Cytokinetics Presents Additional Data From SEQUOIA-HCM at the HFSA Annual Scientific Meeting

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Responder Analyses Show Treatment with Aficamten Demonstrated Improvements on Multiple Assessments of Clinical Significance to Cardiologists

Results Simultaneously Published in the Journal of the American College of Cardiology

SOUTH SAN FRANCISCO, Calif., Sept. 30, 2024 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional analyses synthesizing data 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), were presented virtually at the Heart Failure Society of America (HFSA) Annual Scientific Meeting by Martin Maron, M.D., Director of the Hypertrophic Cardiomyopathy Center at the Lahey Hospital and Medical Center. The presentation was simultaneously published in the *Journal of the American College of Cardiology*[1].

In these responder analyses of data from SEQUOIA-HCM, key integrated clinical assessments, commonly relied upon by practicing cardiologists to inform treatment choice and response, were analyzed following 24 weeks of treatment with *aficamten* or placebo (in addition to standard of care in both cases) in the study population (n=282): 1) complete hemodynamic response (resting and Valsalva left ventricular outflow tract gradient [LVOT-G] <30 mmHg and <50 mmHg, respectively), 2) relief of symptoms (≥1 change in New York Heart Association [NYHA] Functional Class and/or ≥10-point increase in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score [KCCQ-CCS]), 3) enhanced exercise capacity (≥1.5 mL/kg/min change in peak oxygen uptake [pVO_2]), and 4) cardiac biomarker response (≥50% reduction in NT-proBNP).

Comparing patients treated with *aficamten* to placebo, 68% vs 7% demonstrated a complete hemodynamic response, 71% vs 42% experienced relief of limiting symptoms, 46.5% vs 24% showed enhanced exercise capacity and 84% vs 8% demonstrated a substantial response in cardiac biomarkers (for all p<0.002 compared to placebo). Overall, 97% of patients treated with *aficamten* achieved one or more clinically relevant outcomes, 62% achieved at least three outcomes and 23% achieved all four outcomes. For each of the four outcomes assessed in these analyses, the number needed to treat (NNT) was fewer than 5 patients.

In a responder analysis of functional capacity (defined as pVO_2 ≥1.5 mL/kg/min and ≥1 improvement in NYHA class, or pVO_2 ≥3.0 mL/kg/min2 and no worsening in NYHA class), 42% of patients on *aficamten* and 14% of patients on placebo were responders, for a difference vs. placebo of 29% (95% CI: 18.8 - 38.6, p<0.001) and an NNT of 3. Additionally, among patients treated with *aficamten* who were eligible for septal reduction therapy at baseline (n=32), 88% were no longer eligible at 24 weeks (p=0.002 compared to placebo).

“In these prespecified analyses of SEQUOIA-HCM the addition of *aficamten* to standard of care was associated with important improvements in four key clinical markers used by cardiologists to inform HCM patient management strategies and prognosis. Included in these assessments are a complete hemodynamic response which was demonstrated in two-thirds of the patients in SEQUOIA-HCM,” said Stephen Heitner, M.D., Vice President, Head of Clinical Research. “These data elaborate on the primary results from SEQUOIA-HCM and further inform the relevance to clinical practice of *aficamten* as a next-in-class cardiac myosin inhibitor for adult patients with obstructive HCM.”

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.

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**), 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.

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.

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. 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 which were published in the *New England Journal of Medicine*. *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.

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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