NEWS RELEASE

Cytokinetics Announces Additional Results from ACACIA-HCM and MAPLE-HCM Presented in Late Breaking Clinical Trial Session at the European Society of Cardiology (ESC) Congress 2026

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Additional Results from ACACIA-HCM Demonstrate Improvements in Cardiac Structure and Diastolic Function in Patients with Non-Obstructive HCM

New Analysis of MAPLE-HCM Finds Aficamten Outperformed Metoprolol Across Pre-Trial Treatment Groups in Patients with Obstructive HCM

SOUTH SAN FRANCISCO, Calif., Aug. 29, 2026 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional results from ACACIA-HCM (**A**ssessment **C**omparing ***A**ficamten* to Placebo on **C**ardiac Endpoints **I**n **A**dults with Non-Obstructive **HCM**) and MAPLE-HCM (***M**etoprolol* vs ***A**ficamten* in **P**atients with **L**VOT Obstruction on **E**xercise Capacity in **HCM**) were presented in a Late Breaking Clinical Session at the European Society of Cardiology (ESC) Congress 2026 in Munich, Germany and simultaneously published in *Circulation* and the *Journal of the American College of Cardiology: Heart Failure*, respectively.

"The findings from these additional analyses of ACACIA-HCM and MAPLE-HCM elaborate on the primary results from each trial and expand the body of evidence supporting the potential use of *aficamten* across the spectrum of HCM," said Stephen Heitner, M.D., Cytokinetics' Chief Medical Officer. "In particular, the additional results from ACACIA-HCM suggest that the benefits of *aficamten* in non-obstructive HCM extend beyond exercise capacity and symptom burden to also include improvements in wall thickness and diastolic function, pointing to the potential mechanisms by which *aficamten* is effective in these patients. Given the lack of approved therapies for non-obstructive HCM, these findings highlight the potential impact *aficamten* could have on this population independent from relief of left ventricular outflow tract obstruction."

ACACIA-HCM: Effect of *Aficamten* on Cardiac Structure and Function in Patients with Symptomatic Non-Obstructive HCM

Results from a pre-specified exploratory analysis of ACACIA-HCM, the Phase 3 clinical trial of *aficamten*

in patients with symptomatic non-obstructive hypertrophic cardiomyopathy (nHCM), were presented in a Late Breaking Clinical Trial Session and simultaneously published in *Circulation*.[1]

As previously reported, the primary results from ACACIA-HCM showed that treatment with *aficamten* was associated with 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). This analysis showed that treatment with *aficamten* also demonstrated improvements in measures of cardiac structure and diastolic function at the time of the primary analysis (36 weeks) and at end of treatment (EOT) (up to 72 weeks; median time to end of treatment = 49 weeks).

At Week 36 and at EOT, *aficamten* significantly improved measures of diastolic function including peak E velocity (p=0.001 and p=0.034, respectively) and septal e' velocity (p<0.001 for both), suggesting improvement in myocardial relaxation and enhanced early diastolic filling. Septal E/e' showed a trend towards improvement at Week 36 (p=0.07), and a statistically significant improvement at EOT (p<0.001). Similarly, left atrial volume index (LAVI) showed a trend toward stabilization at Week 36 (p=0.06) and a statistically significant improvement with longer treatment exposure at EOT (p=0.022). These results in patients with nHCM show that *aficamten* improves diastolic function independent of reducing left ventricular outflow tract (LVOT) obstruction, providing support for the importance of diastolic function as the potential underlying mechanism for the improvements in functional capacity and symptom relief in this population.

Aficamten was associated with a modest but statistically significant (p<0.001) reduction in systolic function as measured by left ventricular ejection fraction (LVEF) which remained within normal range at EOT. Left ventricular wall thickness decreased by 0.2 cm at EOT (p<0.001) while left ventricular end-systolic and end-diastolic left ventricular volumes increased (p<0.001).

MAPLE-HCM: *Aficamten* vs. *Metoprolol* in Obstructive HCM According to Pre-Trial Treatment

Results of a post-hoc analysis from MAPLE-HCM, the Phase 3 clinical trial of *aficamten* compared to *metoprolol* in patients (n=175) with symptomatic obstructive HCM (oHCM), were presented in a Late Breaking Clinical Trial Session and simultaneously published in the *Journal of the American College of Cardiology: Heart Failure.*[2]

As previously reported, the primary results of MAPLE-HCM demonstrated superiority of *aficamten* to *metoprolol* on pVO_2 (change from baseline to Week 24, least squares mean (LSM) treatment difference (SE), +2.3 (0.39) mL/kg/min, p<0.001). This post-hoc analysis evaluated the effect of treatment with *aficamten* or *metoprolol* on the primary endpoint and key secondary endpoints according to pre-trial medical therapy.

