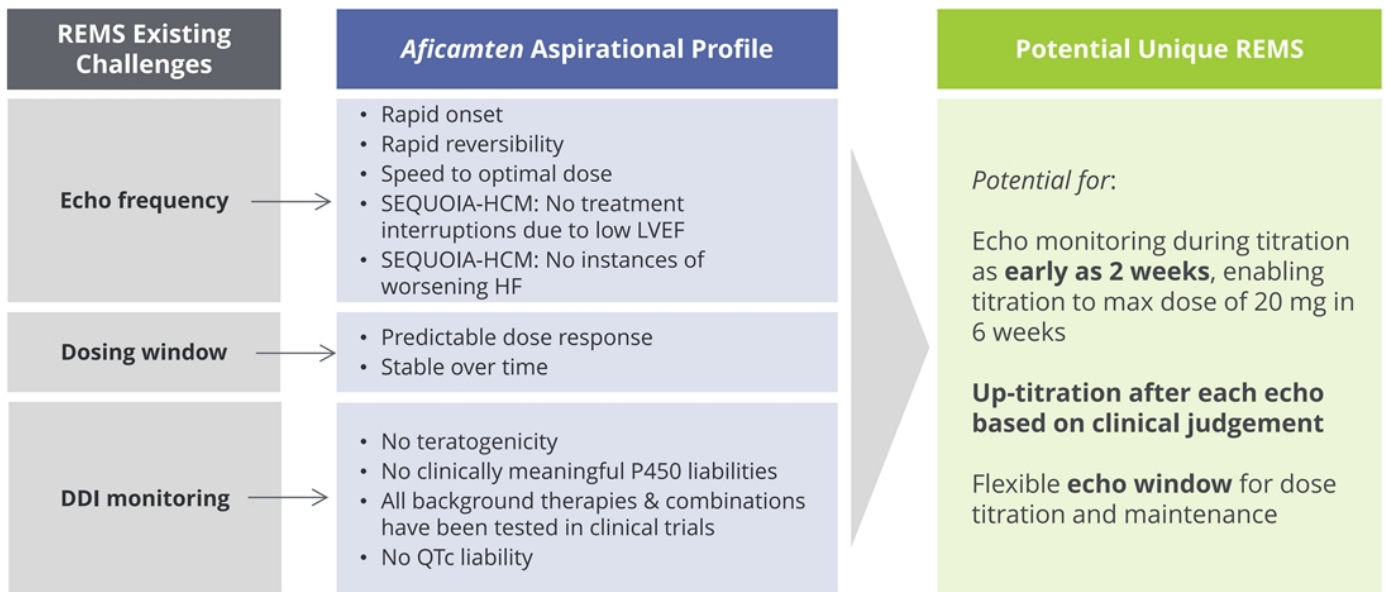


2024

- 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

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# Aspirational Profile of *Aficamten* & Results from SEQUOIA-HCM Inform Potential REMS



# Few Dose Reductions Occurred During Maintenance

FOREST-HCM data cut as of September 15, 2023

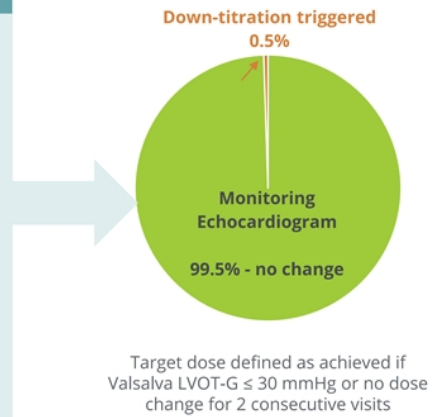


### Dose Titration Phase

- 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



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# Ongoing Clinical Trials of *Aficamten*



