NEWS RELEASE

Cytokinetics Announces Positive Topline Results from ACACIA-HCM, the Pivotal Phase 3 Clinical Trial of Aficamten in Patients with Non-Obstructive Hypertrophic Cardiomyopathy

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Trial Met Dual Primary Endpoints of KCCQ and Maximal Exercise Performance
With Consistent Positive Findings Across Key Secondary Endpoints

Company to Host Conference Call and Webcast Tuesday May 5 at 8:00 AM Eastern Time

SOUTH SAN FRANCISCO, Calif., May 05, 2026 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced positive topline results from ACACIA-HCM (**A**ssessment **C**omparing ***Aficamten*** to Placebo on **C**ardiac Endpoints **I**n **A**dults with **N**on-Obstructive **HCM**), the pivotal Phase 3 clinical trial of *aficamten* in patients with symptomatic non-obstructive hypertrophic cardiomyopathy (HCM).

ACACIA-HCM met both dual primary endpoints, demonstrating statistically significant improvements from baseline to Week 36 compared to placebo in both Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) and maximal exercise performance (pVO_2) (Table 1).

“Patients with non-obstructive HCM have no therapies approved to treat the underlying hypercontractility associated with the disease. We hope that will change with ACACIA-HCM which is the first clinical trial to demonstrate statistically significant improvements in exercise capacity and symptom burden in patients with non-obstructive HCM,” said Fady I. Malik, M.D., Ph.D., Cytokinetics’ Executive Vice President of Research & Development. “We believe that the totality and consistency of evidence favoring *aficamten* across multiple patient-reported and physician-assessed endpoints of symptom improvement and physical function are clinically meaningful for patients with non-obstructive HCM.”

Table 1: Primary Endpoint Results

Primary Endpoints	Change from Baseline to Week 36 LSM (95% CI)	*Aficamten* vs Placebo LSM (95% CI)	p-value

	Aficamten	Placebo		
KCCQ-CSS	11.4 (9.6 – 13.2)	8.4 (6.6 – 10.2)	3.0 (0.5 - 5.5)	0.021
pVO_2 (mL/kg/min)	0.64 (0.32 – 0.95)	-0.03 (-0.35 – 0.28)	0.67 (0.22 - 1.1)	0.003
LSM = least square mean; CI = confidence interval				

The improvement in KCCQ was robust and consistent throughout the treatment period in participants on *aficamten.* Following washout, KCCQ decreased for participants on *aficamten* to match the placebo group. At Week 36, pVO_2 increased for participants on *aficamten*, while it remained unchanged for participants on placebo, consistent with prior trials of *aficamten* in obstructive HCM (oHCM) (Figure 1).

Figure 1: Assessments of KCCQ and pVO_2

Statistically significant (p<0.001) improvements compared to placebo were observed in key secondary endpoints including the proportion of participants with improvements in New York Heart Association (NYHA) Functional Class, the composite z-score of ventilatory efficiency and pVO_2, and NT-proBNP.

There were no new safety signals identified. The percentage of participants completing planned dosing was similar in those receiving *aficamten* or placebo (88.4% vs. 90.3%, respectively). Left ventricular ejection fraction (LVEF) <50% occurred in 27 (10%) participants taking *aficamten* and in two (1%) participants taking placebo. Two participants on *aficamten* experienced a serious adverse event of heart failure associated with LVEF <50%. Treatment interruptions due to LVEF <40% occurred in 3% of participants taking *aficamten*.

“We are grateful to the clinical trial investigators and staff, as well as the patients who participated in this trial,” Dr. Malik added. “We look forward to presenting the results from ACACIA-HCM at an upcoming medical meeting, as well as discussing them with the U.S. FDA and other regulatory authorities.”

Investor Webcast Information

Cytokinetics will host an investor conference call on May 5, 2026, at 8:00 AM Eastern Time to discuss the topline results from ACACIA-HCM. Interested parties can register online at ACACIA-HCM Topline Results. The live webcast will be available on the Investors & Media section of the Cytokinetics website at https://ir.cytokinetics.com/. A replay of the webcast will be archived on the Cytokinetics website for six months.

About ACACIA-HCM

ACACIA-HCM was a Phase 3, multi-center, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the effect of *aficamten* compared to placebo in patients with symptomatic non-obstructive hypertrophic cardiomyopathy (nHCM). The dual primary endpoint was the change in Kansas City Cardiomyopathy Questionnaire (KCCQ) Clinical Summary Score and change in maximal exercise performance (pVO_2) from baseline to Week 36.

