# Cytokinetics Provides Update on Cardiac Myosin Inhibitor Programs and Plans to Build a Specialty Cardiology Franchise at Virtual Investor & Analyst Day

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*New Long-Term Data from FOREST-HCM, the Open-Label Extension Study of Aficamten, Show Sustained Improvements in Clinical Efficacy Endpoints and No Treatment Interruptions for Low Ejection Fraction*

*Commercial Readiness Activities Leverage Insights from Market Research to Inform Market Segmentation and Patient-Centric Strategies*

*New Pre-Clinical Data for CK-586 Shows Improved Diastolic Function and Reduced Cardiac Fibrosis in Animal Model of HFpEF; Phase 1 Study Ongoing*

SOUTH SAN FRANCISCO, Calif., Oct. 19, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) will provide an update on the company's cardiac myosin inhibitor programs and plans to build a specialty cardiology franchise today at its virtual Investor and Analyst Day, "New Horizons in Hypercontractility." The company plans to review the broad development program for *aficamten* and present new long-term data from FOREST-HCM (**F**ollow-up, **O**pen-Label, **R**esearch **E**valuation of **S**ustained **T**reatment with *Aficamten* in **HCM**) and highlight commercial readiness activities in advance of the potential approval and launch of *aficamten*. The company will also present new preclinical data for CK-4021586 (CK-586), a cardiac myosin inhibitor in development for the potential treatment of patients with heart failure with preserved ejection fraction (HFpEF). Today's event will also feature perspectives from leading physician experts and a patient advocate living with hypertrophic cardiomyopathy (HCM).

"Cytokinetics is advancing plans to build a specialty cardiology franchise anchored by *aficamten*. We believe we have a unique opportunity to address the multiple manifestations of cardiac hypercontractility with both our late-stage programs and our earlier-stage pipeline," said Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "We expect that, if *aficamten* is approved, our investment in its clinical development program will support the potential to build a foundation rooted in obstructive HCM, expand into non-obstructive HCM, and bridge to HFpEF while also pursuing opportunities in advanced heart failure. We are uniquely positioned to pursue a specialty cardiology franchise and deliver on the promise of our science to bring forward new medicines for patients given the combination of our pioneering leadership in muscle biology, focused cardiology expertise and strong relationships with institutions, cardiologists and payers."

**New Long-Term Data from FOREST-HCM Support Development Program for *Aficamten***

The company plans to present today new long-term efficacy and safety data from FOREST-HCM, an open-label extension clinical study of *aficamten*. More than 200 patients have been enrolled in FOREST-HCM to date and 143 patients were available for this analysis. Of the 94 patients who had completed the titration period (by Week 12), approximately two-thirds are receiving the 15 mg or 20 mg doses of *aficamten*. During the titration period, there have been no treatment-related instances of left ventricular ejection fraction (LVEF) <50%. During the maintenance phase, there have been no instances of LVEF <40%, which would require dose interruption, and only three instances of LVEF <50% that required a dose down-titration. Therefore, of the 579 monitoring echocardiograms completed during the maintenance phase of treatment, 99.5% of them did not result in a dose reduction.

Additionally, after prolonged treatment for more than two years in some patients, the mean resting left ventricular outflow tract gradients (LVOT-G) and mean Valsalva LVOT-Gs remained reduced and below the diagnostic threshold for obstructive HCM (oHCM). Patients also experienced sustained reductions in cardiac biomarkers and improved symptoms. The KCCQ increased by ≥5 points in 71% of patients, 30% of whom had an improvement of ≥10 points. Approximately half of patients were asymptomatic at one year by NYHA Functional Class assessment, and 80% of patients improved by one or more Functional Class at every visit after starting treatment with *aficamten*. Of patients eligible for septal reduction therapy (SRT) at baseline, 90% were no longer SRT-eligible at the time of this analysis. *Aficamten* has been generally well-tolerated, with 60% of patients experiencing at least one treatment emergent adverse event (TEAE) but no treatment-related serious adverse events (SAEs) as assessed by investigators, and no patient deaths.

Today Cytokinetics management will elaborate on these new long-term data from FOREST-HCM and will also provide an overview of the broad development program for *aficamten* focused to the potential treatment of patients with oHCM and non-obstructive HCM (nHCM).