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



Pivotal **Phase 3** clinical trial in nHCM



Clinical trial in a **pediatric population**



**Open-label extension** clinical study in HCM

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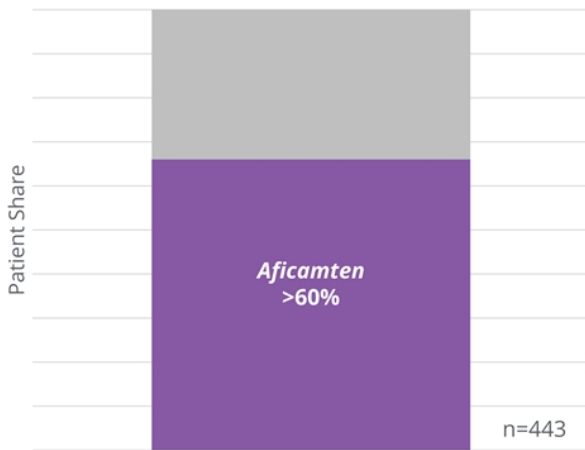
# Cytokinetics Poised to Compete in the Specialty Cardiology Business

## Potential for high return on investment

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

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.

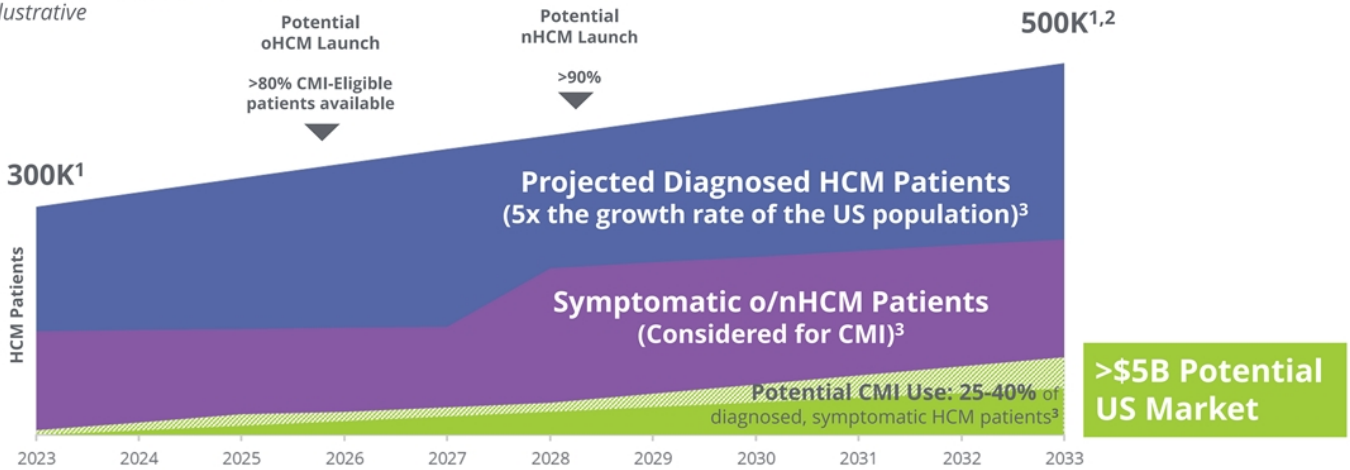
- Potential target product profile for *aficamten* interest creates **share opportunity** in newly treated CMI patients
- *Aficamten* could also be **expected to expand the total CMI market**
- Key attributes that may drive preference include the potential for:
  - LVOT gradient reduction
  - Change 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**

