



Cytokinetics Presents New Data in Patients With Non-Obstructive HCM From Cohort 4 of REDWOOD-HCM in Late-Breaking Clinical Trial Session at The European Society of Cardiology Heart Failure 2023 Congress

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Treatment of Aficamten was Well-Tolerated and Associated with Statistically Significant Improvements in KCCQ, Angina Frequency, NYHA Class, NTpro-BNP and High-Sensitivity Troponin I

Phase 3 Clinical Trial in Non-Obstructive HCM To Begin in 2H 2023

SOUTH SAN FRANCISCO, May 20, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data from Cohort 4 of REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM), a Phase 2, open-label clinical trial of *aficamten* in patients with non-obstructive hypertrophic cardiomyopathy (nHCM), were presented in a Late Breaking Clinical Trial session at Heart Failure 2023 an International Congress of the European Society of Cardiology taking place online and in Prague, Czech Republic from May 20, 2023 – May 23, 2023.

"We're pleased to see that, in addition to the previously reported improvements in both functional class and cardiac biomarkers, patients with nHCM treated with *aficamten* in Cohort 4 of REDWOOD-HCM experienced a statistically significant improvement in patient reported health status, the KCCQ clinical summary score, an important measure of disease burden," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Additionally, this study reported for the first time that patients who suffered from angina, a common and debilitating complaint in patients with nHCM that is a consequence of hypertrophy in the heart, reported a significant reduction in the frequency of anginal symptoms. We look forward to advancing *aficamten* into a Phase 3 clinical trial in patients with nHCM which is expected to begin in the second half of this year."

The new data from Cohort 4, presented today by Ahmad Masri, M.D. M.S., Director of the Hypertrophic Cardiomyopathy Center at Oregon Health & Science University, build on the previously presented initial data from Cohort 4 in REDWOOD-HCM, including analyses of all 41 patients through the end of the 12-week clinical study, and new data relating to the effect of *aficamten* on Kansas City Cardiomyopathy Questionnaire (KCCQ) Clinical Symptom Score (CSS) and angina.

At 10 weeks, treatment with *aficamten* was associated with an average improvement in KCCQ-CSS of 10.6 points ($p < 0.0001$) (Figure 1). Overall, 58% of patients experienced a clinical reduction in symptom burden: 12.5% had a small improvement (≥ 5 -10 points), 20% had a moderate to large improvement (≥ 10 -20 points), and 25% had a large to very large improvement (≥ 20 points). Additionally, 56% of patients demonstrated improvement of ≥ 1 New York Heart Association (NYHA) Functional Class ($p = 0.011$) (Figure 2). By Week 10, 28% of patients were asymptomatic (NYHA Class 1). Furthermore, in the 14 patients who reported some angina at baseline, there was an average reduction in the Seattle Angina Questionnaire Angina Frequency (SAQ-AF) score of 14.3 points ($p = 0.005$) at Week 10, translating to a reduction in angina frequency from daily or weekly, to weekly or monthly (Figure 3).

Figure 1: Kansas City Cardiomyopathy Questionnaire (KCCQ)