**Preparing for Commercial Readiness for the Potential Approval and Launch of *Aficamten***

Cytokinetics commercial leaders will provide an update on the company's commercial readiness activities, including results of market research and customer segmentation exercises which inform positioning, branding, payer access and sales strategies. The company has structured its current commercial planning initiatives with a focus to gaining a deep understanding of the HCM market and designing an optimal physician and patient experience. The company has conducted market research to assess potential patient profiles and available market segments in obstructive HCM which have revealed a symptomatic patient population in need of treatment with a potential next-in-class cardiac myosin inhibitor. By anchoring its commercial strategies to its patient-centric approach, Cytokinetics is preparing to address a high unmet customer need with objective to potentially make a positive impact for patients and shareholders, if *aficamten* will be approved.

**Expanding Clinical Research with CK-586 for the Potential Treatment of HFpEF**

The company plans to present today new pre-clinical data for CK-586, a cardiac myosin inhibitor, which is currently the subject of an ongoing Phase 1 study and is in development for the potential treatment of patients with HFpEF. These preclinical data show improved diastolic function and reduced cardiac fibrosis in an animal model of HFpEF. Cytokinetics' management will also discuss the rationale for the development of CK-586 in a defined subset of patients with HFpEF characterized by hypercontractility resembling nHCM.

**Perspectives from Physician Experts and Patient Advocate**

At today's Investor & Analyst Day, a panel of leading physician experts in the treatment of HCM will discuss perspectives on the evolving HCM landscape. Panelists include:

- **Theodore Abraham, M.D., FACC, FASE,** Meyer Friedman Distinguished Professor of Medicine, Division of Cardiology, University of California, San Francisco; Co-director, UCSF HCM Center of Excellence; Director, UCSF Adult Cardiac Echocardiography Laboratory
- **Caroline Coats, Ph.D.,** Clinical Senior Lecturer, School of Cardiovascular & Metabolic Health, University of Glasgow
- **Carolyn Ho, M.D.,** Associate Professor, Harvard Medical School, Medical Director of the Cardiovascular Genetics Center

In addition, a patient living with HCM will share her experience and perspectives.

**Access to Virtual Event**

Interested parties must register online at https://cytokinetics-new-horizons-in-hypercontractility.open-exchange.net/. Registered attendees may access the virtual event platform by visiting the Investor & Media section of the Cytokinetics website at www.cytokinetics.com. A link to the webcast replay will be archived on the Cytokinetics website until April 19, 2024.

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

*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.

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* is currently the subject of SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A****ficamten* in **HCM**), a pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM), MAPLE-HCM (***M****etoprolol* vs ***A****ficamten* in **P**atients with **L**VOT Obstruction on **E**xercise Capacity in **HCM**), a Phase 3 clinical trial evaluating *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, and ACACIA-HCM (**As**sessment **C**omparing ***A****ficamten* to Placebo on **C**ardiac Endpoints **I**n **A**dults with Non-Obstructive **HCM**), a pivotal Phase 3 clinical trial in patients with symptomatic non-obstructive HCM. Results from SEQUOIA-HCM are expected by the end of 2023. *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. *Aficamten* is a next-in-class cardiac myosin inhibitor, currently the subject of three Phase 3 clinical trials: SEQUOIA-HCM, evaluating *aficamten* in patients with obstructive hypertrophic cardiomyopathy (HCM), MAPLE-HCM, evaluating *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM and ACACIA-HCM, evaluating *aficamten* in patients with non-obstructive HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure. Additionally, Cytokinetics is developing 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, and CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of HFpEF. In 2023, Cytokinetics is celebrating its 25-year history of pioneering innovation in muscle biology and related pharmacology focused to diseases of muscle dysfunction and conditions of muscle weakness.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on X, LinkedIn, Facebook and YouTube.

**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*, CK-586 or any of our other drug candidates, our ability to announce the results of SEQUOIA-HCM by the end of 2023, our ability to submit or obtain approval of a future new drug application or other marketing authorization application for *aficamten* in oHCM or nHCM or commercially launch *aficamten* in the United States or any other jurisdiction, or that any of the long-term efficacy and safety results from FOREST-HCM described in this press release will be replicated in, or that they are otherwise indicative of, any future efficacy or safety results to be released of SEQUOIA-HCM, MAPLE-HCM, ACACIA-HCM or any of our other clinical trials. 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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References:

1. 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.
2. Symphony Health 2016-2021 Patient Claims Data DoF.
3. 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.
4. 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.
5. 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.

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