**US HCM Patients (in '000)**

*Illustrative*

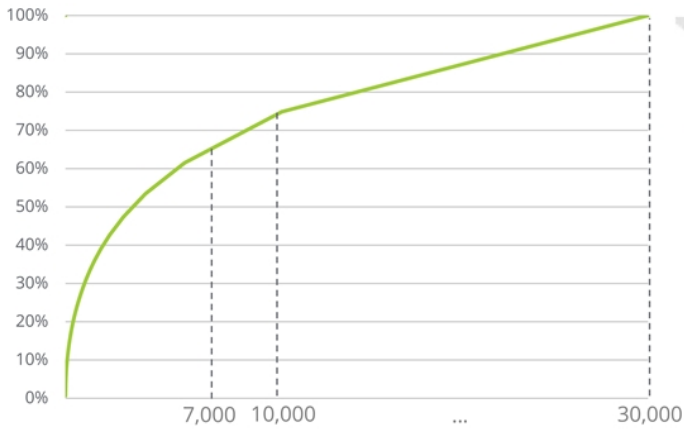


1. DoF: SHA; Symphony PTD (Patient Transaction Data); Includes patients diagnosed since 2016 and having any HC transaction in the claims data universe in the last year June 2022-May 2023;  
 2. Butzner et al 2021 estimated a 8% growth rate in diagnosed HCM patients between 2013-2019 [https://www.ajconline.org/article/S0002-9149\(21\)00783-9/fulltext](https://www.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

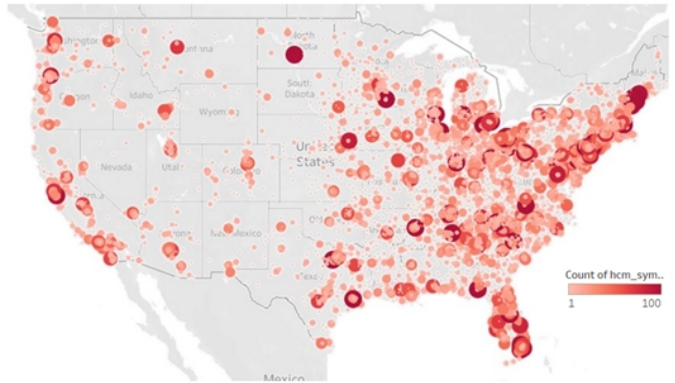
# Cardiologists Located in Concentrated Geographic Clusters Across the US

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

**HCM Patient Concentration by Cardiologist**



**Geographic Distribution of HCM Patients**

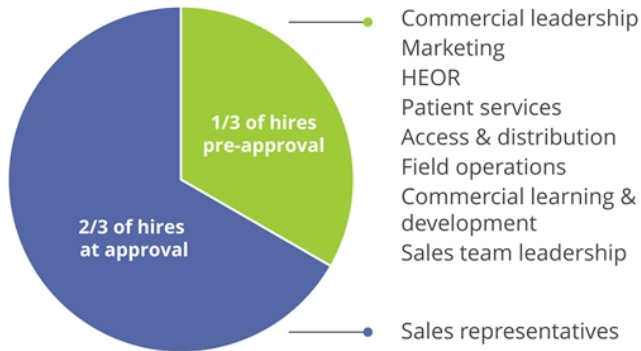


Note: includes only patients who are treated by a cardiologist - not all patients see a cardiologist; sample of 67K HCM patients  
 Source: Symphony PTD (Patient Transaction Data); mapping of HCPs to HCOs using Definitive Healthcare Data 2023 and 7/2023 mapping; Patient volume by dominant Cardiologist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

# 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



## Initiated upon FDA approval

- Payer Pre-approval Information Exchange
- Sales force planning
- Data & Technology Infrastructure build
- Omnichannel execution
- Market development rollout
- Media purchases
- Patient support programs
- Peer to peer engagement
- HCP Omnichannel launched



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# Omecamtiv Mecarbil

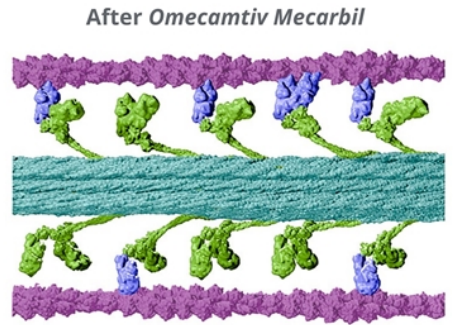
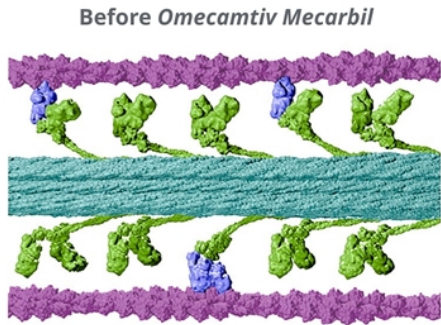
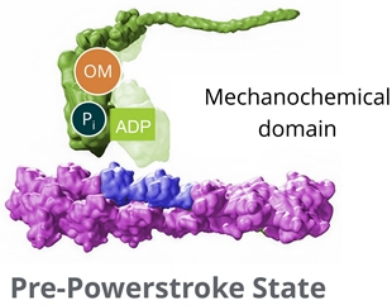