Secondary endpoints included the proportion of participants with ≥1 class improvement in New York Heart Association (NYHA) functional class, and changes in the composite z-score of two

cardiopulmonary exercise testing (CPET) parameters of sub-maximal exercise performance (VE/VCO_2 and pVO_2), NT-proBNP, and left atrial volume index (LAVI) from baseline to Week 36. After 36 weeks of treatment, participants continued treatment with *aficamten* or placebo for up to 72 weeks to evaluate additional secondary and exploratory analyses including the time to first cardiovascular event. The trial (outside Japan) concluded when at least 200 participants completed 52 weeks of treatment.

ACACIA-HCM randomized and treated 516 participants (outside Japan) on a 1:1 basis with *aficamten* or placebo. Randomization was stratified by persistent atrial fibrillation and presence of intracavitary obstruction. At screening, participants enrolled in ACACIA-HCM were required to have resting left ventricular outflow tract gradient (LVOT-G) <30 mmHg and post-Valsalva LVOT-G <50 mmHg in addition to left ventricular ejection fraction (LVEF) ≥60%, respiratory exchange ratio (RER) ≥1.00 and peak VO_2 ≤90% predicted, NT-proBNP ≥300 pg/mL or ≥900 pg/mL if atrial fibrillation or atrial flutter were present at screening, NYHA functional class II or III and KCCQ Clinical Summary Score ≤85.

Each patient received up to four escalating doses of *aficamten* or placebo based on echocardiographic guidance. Participants who received *aficamten* began with 5 mg dosed once daily. At weeks 2, 4 and 6 participants received an echocardiogram to determine if they would be up-titrated to escalating doses of 10, 15 or 20 mg. Dose escalation occurred only if a participant had an LVEF ≥60%. Participants who did not meet escalation criteria continued the same dose or were down-titrated if their LVEF was <50%.

About MYQORZO® (*aficamten*)

MYQORZO® (*aficamten*) is a cardiac myosin inhibitor approved in the U.S., China and European Union for the treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM). In patients with oHCM, myosin inhibition with MYQORZO reduces cardiac contractility and consequently, left ventricular outflow tract (LVOT) obstruction. MYQORZO was engineered to achieve a predictable exposure response, rapid onset of action and reversibility.[1]

Aficamten is also under clinical investigation in CEDAR-HCM, in a pediatric population with oHCM. *Aficamten* has not been deemed safe or effective for use in this patient population. In addition, *aficamten* is being studied in FOREST-HCM, an open-label extension clinical study.

INDICATION

MYQORZO is indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF HEART FAILURE

MYQORZO reduces left ventricular ejection fraction (LVEF) and can cause heart failure due to systolic dysfunction.

Echocardiogram assessments are required prior to and during treatment with MYQORZO to monitor for systolic dysfunction. Initiation of MYQORZO in patients with LVEF <55% is not recommended. Decrease the dose of MYQORZO if LVEF is <50% and ≥40%. Interrupt the dose of MYQORZO if LVEF <40% or if the patient experiences heart failure symptoms or worsening clinical status due to systolic dysfunction.

Because of the risk of heart failure due to systolic dysfunction, MYQORZO is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the MYQORZO REMS Program.

CONTRAINDICATIONS

MYQORZO is contraindicated with concomitant use of rifampin.

WARNINGS AND PRECAUTIONS

Heart Failure

MYQORZO reduces cardiac contractility, which can reduce LVEF and cause heart failure.
Patients who experience a serious intercurrent illness (eg, serious infection) or arrhythmia (eg, new or uncontrolled atrial fibrillation) may be at greater risk of developing systolic dysfunction and heart failure.

Assess patients' clinical status and LVEF prior to and during treatment and adjust the MYQORZO dose accordingly. New or worsening arrhythmia, dyspnea, chest pain, fatigue, leg edema, or elevations in N-terminal pro-B-type natriuretic peptide may be signs and symptoms of heart failure.

Initiation of MYQORZO in patients with LVEF <55% is not recommended.

MYQORZO REMS Program

MYQORZO is available only through a restricted program called the MYQORZO REMS Program, because of the risk of heart failure due to systolic dysfunction.

