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 13, 2024

Cytokinetics, Incorporated

(Exact name of Registrant as Specified in Its Charter)

Delaware	**000-50633**	**94-3291317**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
350 Oyster Point Boulevard South San Francisco, California		**94080**
(Address of Principal Executive Offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (650) 624-3000

N/A
(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, $0.001 par value	CYTK	The Nasdaq Global Select Market

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 13, 2024, Cytokinetics, Incorporated (the "Company") issued a press release announcing the release of the primary results form SEQUOIA-HCM that were presented in a late breaking clinical trial session at the European Society of Cardiology Heart Failure 2024 Congress and published in the New England Journal of Medicine. A selected copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

In addition, also on May 13, 2024, the Company issued a second press release announcing the release of additional results from SEQUOIA-HCM at the late breaking clinical trial session at the European Society of Cardiology Heart Failure 2024 Congress. A selected copy of the press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1 Press Release dated May 13, 2024 (Primary Results)
99.2 Press Release dated May 13, 2024 (Additional Results)

SIGNATURES

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

CYTOKINETICS, INCORPORATED

Date: May 13, 2024

By: /s/ John O. Faurescu

John O. Faurescu, Esq.
Associate General Counsel & Secretary

CYTOKINETICS ANNOUNCES PRIMARY RESULTS FROM SEQUOIA-HCM PRESENTED IN LATE BREAKING CLINICAL TRIAL SESSION AT THE EUROPEAN SOCIETY OF CARDIOLOGY HEART FAILURE 2024 CONGRESS AND PUBLISHED IN THE NEW ENGLAND JOURNAL OF MEDICINE

Statistically Significant and Clinically Meaningful Improvements Observed in Primary Efficacy Endpoint and All Secondary Endpoints; Results Consistent Across All Prespecified Subgroups

Rapid and Sustained Improvements Observed in Symptoms and Function; No Treatment Interruptions Due to Low LVEF

Company to Host Investor Event and Webcast Today at 4:00 PM Western European Summer Time (11:00 AM Eastern Time)

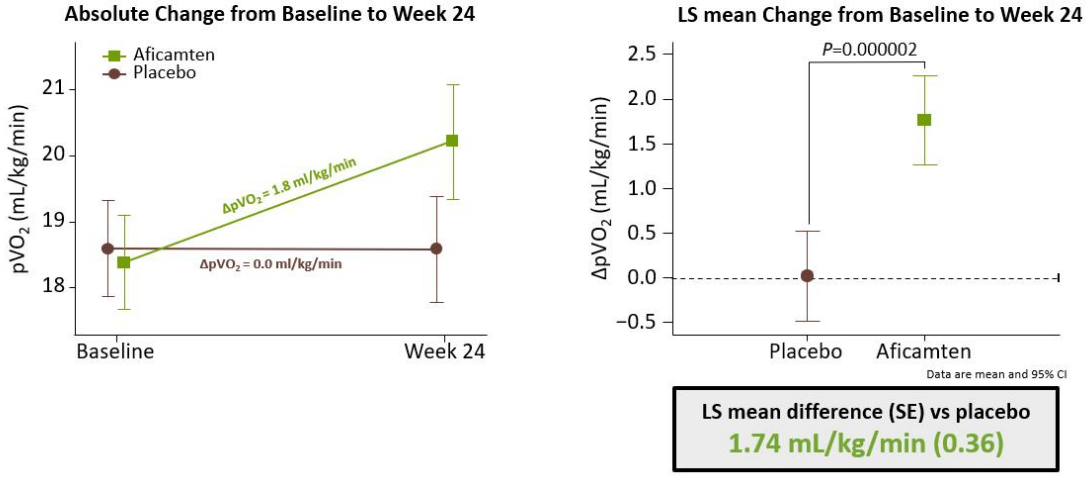
SOUTH SAN FRANCISCO, Calif., May 13, 2024 – Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the primary results from SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***Aficamten*** in **HCM**), the pivotal Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM), were presented by Martin Maron, M.D., Director, Hypertrophic Cardiomyopathy Center, Lahey Hospital and Medical Center, and Principal Investigator of SEQUOIA-HCM, in a Late Breaking Clinical Trial session at Heart Failure 2024, an International Congress of the European Society of Cardiology, and simultaneously published in the *New England Journal of Medicine*.[1]