*Omecamtiv mecarbil is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.*

# Omecamtiv Mecarbil: Mechanism of Action

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

“More hands pulling on the rope”

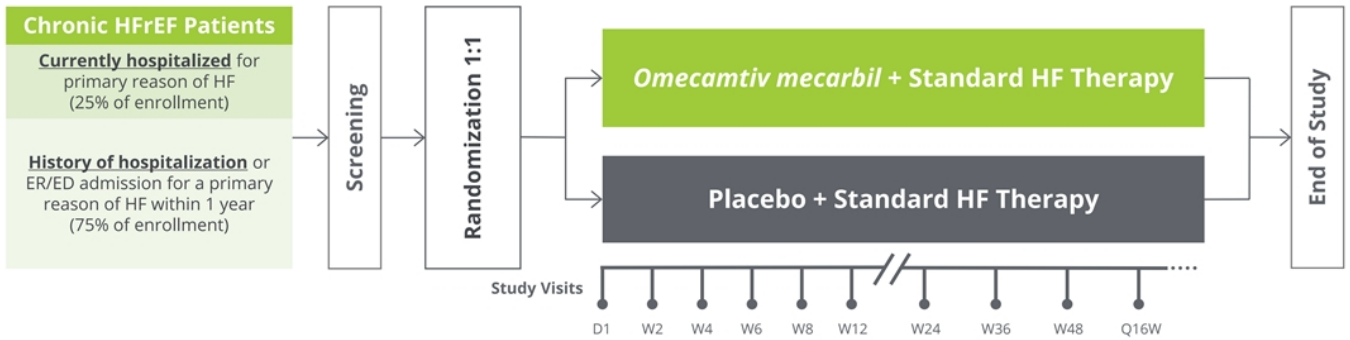


Malik, et al. *Science* 2011; 1439-1443  
Pionelles-Herrero, et al. *Nature Comm* 2017; 1-10  
Shen et al. *Circ HF*, July 2010, 522-527  
Teerlink, et al. *JACC-HF* 2020; 329-340  
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have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