Kansas City Cardiomyopathy Questionnaire

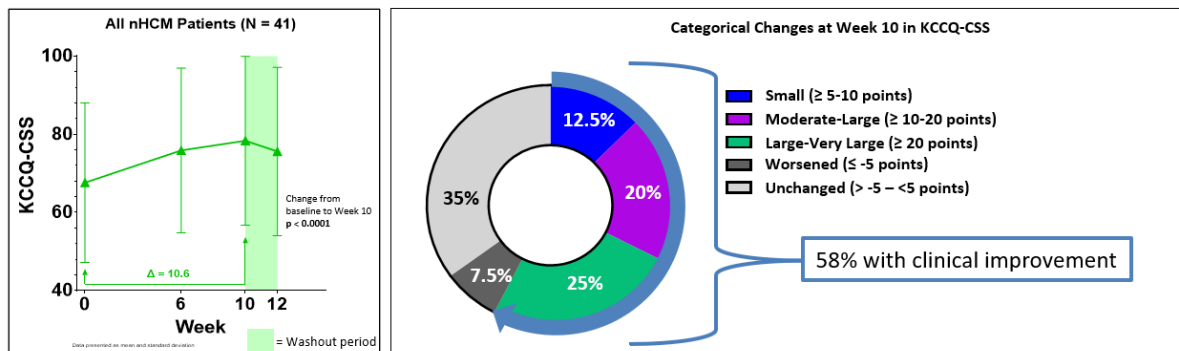


Figure 2: Angina Symptoms

Angina Symptoms

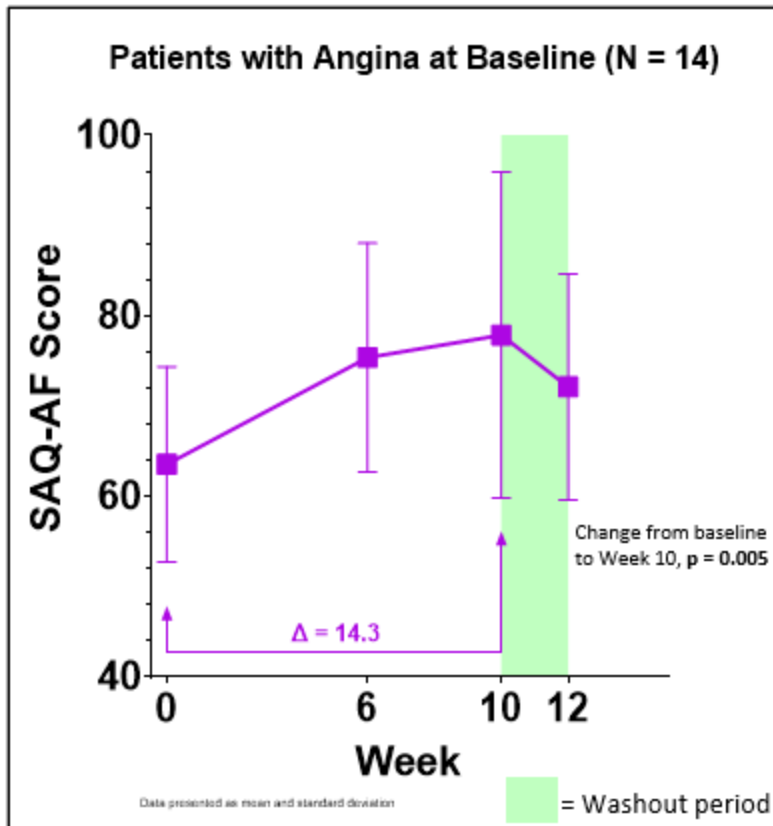
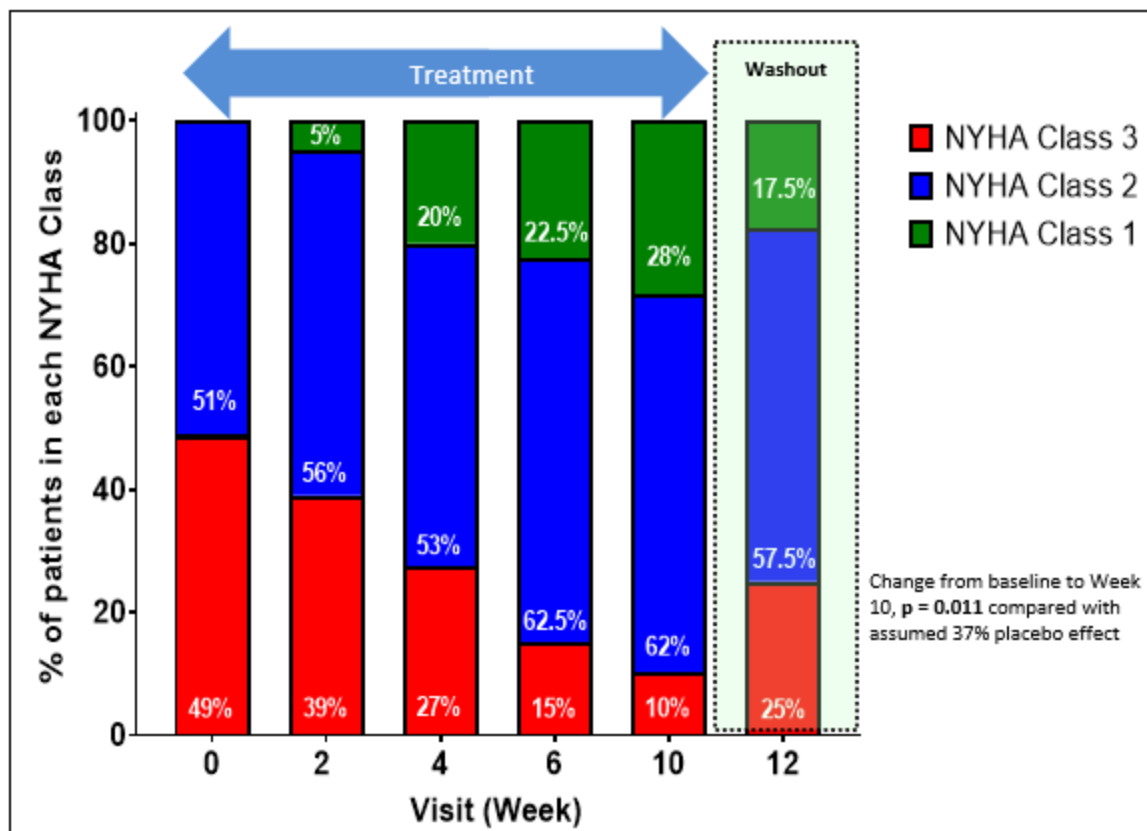