SEQUOIA-HCM enrolled 282 patients with obstructive HCM. The baseline characteristics of patients in SEQUOIA-HCM were well-matched between treatment groups and consistent with a symptomatic patient population that had high resting and post-Valsalva gradients (mean [SD]; 55.1 [29.6] and 83.1 [32.3] mmHg, respectively) reflective of substantial burden of disease. Background therapies consisted of beta-blockers (61.3%), calcium channel blockers (28.7%), and disopyramide (12.8%), with combination background therapies permitted.

The results from SEQUOIA-HCM showed that treatment with *aficamten* for 24 weeks significantly improved exercise capacity compared to placebo, increasing peak oxygen uptake (pVO_2) measured by cardiopulmonary exercise testing (CPET) by 1.8 ml/kg/min compared to

baseline in patients treated with *aficamten* versus 0.0 ml/kg/min in patients treated with placebo (least square mean (LSM) difference [95% CI] of 1.74 mL/kg/min [1.04 - 2.44]; p=0.000002) (Figure 1).

Figure 1. Primary Endpoint – Change in pVO_2



The treatment effect of *aficamten* was consistent across all prespecified subgroups, including age, sex, patient baseline characteristics, and in patients receiving or not receiving background beta-blocker therapy (Figure 2).

Figure 2. Subgroup Analyses – Change in pVO_2

	n (Afi/Plb)	Aficamten LS mean	Placebo LS mean	Mean difference (95% CI)
Age				
<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)
Sex				
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)
Baseline BMI				
<30 kg/m²	97/94	1.9	0.1	1.8 (1.0, 2.7)
≥30 kg/m²	45/46	1.4	−0.2	1.6 (0.3, 2.8)
Baseline Median LVEF				
≤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)
Baseline NYHA FC				
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)
Baseline Median KCCQ-CSS				
≤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)
Baseline Median NT-proBNP				
≤ 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)
CPET Modality				
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)
Baseline Median pVO_2				
≤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)
Baseline Beta-Blocker Use				
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)
Baseline Median Resting LVOT				
≤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)
Genotype				
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)

Favors Placebo — Favors Treatment

Interaction *P* values were >0.05 for all prespecified subgroups

Favors Placebo — Favors Treatment

BMI, body mass index; CPET, cardiopulmonary exercise test; KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score; LVEF, left ventricular ejection fraction; LS, least squares; LVOT, left ventricular outflow tract; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA FC, New York Heart Association functional class; pVO_2, peak oxygen uptake.

Statistically significant improvements were observed in all 10 prespecified secondary endpoints, with functional and symptomatic improvements occurring within two weeks of initiating treatment with *aficamten* and sustained throughout the treatment period. Compared to baseline, at Week 24 patients treated with *aficamten* experienced significant improvements in post-Valsalva left ventricular outflow tract gradient (LVOT-G) with an LSM difference of -50 mmHg ($p<0.0001$) versus placebo. *Aficamten* also substantially reduced the burden of symptoms compared with placebo, with a significant improvement observed in Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) (LSM difference = 7 points; $p<0.0001$) and with 34% of patients experiencing ≥1 class improvement in New York Heart Association (NYHA) Functional Class ($p<0.0001$) (Figure 3). Treatment with *aficamten* substantially reduced the proportion of patients eligible for septal reduction therapy (SRT). Among those eligible for SRT at baseline, over the duration of 24 weeks of treatment, patients receiving *aficamten* spent 78 fewer days eligible for SRT compared with those treated with placebo ($p<0.0001$). Additionally, from baseline to Week 24, treatment with *aficamten* reduced NT-proBNP, a biomarker of cardiac wall stress, by 80% relative to placebo (Figure 4).

