# Cytokinetics Announces FDA Acceptance of New Drug Application for Aficamten for the Treatment of Obstructive Hypertrophic Cardiomyopathy

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*PDUFA Target Action Date Set for September 26, 2025*

SOUTH SAN FRANCISCO, Calif., Dec. 02, 2024 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the U.S. Food & Drug Administration (FDA) has accepted the company's New Drug Application (NDA) for *aficamten*, a next-in-class cardiac myosin inhibitor, for the treatment of obstructive hypertrophic cardiomyopathy (HCM).

The FDA assigned the NDA a standard review with a Prescription Drug User Fee Act (PDUFA) target action date of September 26, 2025. The FDA is not currently planning to hold an advisory committee meeting to discuss the application.

"The NDA acceptance for *aficamten* by FDA is a significant milestone that moves our company another step closer to hopefully translating our pioneering science to the potential benefit of patients suffering from obstructive HCM. The results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial, which form the foundation of the NDA, demonstrated that *aficamten* has a positive impact on exercise capacity, clinical outcomes, symptom burden and cardiac biomarkers in patients with HCM, with a consistent effect across all prespecified subgroups and a favorable safety and tolerability profile," said Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "If approved by FDA, we believe *aficamten* may expand utilization of cardiac myosin inhibitors and become the preferred choice amongst physicians and patients while also anchoring our emerging specialty cardiology franchise arising from Cytokinetics' industry-leading muscle biology directed research."

The NDA is supported by the 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 HCM, which were published in the *New England Journal of Medicine*.[1]

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). Statistically significant improvements were observed in all 10 prespecified secondary endpoints, including Valsalva left ventricular outflow tract (LVOT) gradient, New York Heart Association (NYHA) Functional Class, Kansas City Cardiomyopathy Clinical Summary Score (KCCQ-CSS), and proportion with LVOT gradient <30 mmHg, each at 12 and 24 weeks, as well as duration of guideline eligibility for septal reduction therapy (SRT), and total workload during CPET at 24 weeks. 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. There were no instances of worsening heart failure or treatment interruptions due to low LVEF.

Additional analyses from SEQUOIA-HCM have demonstrated that treatment with *aficamten* is associated with favorable cardiac remodeling as well as improvements in cardiac structure, function, and biomarkers without negatively impacting systolic function.

The FDA previously granted *aficamten* Orphan Drug Designation for the treatment of symptomatic HCM in January 2021 and Breakthrough Therapy Designation for the treatment of obstructive HCM in December 2021.

**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 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* was evaluated in SEQUOIA-HCM, a positive pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (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 where it is currently also under review for potential approval.

*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.

**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, however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed in the U.S.[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 muscle biology-directed drug candidates 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. Following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial evaluating *aficamten,* a next-in-class cardiac myosin inhibitor, in obstructive hypertrophic cardiomyopathy (HCM), Cytokinetics is progressing regulatory submissions for *aficamten* for the treatment of obstructive HCM in the US, Europe, and China. *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 with severely reduced ejection fraction (HFrEF), CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten* for the potential treatment of heart failure with preserved ejection fraction (HFpEF), and CK-089, a fast skeletal muscle troponin activator (FSTA) for the potential treatment of a specific type of muscular dystrophy.

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* 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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