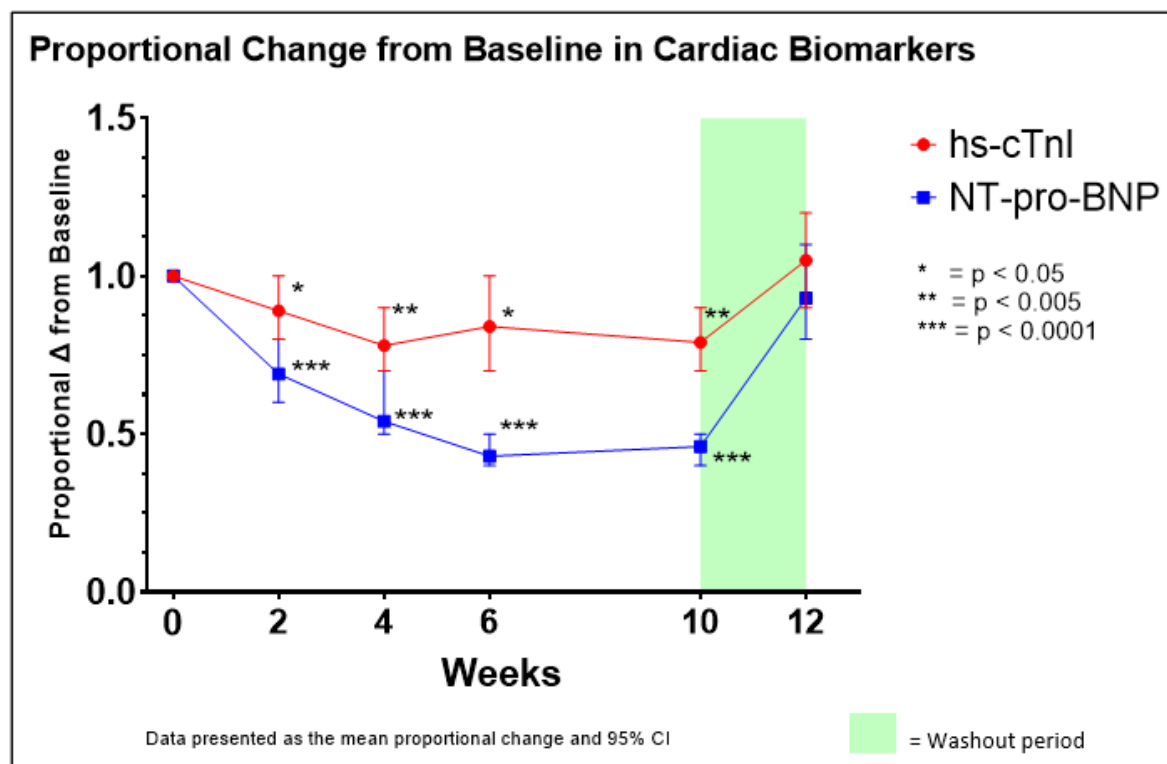
Figure 3: New York Heart Association (NYHA) Functional Class

NYHA Functional Class



Treatment with *aficamten* was associated with a mean relative reduction in high-sensitivity cardiac troponin I of 21% by Week 10 with an absolute mean (SE) reduction of -24.8 ng/L (11.6; $p < 0.005$), and a mean relative reduction in NT-proBNP of 55% by Week 10 with an absolute mean (SE) reduction of -870 pg/mL (155.3; $p < 0.0001$) (Figure 4). After the 2-week washout period, NT-proBNP and high-sensitivity troponin I levels returned to baseline levels.