Figure 3. Secondary and Exploratory Endpoints

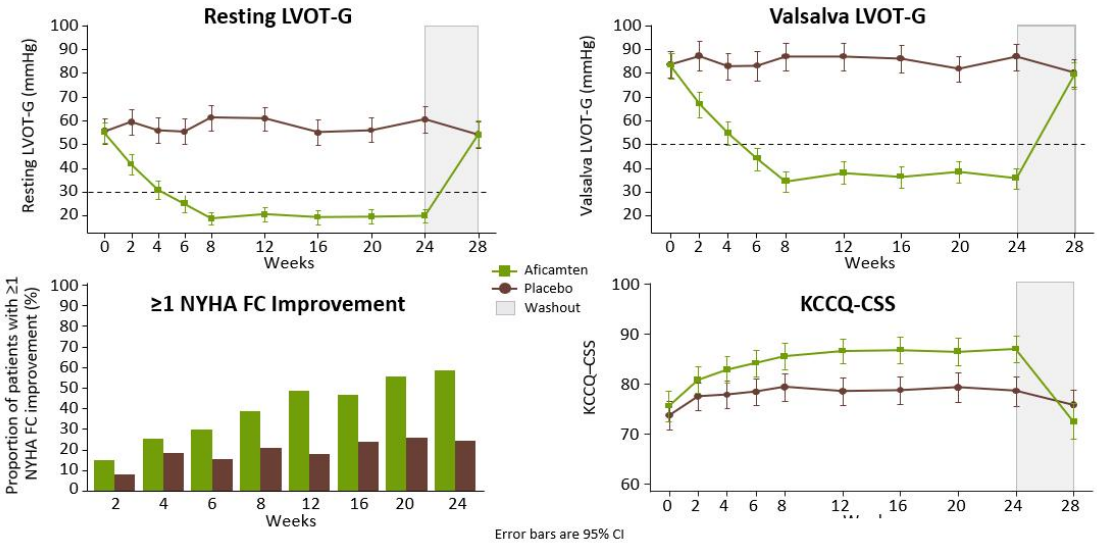
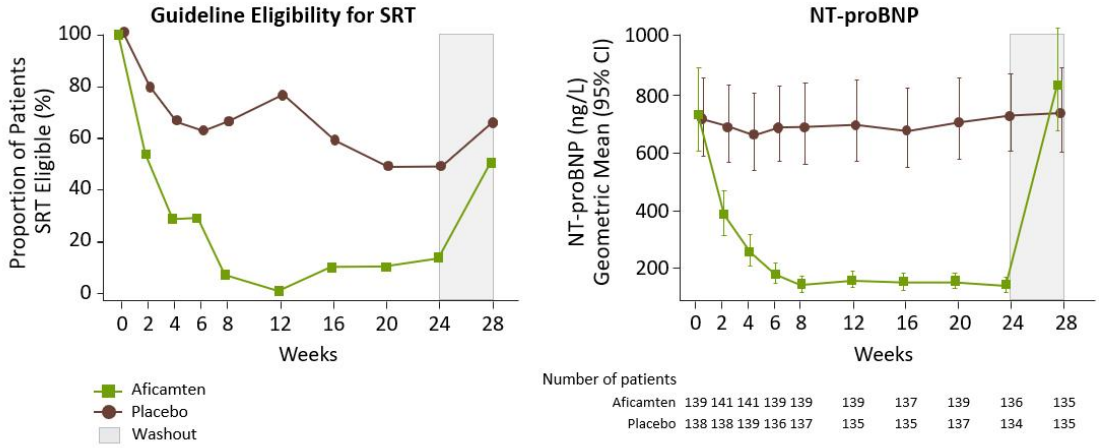


Figure 4. Secondary and Exploratory Endpoints



The prespecified exploratory responder analysis in SEQUOIA-HCM showed that treatment with *aficamten* improved both exercise capacity and symptoms, with 60 (42%) of 142 patients treated with *aficamten* achieving the composite responder endpoint of (1) ≥1.5 mL/kg/min increase in pVO_2 and ≥1 NYHA Functional Class improvement, or (2) ≥3.0 mL/kg/min increase in pVO_2 and no worsening of NYHA Functional Class, compared to 19 (14%) of 140 patients treated with placebo, equating to a placebo-corrected difference of 28.7% (95% CI, 18.8, 38.6; p<0.0001).