At screening, 123 patients were taking a beta blocker while 52 patients were not taking a beta blocker. Of the 52 patients not taking a beta blocker at screening, 22 patients had received no standard of care therapy for at least 12 months before screening. Prior to randomization, all patients underwent a two-week washout period of standard of care therapy.

Independent of pre-trial medical therapy, *aficamten* demonstrated a consistent treatment effect across multiple efficacy endpoints compared with *metoprolol*. *Aficamten* improved pVO_2 compared with *metoprolol* for patients not previously taking beta blockers (LSM difference +3.1 mL/kg/min, p<0.001), as well as for patients previously taking beta blockers (LSM difference +1.9 mL/kg/min, p<0.001) with no difference between groups in the improvement (interaction p = 0.133).

Similarly, compared to *metoprolol*, *aficamten* significantly improved key secondary endpoints independent of pre-trial treatment, including KCCQ-CSS and New York Heart Association (NYHA) Functional Class, Valsalva left ventricular outflow tract gradient (LVOT-G) and NT-proBNP.

There were no differences in the safety profile of *aficamten*, including the rates of serious adverse events, between pre-trial treatment groups.

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 (peak VO_2) from baseline to Week 36.

Secondary endpoints included the proportion of participants with ≥1 class improvement in 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 exploration analyses including the time to first cardiovascular event. The trial (outside Japan) concluded when at least 200 patients completed 52 weeks of treatment.

ACACIA-HCM randomized and treated 517 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 MAPLE-HCM

MAPLE-HCM was a Phase 3, multi-center, randomized, double-blind active-comparator clinical trial of *aficamten* compared to *metoprolol* in patients with symptomatic obstructive HCM (oHCM). The primary endpoint was the change in peak oxygen uptake (pVO_2) from baseline to Week 24 measured by cardiopulmonary exercise testing (CPET). Secondary endpoints include the change from baseline to Week 24 in Kansas City Cardiomyopathy Questionnaire (KCCQ) score, the proportion of patients with ≥1 class improvement in New York Heart Association (NYHA) functional class, and changes in left ventricular mass index (LVMI), left atrial volume index (LAVI), post-Valsalva left ventricular outflow tract gradient (LVOT-G) and NT-proBNP.

MAPLE-HCM enrolled 175 patients, randomized on a 1:1 basis to receive *aficamten* or *metoprolol* as monotherapy in a double-blind, double dummy fashion. Randomization was stratified by CPET exercise

modality (treadmill or bicycle) and recently diagnosed versus chronic obstructive HCM. At screening, patients enrolled in MAPLE-HCM had a resting LVOT-G ≥30 mmHg and/or post-Valsalva LVOT-G ≥50 mmHg in addition to left ventricular ejection fraction (LVEF) ≥ 60%, respiratory exchange ratio (RER) ≥ 1.05 and pVO2 <100% predicted, NYHA functional class II or III and a KCCQ Clinical Summary Score (KCCQ-CSS) score ≥ 35 and ≤ 90. Following the initial screening visit, all participants on standard of care (SOC) therapy underwent a washout period of up to 14 days to wean from SOC therapy, followed by an additional 7 days with no SOC therapy prior to the second screening visit. Each patient received up to four escalating doses of *aficamten* or *metoprolol* based on echocardiographic guidance as well as a matching placebo for the alternate therapy.

About MYQORZO® (*aficamten*)

MYQORZO® (*aficamten*) is a cardiac myosin inhibitor approved in the U.S., China, European Union and United Kingdom 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.[3]

Aficamten is also under clinical investigation in CEDAR-HCM in a pediatric population with oHCM. Safety and efficacy of *aficamten* have not been established in a pediatric 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 approved in the U.S., including Boxed WARNING.

Please see full Summary of Product Characteristics approved in the European Union.

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, affecting approximately 1 out of 350 individuals worldwide.[4]

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.

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 approved in the U.S., China, European Union and United Kingdom for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). Following positive results in ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM (nHCM), the company plans to submit a Supplemental New Drug Application in Q4 2026. 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 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.

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