Figure 4: Cardiac Biomarkers



As previously reported, *aficamten* was generally well-tolerated. The most common adverse events reported were mild fatigue (9.8%) and dizziness (7.3%). By Week 6, 35 (85%) of patients achieved the highest available dose of 15 mg of *aficamten*, and 6 (15%) achieved 10 mg. From baseline to Week 10 there was a modest and reversible reduction in left ventricular ejection fraction (LVEF) of -5.5% (9.9%). There were no drug discontinuations due to adverse events, no treatment interruptions or down-titration events related to LVEF <50%, and no events with LVEF <40%. Three patients (7.3%) had LVEF <50% at Week 10; all three patients returned to baseline LVEF after the 2-week washout period, and none were associated with adverse events. No adverse events of heart failure were reported. Four patients (9.8%) had serious adverse events, including one previously reported death, and none were attributed to *aficamten*.

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* 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. 78.6% of patients treated with *aficamten* in Cohort 1 and 92.9% of patients treated with *aficamten* in Cohort 2 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. 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.

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* 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, specialty cardiovascular 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 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. *Aficamten* is 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 and the company plans to begin a Phase 3 trial later this year. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator in patients with heart failure. Additionally, Cytokinetics is developing CK-3828136 (CK-136), a cardiac troponin activator for the potential treatment HFrEF and other types of heart failure, such as right ventricular failure, resulting from impaired cardiac contractility, as well as CK-4021586 (CK-586), a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten*. 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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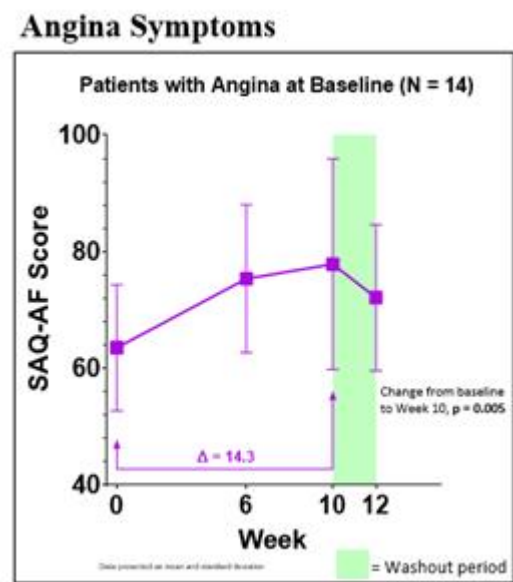
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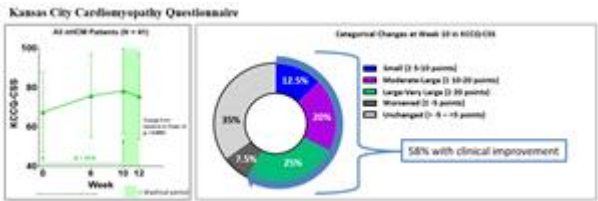
Source: Cytokinetics, Incorporated

Figure 2



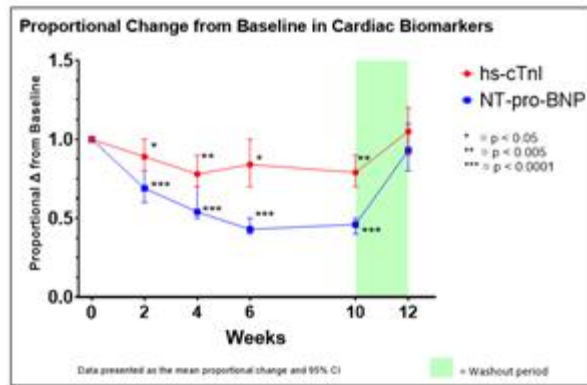
REDWOOD-HCM Cohort 4: Angina Symptoms

Figure 1



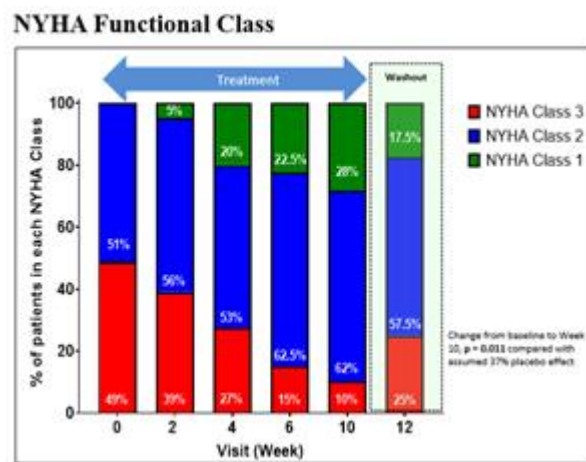
REDWOOD-HCM Cohort 4: Kansas City Cardiomyopathy Questionnaire (KCCQ)

Figure 4



REDWOOD-HCM Cohort 4: Cardiac Biomarkers

Figure 3



REDWOOD-HCM Cohort 4: New York Heart Association (NYHA) Functional Class