[…]

[…]

Aficamten was well-tolerated in SEQUOIA-HCM with an adverse event profile comparable to placebo. Treatment emergent serious adverse events occurred in 5.6% and 9.3% of patients on *aficamten* and placebo, respectively. Core echocardiographic left ventricular ejection fraction (LVEF) was observed to be <50% in 5 patients (3.5%) on *aficamten* compared to 1 patient (0.7%) on placebo. One of the 5 patients on *aficamten* with low LVEF had LVEF <40% following infection with COVID-19 but did not interrupt treatment as the site-read LVEF remained greater than 40% and the patient did not have symptoms of heart failure due to systolic dysfunction. Overall, there were no instances of worsening heart failure or treatment interruptions due to low LVEF.

Investor Event and Webcast Information

[…]

About *Aficamten*

Aficamten is an investigational selective, small molecule cardiac myosin inhibitor discovered following an extensive chemical optimization program that was conducted with careful attention to therapeutic index and pharmacokinetic properties and as may translate into next-in-class potential in clinical development if approved. *Aficamten* was designed to reduce the number of active actin-myosin cross bridges during each cardiac cycle and consequently suppress the myocardial hypercontractility that is associated with hypertrophic cardiomyopathy (HCM). In preclinical models, *aficamten* reduced myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state.

About the Broad Phase 3 Clinical Trials Program for *Aficamten*

The development program for *aficamten* is assessing its potential as a treatment that improves exercise capacity and relieves symptoms in patients with HCM as well as its potential long-term effects on cardiac structure and function.

Aficamten was evaluated in SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A**ficamten* in **HCM**), the pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, CEDAR-HCM, a trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA) as well as the National Medical Products Administration (NMPA) in China.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart's pumping function, resulting in reduced exercise capacity and symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. HCM is the most common monogenic inherited cardiovascular disorder, with approximately 280,000 patients diagnosed in the U.S., however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed.[2,3,4] Two-thirds of patients with HCM have obstructive HCM (oHCM), where the thickening of the cardiac muscle leads to left

ventricular outflow tract (LVOT) obstruction, while one-third have non-obstructive HCM (nHCM), where blood flow isn't impacted, but the heart muscle is still thickened. People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease.[5] People with HCM are at risk for potentially fatal ventricular arrhythmias and it is one of the leading causes of sudden cardiac death in younger people or athletes.[6] A subset of patients with HCM are at high risk of progressive disease leading to dilated cardiomyopathy and heart failure necessitating cardiac transplantation.

About Cytokinetics

Cytokinetics is a late-stage, specialty cardiovascular biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors as potential treatments for debilitating diseases in which cardiac muscle performance is compromised. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to impact myocardial muscle function and contractility. Cytokinetics is preparing for regulatory submissions for *aficamten*, its next-in-class cardiac myosin inhibitor, following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in obstructive hypertrophic cardiomyopathy. *Aficamten* is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure. Additionally, Cytokinetics is developing CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of HFpEF, and CK-136, a cardiac troponin activator for the potential treatment HFrEF and other types of heart failure, such as right ventricular failure resulting from impaired cardiac contractility.