# GALACTIC-HF: Clinical Trial Overview

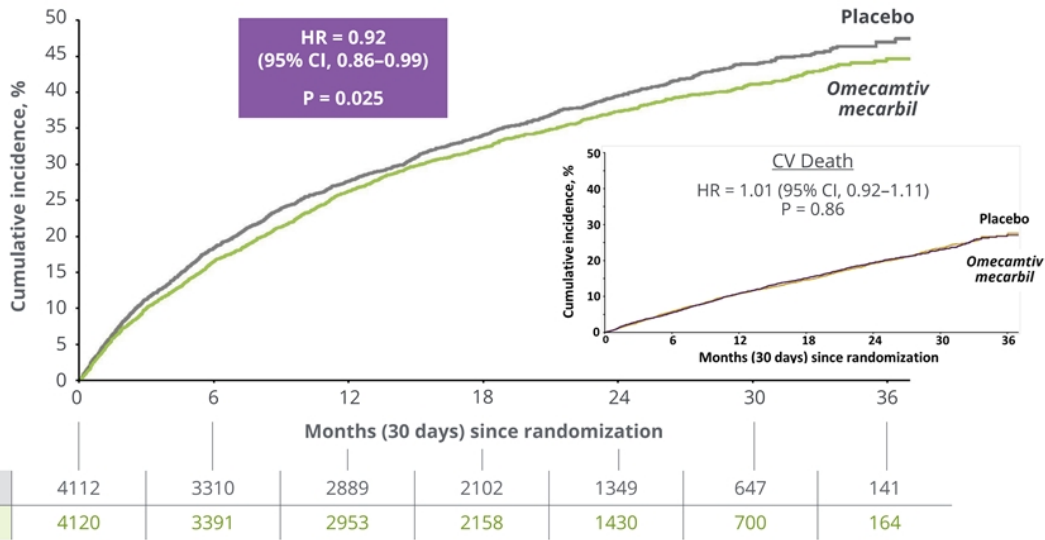
## Phase 3 clinical trial

Event-driven clinical trial; 8256 patients randomized in 35 countries at 944 clinical trial sites



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

# Primary Composite Endpoint



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**ORIGINAL ARTICLE**

**Cardiac Myosin Activation with Omecamtiv Mecarbil in Symptomatic Heart Failure**

**ABSTRACT**

**Background** Omecamtiv mecarbil, a cardiac myosin activator, may have been shown to improve clinical outcomes in patients with heart failure with reduced ejection fraction. We evaluated its effect on cardiovascular mortality in patients with symptomatic heart failure.

**Methods** We conducted a randomized, controlled trial comparing omecamtiv mecarbil with placebo in patients with symptomatic heart failure with reduced ejection fraction. The primary end point was cardiovascular mortality. Secondary end points included all-cause mortality, hospitalization for heart failure, and quality of life.

**Results** In a total of 36 months, a primary end point was reached in 100% of patients in the placebo group and in 100% of patients in the omecamtiv mecarbil group. The primary end point was not reached in either group. The secondary end points were not reached in either group. The quality of life was not significantly different between groups.

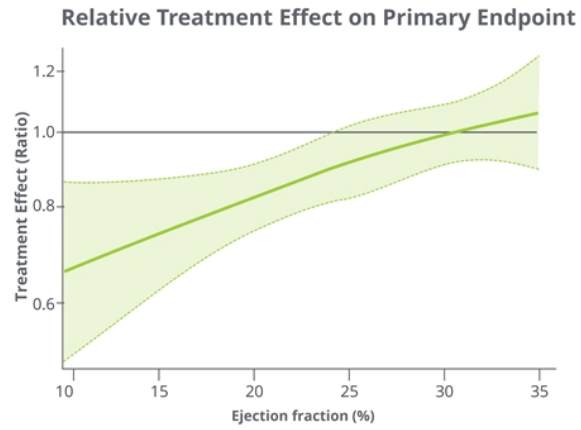
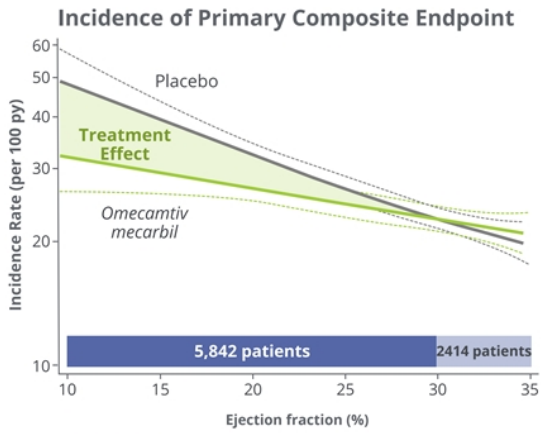
**Conclusions** Omecamtiv mecarbil did not improve cardiovascular mortality or all-cause mortality in patients with symptomatic heart failure with reduced ejection fraction. The quality of life was not significantly different between groups.

**Keywords** Omecamtiv mecarbil, heart failure, cardiovascular mortality, all-cause mortality, quality of life.

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










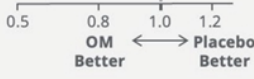
Pre-specified Subgroup	Baseline LVEF	≤ median (28%)	> median (28%)
		0.84 (0.77, 0.92)	1.04 (0.94, 1.16)
Interaction P-value = 0.004			

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.



