NEWS RELEASE

Cytokinetics Presents Additional Data Related to Aficamten at the European Society of Cardiology Heart Failure 2025 Congress

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Two New Analyses from SEQUOIA-HCM on Effect of Aficamten Between Patients with Mild and Moderate-to-Severe Symptoms, and Across Geographic Regions

HEOR Analyses of Real-World Data Reveal Disparities in Outcomes In Females and Older Patients with Non-Obstructive HCM

SOUTH SAN FRANCISCO, Calif., May 18, 2025 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data arising from two analyses 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), and results from a real-world analysis related to non-obstructive HCM were presented at the European Society of Cardiology Heart Failure 2025 Congress. The results from an analysis of the efficacy of *aficamten* in patients with obstructive HCM and mild symptoms in SEQUOIA-HCM were also simultaneously published in *The European Heart Journal*.[1]

“These analyses from SEQUOIA-HCM demonstrate that the effect of *aficamten* on exercise capacity, symptoms, hemodynamics and cardiac biomarkers is consistent in patients with obstructive HCM regardless of baseline symptom severity and geographic region,” said Stephen Heitner, M.D., Vice President, Head of Clinical Research. “These findings are informative as we continue to explore the potential application of *aficamten* across a range of patient phenotypes in obstructive HCM.”

Effect of *Aficamten* in Patients with Mild Symptoms and Moderate-to-Severe Symptoms

Data from an additional analysis from SEQUOIA-HCM related to the effect of *aficamten* in patients with mild symptoms were presented in a Late Breaking Clinical Trial session and simultaneously published in *The European Heart Journal*. Patients in SEQUOIA-HCM (n=282) were divided into two groups according to baseline symptom severity: mild symptoms, defined as New York Heart Association (NYHA) Functional Class II and Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) ≥80 (n=118; 62 randomized to *aficamten*), and moderate-to-severe symptoms defined as NYHA Functional Class II/III/IV and KCCQ-CSS <80 (n=150; 71 randomized to *aficamten*). The effect of

aficamten on the primary endpoint of change from baseline to Week 24 in peak oxygen uptake (pVO_2) was similar between symptom groups (1.6 and 1.8 mL/kg/min in mild and moderate-to-severe symptom groups respectively; interaction p=0.8). While both groups experienced improvements in KCCQ-CSS, the magnitude of improvement was greater in the moderate-to-severe symptom group compared to the mild symptom group (interaction p=0.02) as expected given the lower baseline KCCQ-CSS score. At the end of the treatment period, 54% of patients with mild symptoms and 36% of patients with moderate-to-severe symptoms were asymptomatic. Additionally, more than half of patients in both groups had an improvement of at least one NYHA Functional Class (interaction p=0.6). Improvements in resting and Valsalva left ventricular outflow tract (LVOT) gradients and NT-proBNP also did not differ significantly between the two groups (all interaction p≥0.3). The safety and tolerability profile of *aficamten* was similar to placebo in both subgroups. These data indicate that, in SEQUOIA-HCM, the effect of *aficamten* was observed independent of baseline symptom burden in patients with obstructive HCM.

Effect of *Aficamten* in Patients with Obstructive HCM Consistent Across Geographic Regions

Data from an additional analysis from SEQUOIA-HCM evaluating geographical differences in the effect of *aficamten* were presented in a Late Breaking Clinical Trial session. Participants from SEQUOIA-HCM (n=282) were classified into three geographic regions: Europe, including Israel (n=142; 50%), North America (n=94; 33%) and China (n=46; 16%). At baseline, patients in Europe and North America were on average older, with a higher BMI, lower LVOT gradients, lower KCCQ-CSS and were more likely to have comorbidities than those in China. A greater proportion of patients in North America were NYHA Functional Class III/IV compared to Europe and China. Peak VO_2, Valsalva LVOT gradient, NT-proBNP and hs-cardiac troponin I were similar across geographical regions. The distribution of doses of *aficamten* was similar across regions. The effect of *aficamten* on the primary endpoint of change in pVO_2 and all secondary endpoints was consistent, with no significant differences across regions (all interaction p>0.15). The incidence of serious adverse events was similar in the *aficamten* and placebo groups across regions, and occurrences of left ventricular ejection fraction (LVEF) <50% were infrequent. These results demonstrate that in SEQUOIA-HCM, while there were regional differences in patient baseline characteristics, the dosing, safety profile and effect of *aficamten* was consistent across the geographic regions studied.