[…]

Forward-Looking Statements

This press release 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 relating to the properties or potential benefits of *aficamten* or any of our other drug candidates, our ability to obtain regulatory approval for *aficamten* for the treatment of obstructive hypertrophic cardiomyopathy or any other indication from FDA or any other

regulatory body in the United States or abroad, and the labeling or post-marketing obligations that may be required by FDA or any other regulatory body in the United States or abroad as a condition to regulatory approval. 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 the risks related to Cytokinetics' business outlines in Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and Cytokinetics' actual results of operations, financial condition and liquidity, and the development of the industry in which it operates, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that Cytokinetics makes in this press release speak only as of the date of this press release. Cytokinetics assumes no obligation to update its forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Contact:
Cytokinetics
Diane Weiser
Senior Vice President, Corporate Affairs
(415) 290-7757

References:

1. Maron, MS, et al. *Aficamten* for Symptomatic Obstructive Hypertrophic Cardiomyopathy. N Engl J Med. DOI: 10.1056/NEJMoa2401424
2. CVrg: Heart Failure 2020-2029, p 44; Maron et al. 2013 DOI: 10.1016/S0140-6736(12)60397-3; Maron et al 2018 10.1056/NEJMra1710575
3. Symphony Health 2016-2021 Patient Claims Data DoF;
4. Maron MS, Hellawell JL, Lucove JC, Farzaneh-Far R, Olivotto I. Occurrence of Clinically Diagnosed Hypertrophic Cardiomyopathy in the United States. Am J Cardiol. 2016; 15;117(10):1651-1654.
5. Gersh, B.J., Maron, B.J., Bonow, R.O., Dearani, J.A., Fifer, M.A., Link, M.S., et al. 2011 ACCF/AHA guidelines for the diagnosis and treatment of hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Journal of the American College of Cardiology and Circulation, 58, e212-260.

6. Hong Y, Su WW, Li X. Risk factors of sudden cardiac death in hypertrophic cardiomyopathy. Current Opinion in Cardiology. 2022 Jan 1;37(1):15-21

CYTOKINETICS ANNOUNCES ADDITIONAL RESULTS FROM SEQUOIA-HCM PRESENTED IN LATE BREAKING CLINICAL TRIAL SESSION AT THE EUROPEAN SOCIETY OF CARDIOLOGY HEART FAILURE 2024 CONGRESS

Analyses of SEQUOIA-HCM Elaborate on Dosing and Measures of Safety During Treatment with Aficamten

Results from Cardiopulmonary Exercise Testing Showed Improvement in Exercise Performance were Strongly Correlated to Other Measures of Clinical Improvement

Company to Host Investor Event and Webcast Today at 4:00 PM Western European Summer Time (11:00 AM Eastern Time)

SOUTH SAN FRANCISCO, Calif., May 13, 2024 – Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional results from SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A****ficamten* in **HCM**), the pivotal Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM), elaborating on dosing and safety data as well as the effect of *aficamten* on exercise performance were presented at Heart Failure 2024, an International Congress of the European Society of Cardiology. The primary results from SEQUOIA-HCM were also presented in the same Late Breaking Clinical Trial session at the Congress and simultaneously published in the *New England Journal of Medicine.*[1]

[...]

Aficamten **Demonstrates Predictable Dosing with No Dose Interruptions Due to LVEF <50%**

Results from prespecified analyses from SEQUOIA-HCM on dosing and measures of safety during treatment with *aficamten* were presented by Caroline Coats, M.D., Ph.D., Lead Clinician, West of Scotland Inherited Cardiac Conditions Service, Honorary Senior Lecturer, School of Cardiovascular and Metabolic Health, University of Glasgow. In SEQUOIA-HCM, there were no major adverse cardiovascular events associated with treatment with *aficamten.* Serious adverse events occurred in 8 (5.6%) patients in the *aficamten* group and 13 (9.3%) patients in the placebo

group, none of which were determined to be related to study drug. There was no difference in the incidence of adverse events by dose strength. Over the duration of the 24-week double-blind treatment period, patients treated with *aficamten* had a placebo-corrected average change in left ventricular ejection fraction (LVEF) of -4.8% (95% CI -6.3 to -3.2). This modest reduction in LVEF in patients treated with *aficamten* resulted in large reductions in left ventricular outflow tract gradient (LVOT-G).