# In Post-Hoc Analysis, Greater Benefit in Patients with Worsening HF

Subgroup	No. of Events/ No. of Patients		Hazard Ratio (95% CI)	Norm p-value	ARR
All Patients	3103/8232		0.92 (0.86, 0.99)	0.025	2.1%
<b>LVEF ≤28%</b>	<b>1821/4456</b>		<b>0.84 (0.77, 0.92)</b>	<b>&lt;0.001</b>	<b>4.9%</b>
+ Inpatients	566/1152		0.86 (0.73, 1.02)	0.084	3.9%
+ Hosp <3 mos	1200/2688		0.83 (0.74, 0.93)	0.001	5.2%
+ Class III/IV	1055/2132		0.80 (0.71, 0.90)	<0.001	7.0%
+ NT-proBNP >2000	1249/2431		0.77 (0.69, 0.87)	<0.001	8.1%
+ SBP <110	843/1820		0.81 (0.70, 0.92)	0.002	7.4%



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

# Safety Results in Low LVEF Subgroup Were Observed to Continue

Incidences of SAEs, ventricular arrhythmias, & cardiac ischemic events were similar  
 Incidence of stroke was lower with *omecantiv mecarbil*

	Overall Population		LVEF ≤28%	
	<i>Omecantiv Mecarbil</i> N=4110 %	Placebo N=4101 %	<i>Omecantiv 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  
*Omecantiv mecarbil* is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

# Omecamtiv Mecarbil: Current Status

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## Received CRL from FDA

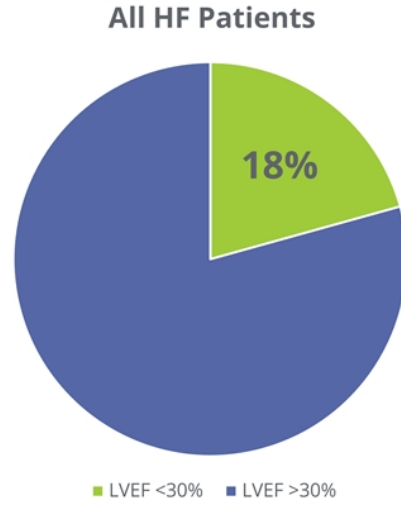
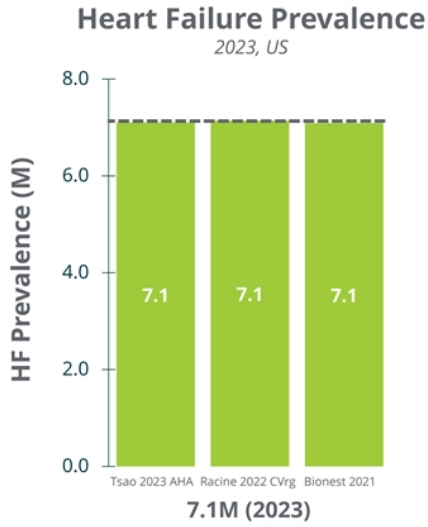
GALACTIC-HF not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic HFrEF

## Withdrew MAA from EMA

Withdrew the MAA from the EMA based on feedback from the CHMP indicating that the Committee will not be able to conclude that the benefits outweigh the risks on the basis of the results from GALACTIC-HF alone

