



Cytokinetics Announces Additional Data From REDWOOD-HCM Presented at the American Society of Echocardiography 33rd Annual Scientific Sessions

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*Echocardiographic Data Show Treatment with Aficamten for 10 Weeks Results
In Improved Cardiac Structure, Myocardial Relaxation and Mitral Valve Mechanics*

SOUTH SAN FRANCISCO, Calif., June 13, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data from a new analysis of REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM) relating to the effect of treatment with *aficamten* on measures of cardiac structure and function were presented at the American Society of Echocardiography (ASE) 33rd Annual Scientific Sessions by Theodore Abraham, M.D., F.A.C.C., Meyer Friedman Distinguished Professor of Medicine, Clinical Chief of Cardiology, Director of Echocardiography, University of California, San Francisco.

This new analysis investigated changes from baseline in echocardiographic measures of cardiac structure and function after 10 weeks of treatment with *aficamten* compared with placebo. At baseline, all patients (n=41) enrolled in Cohorts 1 and 2 of REDWOOD-HCM had severe left ventricular outflow tract (LVOT) obstruction, 88% had associated systolic anterior motion (SAM) of the mitral valve, and 90% had mitral regurgitation. SAM occurs when the mitral valve leaflet gets pushed against the interventricular septum during systole, resulting in obstruction of the LVOT and mitral regurgitation.

Measures of cardiac structure, diastolic and mitral valve function (Table 1) improved at Week 10 in patients treated with *aficamten*. There was a significant reduction in left atrial volume index ($p<0.01$) and a trend towards a reduction in left ventricular hypertrophy (left ventricular mass index; $p=0.06$). Treatment with *aficamten* also resulted in improved ventricular relaxation and filling, as indicated by a reduction in lateral E/e' ($p<0.01$) and an increase in lateral e' ($p<0.05$). Additionally, treatment with *aficamten* improved mitral valve dynamics as noted by a reduction in the proportion of patients with SAM (placebo: 92.3% at baseline to 75.0% at Week 10; *aficamten*: 85.7% at baseline to 35.7% at Week 10; $p=0.038$ for comparison to placebo) and a trend towards a reduction in those with eccentric mitral regurgitation (placebo: 25.0% at baseline to 33.3% at Week 10; *aficamten*: 42.9% at baseline to 7.1% at Week 10; $p=0.055$ for comparison to placebo) at Week 10. Together, these data point to evidence of early signs of improved cardiac function and structure and improved mitral valve dynamics after a 10-week treatment period with *aficamten*.

Table 1: Measures of Cardiac Structure and Diastolic Function

Parameters	Placebo (n=13)		Aficamten (n=28)	
	Baseline	Change at 10 weeks	Baseline	Change at 10 weeks
Left Atrial Volume Index (mL/m ²)	31.4 (7.5)	2.2 (1.5)	32.5 (8.1)	-2.9 (1.0)
Left Ventricular Mass Index (g/m ²)	103.3 (25)	3.3 (3.6)	109.8 (29)	-4.8 (2.4)
Mitral E Wave to Lateral Annular Early Diastolic Velocity Ratio	17.4 (10)	1.8 (1.1)	13.8 (6.3)	-2.0 (0.8)
Mitral Lateral Annular Early Diastolic Velocity (cm/sec)	5.8 (2.1)	-0.5 (0.4)	6.7 (2.3)	0.5 (0.3)

Baseline values are mean (SD) and change from baseline are least square mean (SE)

"Obstructive HCM is a disease characterized by left ventricular hypertrophy, impaired cardiac relaxation, and induced mitral regurgitation," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "These data show that in addition to the previously reported improvements in left ventricular outflow tract gradients, cardiac biomarkers and symptoms, treatment with *aficamten* improves other key echocardiographic measures of cardiac structure and function. We will continue to further explore the longer-term effect of *aficamten* on these measures in REDWOOD-HCM OLE, the ongoing open label extension and SEQUOIA-HCM, the ongoing Phase 3 clinical trial of *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. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA).

About REDWOOD-HCM

REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease 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*. Cohort 3 of REDWOOD-HCM enrolled patients with symptomatic obstructive HCM whose background therapy included *disopyramide* and, in the majority, a beta-adrenergic blocker. Data from Cohort 3

show that the addition of *aficamten* to standard of care therapy in more treatment-resistant patients treated with *disopyramide* resulted in well tolerated, clinically meaningful improvements in LVOT gradients, functional class and cardiac biomarkers supporting inclusion of patients on background therapy with *disopyramide* in further clinical trials. Cohort 4 of REDWOOD-HCM is enrolling, in an open label fashion, patients with symptomatic non-obstructive HCM receiving background medical therapy with primary objective to determine safety and tolerability of *aficamten* in patients with non-obstructive 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 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 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 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). 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 relating to any of our other clinical trials, including statements relating to the potential benefits of *aficamten* for patients with obstructive hypertrophic cardiomyopathy. 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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