Cytokinetics Presents Positive Results From Cohort 4 of REDWOOD-HCM and Long-Term Results From FOREST-HCM at the American College of Cardiology 72nd Annual Scientific Session

March 4, 2023 3:00 PM EST

Treatment with Aficamten Resulted in Significant Improvements in Heart Failure Symptoms and Cardiac Biomarkers in Patients with Non-Obstructive HCM, Supporting Advancement to Phase 3

Additional Results from FOREST-HCM Demonstrate Long-Term Treatment with Aficamten for 48 Weeks is Well-Tolerated and Associated with Sustained Treatment Effect

Company to Host Investor Event and Conference Call on March 6, 2023 at 8:30 AM Eastern Time

SOUTH SAN FRANCISCO, Calif., March 04, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that positive results from Cohort 4 of REDWOOD-HCM (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM**), a Phase 2 clinical trial of *aficamten* in patients with non-obstructive hypertrophic cardiomyopathy (nHCM), were presented at the American College of Cardiology 72nd Annual Scientific Session (ACC.23). Additionally, 48-week data from FOREST-HCM (**F**ollow-up, **O**pen-Label, **R**esearch **E**valuation of **S**ustained **T**reatment with *Aficamten* in **HCM**) were also presented at the meeting.

“Patients with non-obstructive HCM have no effective medical therapies and lack an apparent therapeutic target like reducing or eliminating the LVOT obstruction, underscoring the need for a therapy to address the underlying cause of the disease,” said Fady I. Malik, M.D., Ph.D., Cytokinetics’ Executive Vice President of Research & Development. “The results from Cohort 4 of REDWOOD-HCM demonstrate that treatment with *aficamten* is well-tolerated and associated with significant improvements in heart failure symptoms and cardiac biomarkers in patients with non-obstructive HCM and support the advancement of *aficamten* into a pivotal Phase 3 clinical trial in patients with non-obstructive HCM. Additionally, *aficamten* continues to demonstrate sustained hemodynamic and biomarker improvement after nearly a year of treatment with the majority of oHCM patients becoming either asymptomatic or mildly symptomatic.”

REDWOOD-HCM Cohort 4: *Aficamten* Improved Heart Failure Symptoms and Cardiac Biomarkers in Patients with Non-Obstructive HCM

Ahmad Masri, M.D., Director of the Hypertrophic Cardiomyopathy Center at Oregon Health & Science University, presented results from Cohort 4 of REDWOOD-HCM. Cohort 4 enrolled 41 patients with nHCM, who were New York Heart Association (NYHA) Class II/III with left ventricular ejection fraction (LVEF) ≥60% without a resting or provoked left ventricle outflow tract (LVOT) gradient (<30 mm Hg). Eligible patients had a NT-proBNP ≥300 pg/mL and no history of LVEF <45%. All patients received up to three escalating doses of *aficamten*, beginning with 5 mg once daily and increasing to 10 and 15 mg once daily guided by echocardiographic assessment of LVEF. Overall treatment duration was 10 weeks with a 2-week washout period.

At 10 weeks, patients in Cohort 4 experienced significant improvements in NT-proBNP, with an average decrease of 66% ($p<0.0001$). High-sensitivity troponin I levels also improved significantly proportional to baseline at each study visit ($p<0.05$). An improvement of ≥1 NYHA Functional Class was observed in 22 of 41 (54%) patients. After the 2-week washout period, NT-proBNP and high-sensitivity troponin I levels returned to baseline levels.

Aficamten was generally well-tolerated. By Week 6, 35 (85%) of patients achieved the highest dose of 15 mg of *aficamten*, and 6 (15%) achieved 10 mg. There were no drug discontinuations due to adverse events. One dose reduction to 10 mg occurred due to fatigue, and one temporary dose interruption occurred due to palpitation. Three patients had serious adverse events, but none were attributed to *aficamten*. In 27 patients (66%), at least one treatment emergent adverse event was reported. Three patients (7.3%) had LVEF <50% at Week 10; all three patients returned to baseline LVEF after the 2-week washout period. No adverse events of heart failure were reported.

FOREST-HCM: *Aficamten* Well Tolerated with Sustained Treatment Effect Up to 48 Weeks

Sara Saberi, M.D., Assistant Professor of Internal Medicine at the University of Michigan Health Frankel Cardiovascular Center, presented the 48-week data from FOREST-HCM. Previously presented data from FOREST-HCM showed that treatment with *aficamten* was associated with significant and sustained reductions in LVOT-G, improvements in New York Heart Association (NYHA) Functional Class, improvements in cardiac biomarkers, and improvement in self-reported health status using the Kansas City Cardiomyopathy Questionnaire (KCCQ) through 24 weeks.

New data through 48 weeks of treatment showed that *aficamten* was associated with significant reductions in the average resting LVOT-G (mean change from baseline (SD) = -32 (28) mmHg, $p<0.0002$) and Valsalva LVOT-G (mean change from baseline (SD) = -47 (28) mmHg, $p<0.0001$). Treatment with *aficamten* also resulted in significant improvements in NYHA class, with 88% of patients experiencing a ≥1 NYHA Functional Class improvement, and significant improvements in NT-proBNP, with an average decrease of 70% from baseline to Week 48 ($p<0.0001$). At baseline, 19 patients met eligibility criteria for septal reduction therapy (SRT), defined as NYHA Class III and peak LVOT-G ≥50 mmHg, but treatment with *aficamten* eliminated SRT eligibility in all 19 patients at 48 weeks.

Aficamten was safe and well-tolerated, with no treatment-related serious adverse events (SAEs). There were no instances of LVEF <50% attributed to *aficamten.* One dose reduction and one temporary dose interruption occurred, neither of which were attributed to treatment with *aficamten.*

Investor Event and Conference Call

Cytokinetics will host an investor event and conference call on March 6, 2023 at 8:30 AM Eastern Time. The event will be held at the Omni Riverfront Hotel in New Orleans, LA in the Bacchus B room. The conference call will be simultaneously webcast online and will be accessible from the homepage and in the Investors & Media section of Cytokinetics’ website at **www.cytokinetics.com**. The live audio of the conference call can also be accessed by telephone by registering in advance at the following link: **Cytokinetics ACC.23 Conference Call**. Upon registration, participants will receive a dial-in number and a unique passcode to access the call. An archived replay of the webcast will be available via Cytokinetics’ website for twelve months.

About REDWOOD-HCM

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* divided into 4 Cohorts. Cohorts 1, 2 and 3 enrolled patients with obstructive HCM (oHCM) and Cohort 4 enrolled patients with non-obstructive HCM (nHCM). In Cohorts 1 and 2, patients continued taking background medications exclusive of *disopyramide*. Results from Cohorts 1 and 2 showed that treatment with *aficamten* or 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*. Cohort 3 showed that *aficamten* was associated with reductions in LVOT-G and Valsalva LVOT-G, and improvements in NYHA Class and NT-proBNP in patients with obstructive HCM whose background therapy included *disopyramide*, with safety and tolerability consistent with Cohorts 1 and 2.

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.

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 developing *omecamtiv mecarbil*, a cardiac muscle activator in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-in-class cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in non-obstructive HCM in Cohort 4 of the Phase 2 clinical trial, REDWOOD-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). In 2023, Cytokinetics is celebrating its 25-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, express or implied, relating to REDWOOD-HCM or any of our other clinical trials, statements relating to the potential benefits of *aficamten* or any of our other drug candidates, and the design, timing, results, significance and utility of preclinical and clinical results. 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; 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; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission.

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