Cytokinetics Announces Positive Topline Results from Cohort 3 of REDWOOD-HCM

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Aficamten Reduced LVOT Gradients in Patients on Disopyramide
With No Instances of Left Ventricular Ejection Fraction Below 50%

Findings Support Inclusion of Patients on Disopyramide in SEQUOIA-HCM

SOUTH SAN FRANCISCO, Calif., Feb. 01, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced positive topline results from Cohort 3 of REDWOOD-HCM (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM**), the Phase 2 clinical trial of *aficamten,* an investigational next-generation cardiac myosin inhibitor in development for the potential treatment of hypertrophic cardiomyopathy (HCM).

Cohort 3 of REDWOOD-HCM enrolled patients with symptomatic obstructive HCM and a resting or post-Valsalva left ventricular outflow tract gradient (LVOT-G) of ≥50 mmHg whose background therapy included *disopyramide* and in the majority a beta-adrenergic blocker. All patients received up to three escalating doses of *aficamten* once daily (5, 10, 15 mg), titrated based on echocardiographic guidance. The doses employed were the same as those used in Cohort 1 of REDWOOD-HCM. Overall treatment duration was 10 weeks with a 4-week follow up period after the last dose. In total, thirteen patients were enrolled and all patients completed the study on treatment.

Results from Cohort 3 showed that substantial reductions in the average resting LVOT-G as well as the post-Valsalva LVOT-G (defined as resting gradient <30 mmHg and post-Valsalva gradient <50 mmHg) were achieved. These clinically relevant decreases in pressure gradients were achieved with only modest decreases in average left ventricular ejection fraction (LVEF); there were no patients whose LVEF fell below the prespecified safety threshold of 50%. New York Heart Association functional class was improved in the majority of patients participating in Cohort 3 of the trial. Pharmacokinetic data were similar to those observed in Cohorts 1 and 2. In addition, the safety and tolerability of *aficamten* were consistent with prior experience in REDWOOD-HCM with no treatment interruptions and no serious adverse events attributed to treatment reported by the investigators. The results from Cohort 3 of REDWOOD-HCM have been accepted for presentation at the American College of Cardiology 71st Annual Scientific Session & Expo in Washington, DC in April.

"We are encouraged by the clinically relevant reductions in the LVOT gradient observed in these medically refractory patients and are pleased with the safety profile of *aficamten* when administered in combination with *disopyramide*," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "These results represent the first report of patients with obstructive HCM treated with a combination of a cardiac myosin inhibitor and *disopyramide* and support our plan to include this patient population in SEQUOIA-HCM, our Phase 3 trial, which is important given these patients have exhausted other available medical therapies. We look forward to initiating screening of patients in SEQUOIA-HCM soon and look forward to sharing these results from Cohort 3 with the medical community in April."

About REDWOOD-HCM (Cohorts 1 and 2)

REDWOOD-HCM HCM (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM**) is a Phase 2, multi-center, randomized, placebo-controlled, double-blind, dose finding clinical trial of *aficamten* in patients with symptomatic obstructive HCM (oHCM). In Cohorts 1 and 2, patients continued taking background medications exclusive of *disopyramide*. Results from Cohorts 1 and 2 showed that treatment with *aficamten* for 10 weeks resulted in statistically significant 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. A large majority of patients treated with *aficamten* achieved the target goal of treatment, defined as resting gradient <30 mmHg and post-Valsalva gradient <50 mmHg at Week 10, compared to placebo. Patients treated with *aficamten* also saw improvements in heart failure symptoms and reductions in NT-proBNP, a biomarker of cardiac wall stress. Treatment with *aficamten* in REDWOOD-HCM was generally well tolerated and the incidence of adverse events on *aficamten* was similar to that of placebo. No serious adverse events were attributed to *aficamten*, and no treatment interruptions occurred on *aficamten*.

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. Cytokinetics is currently conducting start-up activities for SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***Aficamten*** in **HCM**), the Phase 3 clinical trial of *aficamten* in patients with symptomatic oHCM.

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 novel cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is conducting

METEORIC-HF, a second Phase 3 clinical trial of *omecamtiv mecarbil*. Cytokinetics is also developing *aficamten*, a next-generation cardiac myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies (HCM). The company has announced positive results from Cohorts 1, 2 and 3 in REDWOOD-HCM, a Phase 2 clinical trial of *aficamten* in patients with symptomatic obstructive HCM. Cytokinetics is conducting start-up activities for SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with obstructive 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.

Cytokinetics 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: the properties and potential benefits of Cytokinetics' drug candidates, including *aficamten*, *omecamtiv mecarbil* and *reldesemtiv*, and the likelihood or timing of regulatory approvals for any such 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, potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval; patient enrollment for or conduct of clinical trials may be difficult or delayed; Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; standards of care may change, rendering Cytokinetics' drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission, particularly under the caption "Risk Factors" in Cytokinetics' latest Quarterly Report on Form 10-Q.

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