Titration of patients to their individually determined target dose of *aficamten* resulted in dose-related increases in plasma drug concentrations with the majority of patients achieving one of the two highest doses (15 mg in 35.0% and 20 mg in 48.6%). Following the completion of dose titration, during the maintenance phase, plasma drug concentrations of *aficamten* remained stable with low variability for the duration of the treatment.

Overall, there was a low frequency of LVEF <50% in SEQUOIA-HCM. LVEF determined by the core laboratory was the prespecified analysis; 5 patients (3.5%) on *aficamten* compared to 1 patient (0.7%) on placebo had LVEF <50%. One of the 5 patients on *aficamten* had LVEF <40% following infection with COVID-19 but did not interrupt treatment as the site-read LVEF remained greater than 40% and the patient did not have symptoms of heart failure due to systolic dysfunction. Overall, there were no instances of worsening heart failure or treatment interruptions due to low LVEF.

To enable same-day dose adjustments, the dosing algorithm in SEQUOIA-HCM used site-interpreted LVEF and LVOT gradients for dose adjustments per protocol as implemented by the interactive Web-response system. There were 7 (4.9%) patients treated with *aficamten* who underwent per-protocol dose reductions for site-read LVEF <50%. Only one patient treated with *aficamten* had both core laboratory and site-read LVEF <50%. There were no dose interruptions and none of the patients treated with *aficamten* experienced symptoms of heart failure due to systolic dysfunction.

[…]

Aficamten Improved Novel Integrated Exercise Performance Metric; Improvements in Exercise Performance Correlated with Improvements in Cardiac Structure and Function

Results from a prespecified analysis of cardiopulmonary exercise testing (CPET) metrics in SEQUOIA-HCM were presented by Gregory Lewis, M.D., Jeffrey and Mary Ellen Jay Chair and Section Head, Heart Failure Medical Director, Cardiopulmonary Exercise Testing Laboratory, Professor of Medicine, Harvard Medical School. In addition to significantly improving peak oxygen uptake (pVO_2), this prespecified analysis demonstrated that treatment with *aficamten* for

24 weeks improved a novel integrated exercise performance metric. Additionally, improvements in pVO_2 were highly correlated with improvements in other clinically important measures.

To capture both maximal and submaximal exercise performance (pVO_2 and ventilatory efficiency [V_E/VCO_2], respectively) an integrated CPET Z-score metric was developed that combines the two measurements into a composite endpoint. It integrates the effect of *aficamten* on exercise across the entire test, representing a more complete view of the therapeutic effect of *aficamten* on functional capacity. *Aficamten* substantially improved overall performance of the integrated CPET Z-score by a placebo-adjusted difference of 0.35 (95% CI, 0.25, 0.46; $p<0.001$). Additionally, of patients treated with *aficamten*, 72.2% experienced an improvement in pVO_2, compared to 43.8% of patients treated with placebo. Among the patients treated with *aficamten,* 27.8% had a large improvement (≥3.0 mL/kg/min) in pVO_2, 21.8% had a moderate improvement (≥1.5 to <3.0 mL/kg/min) and 22.6% had a small improvement (0 to <1.5).

Furthermore, enhanced exercise performance was shown to be correlated with improvements in clinically important measures including Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) ($p=0.001$), New York Heart Association (NYHA) Functional Class ($p<0.001$), resting LVOT-G ($p=0.003$), Valsalva LVOT-G ($p=0.001$), NT-proBNP ($p<0.001$) and high-sensitivity cardiac troponin I ($p=0.010$). Importantly, these correlations demonstrate that the therapeutic effects of *aficamten* manifest broadly and are interrelated.

[…]

Investor Event and Webcast Information

[…]

About *Aficamten*

Aficamten is an investigational selective, small molecule cardiac myosin inhibitor discovered following an extensive chemical optimization program that was conducted with careful attention to therapeutic index and pharmacokinetic properties and as may translate into next-in-class potential in clinical development. *Aficamten* was designed to reduce the number of active actin-myosin cross bridges during each cardiac cycle and consequently suppress the myocardial hypercontractility that is associated with hypertrophic cardiomyopathy (HCM). In preclinical models, *aficamten* reduced myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state.