Notable requirements of the MYQORZO REMS Program include:

- Prescribers must be certified by enrolling in the MYQORZO REMS Program
- Patients must enroll in the MYQORZO REMS Program and comply with ongoing monitoring requirements
- Pharmacies must be certified by enrolling in the MYQORZO REMS Program and must only dispense to patients who are authorized to receive MYQORZO
- Wholesalers and distributors must only distribute to certified pharmacies

Further information is available at www.MYQORZOREMS.com, or at 1-844-285-7367.

Cytochrome P450 Interactions Leading to Heart Failure or Loss of Effectiveness

MYQORZO is metabolized primarily by CYP2C9, and to a lesser extent by CYP3A, CYP2D6, and CYP2C19 enzymes. Initiation of medications that inhibit multiple P450 pathways of MYQORZO elimination (eg, fluconazole, voriconazole, or fluvoxamine) or strong CYP2C9 inhibitors, and discontinuation of moderate-to-strong CYP3A inducers may lead to increased blood concentrations of *aficamten* and increase the risk of heart failure due to systolic dysfunction. Conversely, initiation of medications that induce P450 pathways of MYQORZO (eg, rifampin, moderate-to-strong CYP3A inducers) may lead to decreased blood concentrations of *aficamten* and potential loss of effectiveness. Assess LVEF 2 to 8

weeks after initiation of such inhibitors or after discontinuation of such inducers and adjust the dose of MYQORZO accordingly.

Advise patients of the potential for drug interactions. Advise patients to inform their healthcare provider of all concomitant medications prior to and during MYQORZO treatment.

ADVERSE REACTIONS

Hypertension (8% vs 2%) was the only adverse reaction occurring in >5% of patients and more commonly on MYQORZO than on placebo in the pivotal trial.

INDICATIONS AND USAGE

MYQORZO is indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms.

Please see full Prescribing Information, including Boxed WARNING.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a disease in which the heart muscle becomes abnormally thick. HCM can be obstructive, when thickened muscle blocks blood flow, or non-obstructive, when blood flow is not blocked but heart function is still affected. In obstructive HCM, the thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller, stiffer and less able to relax and fill with blood. Ultimately, HCM limits the heart's pumping function, leading to reduced exercise capacity and a variety of symptoms.

HCM is the most common monogenic inherited cardiovascular disorder, with well over 300,000 patients diagnosed in the U.S. However, there are an estimated 400,000-800,000 additional patients who remain undiagnosed.[2,3,4] Recent analysis of a large claims database indicates that approximately half of patients with HCM have obstructive HCM (oHCM) and half have non-obstructive HCM (nHCM).[5]

People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease.[6] People with HCM are at risk for potentially fatal ventricular arrhythmias and it is one of the leading causes of sudden cardiac death in younger people or athletes.[7] A subset of patients with HCM are at high risk of progressive disease leading to dilated cardiomyopathy and heart failure necessitating cardiac transplantation. There are no currently approved therapies for nHCM.

About Cytokinetics

Cytokinetics is a specialty cardiovascular biopharmaceutical company, building on its over 25 years of pioneering scientific innovations in muscle biology, and advancing a pipeline of potential new medicines for patients suffering from diseases of cardiac muscle dysfunction. Cytokinetics' MYQORZO® (*aficamten*) is a cardiac myosin inhibitor approved in the U.S., European Union and China for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). Cytokinetics is also developing *omecamtiv mecarbil*, an investigational cardiac myosin activator for the potential treatment of patients with heart failure with severely reduced ejection fraction and *ulacamten*, an investigational cardiac myosin inhibitor for the potential treatment of heart failure with

preserved ejection fraction, while continuing pre-clinical research and development in muscle biology.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on X, 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 the enrollment, expected results or timing of completion of any of our clinical trials, the clinical meaningfulness, persuasiveness or interpretation of clinical trial results, including for purposes of regulatory approval, labeling, or market acceptance, the results of long-term, secondary or exploratory analyses, including analyses of time to first cardiovascular event, statements relating to our ability to obtain regulatory approval for *aficamten* in nonobstructive hypertrophic cardiomyopathy in any jurisdiction by any particular date, if ever, the number of patients comprising the eligible treatment population for *aficamten*, or market acceptance of *aficamten* for the treatment of nonobstructive 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 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 including the risk factors included in Cytokinetics' most recent Annual Report on Form 10-K and subsequent reports filed with the SEC.

References

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/adcf634e-a2a7-4cdf-98b3-ca658eab1b35

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