Cytokinetics Announces Start of SEQUOIA-HCM, a Phase 3 Clinical Trial of Aficamten in Patients With Symptomatic Obstructive Hypertrophic Cardiomyopathy

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Pivotal Trial to Assess the Potential of Aficamten to Improve Exercise Capacity, Heart Failure Symptoms and Functional Class

SOUTH SAN FRANCISCO, Calif., Feb. 23, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A**ficamten* in **HCM**), a Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM), is open to enrollment. *Aficamten* is a next-generation cardiac myosin inhibitor in development for the potential treatment of HCM. SEQUOIA-HCM builds on the positive results from REDWOOD-HCM, a Phase 2 clinical trial of *aficamten*, that demonstrated that treatment with *aficamten* for 10 weeks resulted in reductions from baseline compared to placebo in the average resting left ventricular outflow tract pressure gradient (LVOT-G) and the average post-Valsalva LVOT-G, with no treatment interruptions or discontinuations, nor any treatment related serious adverse events.

"We are pleased to announce the start of SEQUOIA-HCM, especially today which marks HCM Awareness Day," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "With this registrational trial we are investigating the potential of *aficamten* to improve exercise capacity measured by peak VO_2, as well as heart failure symptoms and functional class in patients who have substantial resting and provoked gradients despite standard of care therapy. Like in REDWOOD-HCM, we will use a personalized dosing scheme employing echo-guided dose titration to maximize the potential treatment effect and enable patients to reach a target dose quickly. For patients who complete SEQUOIA-HCM, we are also pleased to offer enrollment in the open label extension trial to provide patients with continued access to *aficamten*, and to gather longer term data on its safety and efficacy."

SEQUOIA-HCM: Clinical Trial Design

SEQUOIA-HCM is a Phase 3 randomized, placebo-controlled, double-blind, international multi-center clinical trial designed to evaluate *aficamten* in patients with symptomatic obstructive HCM on background medical therapy for 24 weeks. The primary endpoint is the change in peak oxygen uptake (pVO_2) measured by cardiopulmonary exercise testing (CPET) from baseline to Week 24. Secondary endpoints include the change from baseline to Week 12 and Week 24 in Kansas City Cardiomyopathy Questionnaire (KCCQ) score, proportion of patients with ≥1 class improvement in New York Heart Association (NYHA) functional class, post-Valsalva left ventricular outflow tract gradient (LVOT-G), and proportion of patients with post-Valsalva LVOT-G <30 mmHg, as well as the change from baseline to Week 24 in total workload during CPET.

SEQUOIA-HCM is expected to enroll 270 patients, randomized on a 1:1 basis to receive *aficamten* or placebo in addition to standard-of-care treatment. Following the positive results from Cohort 3 of REDWOOD-HCM, patients whose background therapy includes *disopyramide* are eligible for enrollment. Randomization will be stratified by use of beta-blockers and CPET exercise modality (treadmill or bicycle). At screening, patients enrolled in SEQUOIA-HCM must have a resting LVOT-G ≥30 mmHg, post-Valsalva peak LVOT-G ≥50 mmHg, be NYHA functional class II or III, and have a pVO_2 <80% predicted. Each patient will receive up to four escalating doses of *aficamten* or placebo based on echocardiographic guidance alone. Patients receiving *aficamten* will begin with 5 mg dosed once daily. At weeks 2, 4 and 6 patients will receive an echocardiogram to determine if they will be up-titrated to escalating doses of 10, 15 or 20 mg. Dose escalation will occur only if a patient has a post-Valsalva LVOT-G ≥30 mmHg and a biplane left ventricular ejection fraction (LVEF) ≥55%. Patients who do not meet escalation criteria will continue to receive their current dose or may be down-titrated if their LVEF is below 50%. Patients who complete SEQUOIA-HCM will be eligible to participate in an open label extension trial. Additional information can be found on www.clinicaltrials.gov.

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 long-term effects on cardiac structure and function. *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 symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. A subset of patients with HCM are at high risk of progressive disease which can lead to atrial fibrillation, stroke and death due to arrhythmias. There are no FDA approved medical treatments that directly address the hypercontractility that underlies HCM.

About Cytokinetics

Cytokinetics is a late-stage 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 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 muscle function and contractility. Cytokinetics is readying for the potential commercialization of *omecamtiv mecarbil*, its cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-generation cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with

hypertrophic cardiomyopathy (HCM). Cytokinetics is also developing *reldesemtiv*, an investigational fast skeletal muscle troponin activator, currently the subject of COURAGE-ALS, a Phase 3 clinical trial in patients with amyotrophic lateral sclerosis (ALS). Cytokinetics continues its over 20-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 Twitter, 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 expressed or implied relating to the properties or potential benefits of *aficamten* or any of our other drug candidates, our ability to fully enroll SEQUOIA-HCM by any particular time, if at all, and the likelihood or timing of regulatory approval for *aficamten* or any of our other drug candidates. 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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