About the Broad Phase 3 Clinical Trials Program for *Aficamten*

The development program for *aficamten* is assessing its potential as a treatment that improves exercise capacity and relieves symptoms in patients with HCM as well as its potential long-term effects on cardiac structure and function.

SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A****ficamten* in **HCM**), was the pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). The results from SEQUOIA-HCM showed that treatment with *aficamten* for 24 weeks significantly improved exercise capacity compared to placebo, increasing peak oxygen uptake (pVO_2) measured by cardiopulmonary exercise testing (CPET) by 1.8 ml/kg/min compared to baseline in patients treated with *aficamten* versus 0.0 ml/kg/min in patients treated with placebo (least square mean (LSM) difference [95% CI] of 1.74 mL/kg/min [1.04 - 2.44]; p=0.000002). The treatment effect with *aficamten* was consistent across all prespecified subgroups reflective of patient baseline characteristics and treatment strategies, including patients receiving or not receiving background beta-blocker therapy. Statistically significant ($p<0.0001$) and clinically meaningful improvements were also observed in all 10 prespecified secondary endpoints. *Aficamten* was well-tolerated with an adverse event profile comparable to placebo. Treatment emergent serious adverse events occurred in 5.6% and 9.3% of patients on *aficamten* and placebo, respectively. Core echocardiographic left ventricular ejection fraction (LVEF) was observed to be <50% in 5 patients (3.5%) on *aficamten* compared to 1 patient (0.7%) on placebo. Overall, there were no instances of worsening heart failure or treatment interruptions due to low LVEF.

Aficamten is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, and CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA) as well as the National Medical Products Administration (NMPA) in China.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart's pumping function, resulting in reduced exercise capacity and symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. HCM is the most common monogenic inherited cardiovascular disorder,

with approximately 280,000 patients diagnosed in the U.S., however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed.[1,2,3] Two-thirds of patients with HCM have obstructive HCM (oHCM), where the thickening of the cardiac muscle leads to left ventricular outflow tract (LVOT) obstruction, while one-third have non-obstructive HCM (nHCM), where blood flow isn't impacted, but the heart muscle is still thickened. People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease.[4] People with HCM are at risk for potentially fatal ventricular arrhythmias and it is one of the leading causes of sudden cardiac death in younger people or athletes.[5] A subset of patients with HCM are at high risk of progressive disease leading to dilated cardiomyopathy and heart failure necessitating cardiac transplantation.

About Cytokinetics

Cytokinetics is a late-stage, specialty cardiovascular biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors as potential treatments for debilitating diseases in which cardiac muscle performance is compromised. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to impact myocardial muscle function and contractility. Cytokinetics is preparing for regulatory submissions for *aficamten*, its next-in-class cardiac myosin inhibitor, following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in obstructive hypertrophic cardiomyopathy. *Aficamten* is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM, CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure. Additionally, Cytokinetics is developing CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of HFpEF, and CK-136, a cardiac troponin activator for the potential treatment HFrEF and other types of heart failure, such as right ventricular failure resulting from impaired cardiac contractility.

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Forward-Looking Statements

This press release 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 relating to the properties or potential benefits of *aficamten* or any of our other drug candidates, our ability to obtain regulatory approval for *aficamten* for the treatment of obstructive hypertrophic cardiomyopathy or any other indication from FDA or any other regulatory body in the United States or abroad, and the labeling or post-marketing conditions that FDA or another regulatory body may require in connection with the approval of *aficamten.* 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 the risks related to Cytokinetics' business outlines in Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and Cytokinetics' actual results of operations, financial condition and liquidity, and the development of the industry in which it operates, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that Cytokinetics makes in this press release speak only as of the date of this press release. Cytokinetics assumes no obligation to update its forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Contact:
Cytokinetics
Diane Weiser
Senior Vice President, Corporate Affairs
(415) 290-7757

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