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



## 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

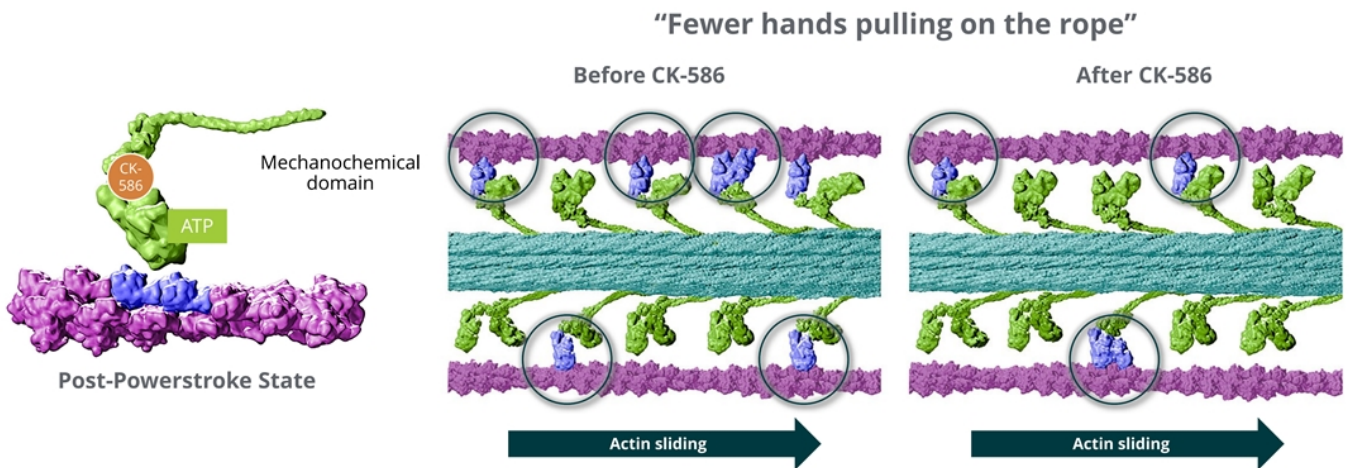
Omecamtiv mecarbil is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

# CK-586



*CK-586 is an investigational agent and has not been approved for use by the U.S. Food & Drug Administration (FDA) or any regulatory agency. The safety and effectiveness of this product has not been established.*

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



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 poor<sup>1</sup>



Americans will have heart failure by 2030<sup>2</sup>



HF patients have HFpEF<sup>3</sup> & prevalence of HFpEF is increasing<sup>2,4</sup>



HFpEF patients will die within five years of initial hospitalization<sup>2</sup>



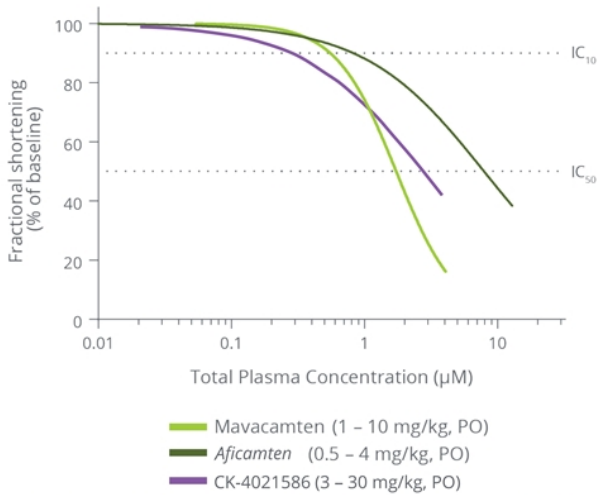
HFpEF patients will be rehospitalized<sup>2</sup>

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 <sub>50</sub> /IC <sub>10</sub> ratio	
mavacamten	2.8x
<i>aficamten</i>	9.9x
CK-586	9.3x

IC<sub>10</sub>: plasma concentration at 10% relative reduction in fractional shortening  
 IC<sub>50</sub>: 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	TBD	15 hours

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 series adverse events** were observed
- **Stopping criteria were not met**