Analyses of Real-World Data Reveal Association Between Age, Sex and Cardiovascular Outcomes in Patients with Non-Obstructive HCM

Data presented from a health economics and outcomes research (HEOR) analysis evaluated the association between age, sex and cardiovascular outcomes in patients with non-obstructive HCM. This retrospective cohort study included adult patients diagnosed with non-obstructive HCM from January 1, 2013 to December 31, 2021 using real-world data from Optum Market Clarity database. Of the 9,842 patients included, 46.2% were female, 53.8% were male and the age distribution was as follows: 24.2% were ages 55 to 64 years, 22.1% were ages 75 or older, 22.1% were ages 65 to 74, 19.9% were ages 40 to 54 and 11.7% were ages 18 to 39. Female patients had increased rates of stroke (risk ratio [RR] 1.32), heart failure (RR 1.22), cardiovascular hospitalization (RR 1.23) and cardiovascular rehospitalization (RR 1.15) compared to male patients (all p<0.01). However, female patients were less likely to have atrial fibrillation (RR 0.83) and ventricular tachycardia (RR 0.69) (p<0.001). Compared to patients aged 75 years or older, younger patients were less likely to have atrial fibrillation, stroke, heart failure, cardiovascular hospitalization and cardiovascular rehospitalization (all p<0.001). All-cause mortality was significantly greater in female patients compared to male patients (p=0.002). Patients aged 75 years or older had the highest all-cause mortality (16.6%; p<0.001), followed by patients aged 65 to 74 (8.3%), 55 to 64 (3.5%), 40 to 54 (3.1%) and 18 to 39 years (1.4%). These findings highlight disparities in morbidity and survival among females and older patients with non-obstructive HCM, emphasizing the potential role for novel treatments to help reduce the clinical burden.

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.[2] *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 as measured by peak oxygen uptake (pVO_2) and relieves symptoms in patients with HCM. *Aficamten* was evaluated in SEQUOIA-HCM, a positive pivotal Phase 3 clinical trial in patients symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic HCM from the U.S. Food & Drug Administration (FDA) and for the treatment of symptomatic obstructive HCM from the National Medical Products Administration (NMPA) in China.

Aficamten is also currently being evaluated in 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.

This communication contains a summary of new data related to the clinical development of *aficamten* presented at the European Society of Cardiology Heart Failure 2025 Congress. *Aficamten* is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established. *Aficamten* is currently under regulatory review in the U.S, where the FDA is reviewing a New Drug Application (NDA) for *aficamten* with a Prescription Drug User Fee Act (PDUFA) target action date of December 26, 2025. Additionally, the European Medicines Agency (EMA) is reviewing a Marketing Authorization Application (MAA) for *aficamten*, and The Center for Drug Evaluation (CDE) of the China National Medical Products Administration (NMPA) is reviewing an NDA for *aficamten* with Priority Review.

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.[3,4,5] 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.[6] 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.[7] 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 specialty cardiovascular biopharmaceutical company, building on its over 25 years of pioneering scientific innovations in muscle biology to advance a pipeline of potential new medicines for patients suffering from diseases of cardiac muscle dysfunction. Cytokinetics is readying for potential regulatory approvals and commercialization of *aficamten,* a cardiac myosin inhibitor following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in patients with obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in additional clinical trials enrolling patients with obstructive and non-obstructive HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac myosin 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 with potential therapeutic application to a specific type of muscular dystrophy and other conditions of impaired skeletal muscle function.

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, treatment effect or potential benefits of *aficamten* or any of our other drug candidates or 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 by any particular date, if ever. 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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