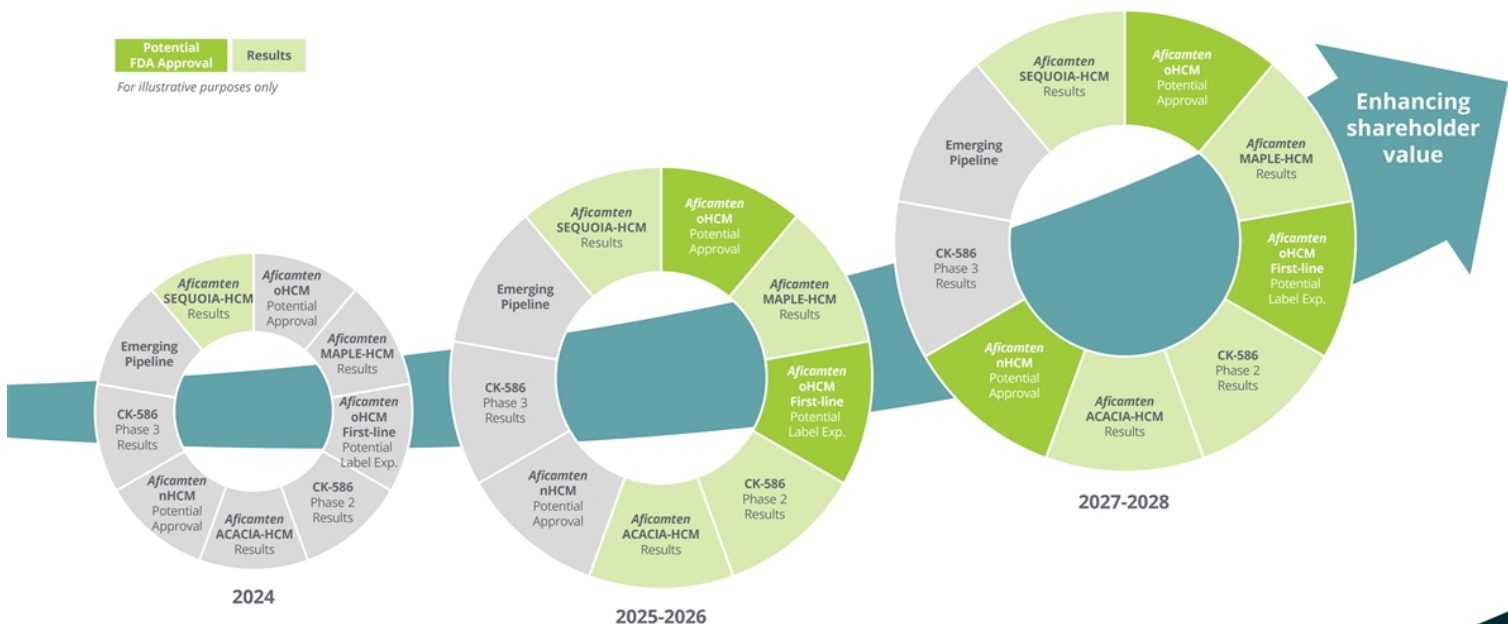
CK-586 is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established.

# Corporate Profile

# Myosin Platform Drives Multiple Data Milestones and Potential Approvals

Potential FDA Approval    Results

For illustrative purposes only



# 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
<b>Total Assets</b>	<b>\$808.1</b>
Convertible Debt, net	\$549.8
Liability related to sale of future royalties	\$390.2
Lease liability	\$136.8
Other liabilities	\$127.4
<b>Total Liabilities</b>	<b>\$1,204.2</b>
Working capital	\$549.8
Accumulated deficit	(\$2,247.9)
Stockholders' deficit	(\$396.2)
<b>Wtd Avg Basic Shares Outstanding (million)</b>	<b>101.9</b>

## 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		CK-586
Submit NDA to FDA in Q3 2024 and MAA to EMA in Q4 2024	Complete enrollment of MAPLE-HCM in Q3 2024	Share full data from Phase 1 study of CK-586 in 2H 2024
Continue enrollment in ACACIA-HCM In 2024	Continue enrollment of CEDAR-HCM in 2024	Initiate Phase 2 study of CK-586 in Q4 2024
Begin Phase 1 study of <i>aficamten</i> in healthy Japanese volunteers in Q2 2024		<b>Pre-Clinical Development &amp; Ongoing Research</b>
		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  
Afonne, diagnosed with HCM  
John, diagnosed with heart failure

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