NEWS RELEASE

# Cytokinetics Presents Additional Data from MAPLE-HCM at the Hypertrophic Cardiomyopathy Medical Society Scientific Sessions and American Heart Association Scientific Sessions 2025

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*Three Late Breaking Science Presentations from MAPLE-HCM Provide Additional Data Including Responder Analyses, Patient Reported Outcomes, and Cardiac Biomarkers*

SOUTH SAN FRANCISCO, Calif., Nov. 10, 2025 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data from MAPLE-HCM (***M****etoprolol* vs ***A****ficamten* in **P**atients with **L**VOT Obstruction on **E**xercise Capacity in **HCM**) were presented in three Late Breaking Science sessions at the Hypertrophic Cardiomyopathy Medical Society Scientific Sessions and the American Heart Association Scientific Sessions 2025 in New Orleans, LA. Two of the presentations were simultaneously published in the *Journal of the American College of Cardiology.*[1,2]

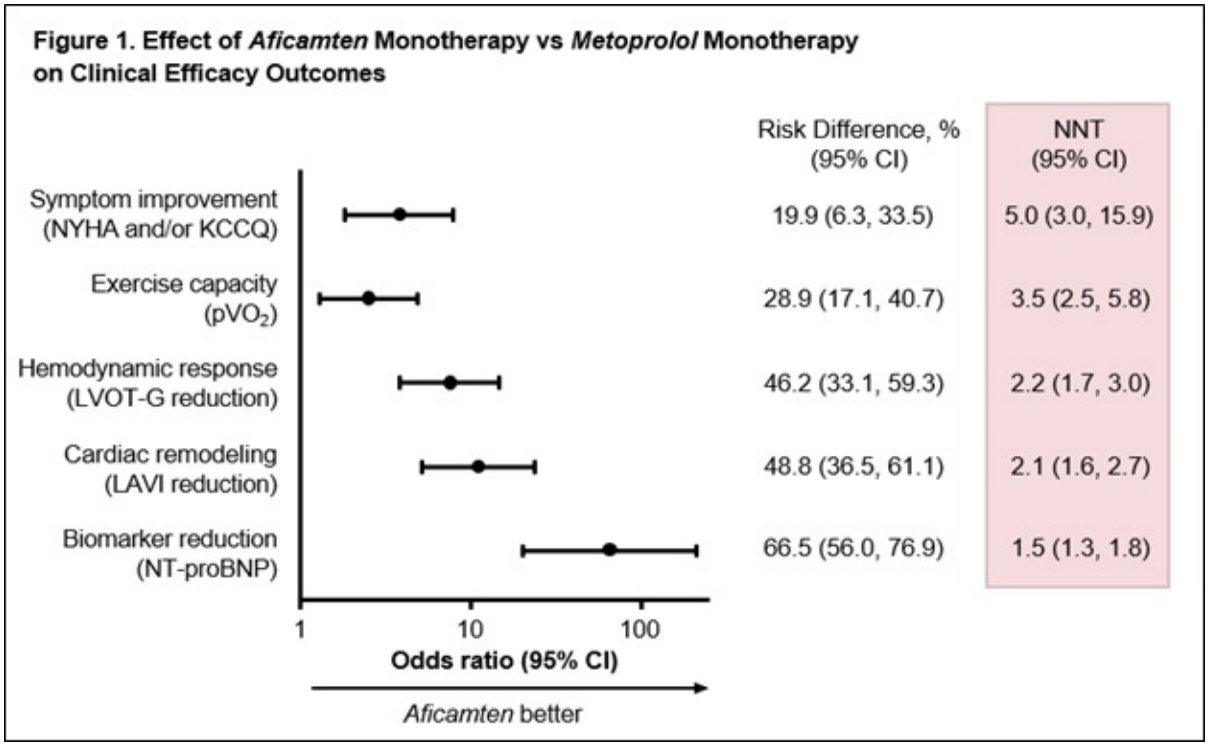
"These additional analyses from MAPLE-HCM expand on the primary finding that *aficamten* is superior to *metoprolol* on exercise capacity, with new insights into the overall treatment effect of *aficamten* as well as its effect on symptoms and biomarkers in comparison to *metoprolol*," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "What's notable is patients treated with *aficamten* achieved a significantly greater number of clinical response categories compared with *metoprolol,* and that nearly 40% achieved significant improvements in patient reported symptoms."

**Responder Analysis Shows Significantly More Patients on *Aficamten* Achieved Positive or Complete Response Compared to *Metoprolol***

Andrew Wang, M.D., Cardiologist and Professor of Medicine, Duke University School of Medicine presented a pre-specified responder analysis from MAPLE-HCM evaluating five clinically relevant measures of disease burden: complete hemodynamic response, symptom improvement, cardiac biomarker response, enhanced exercise capacity and favorable cardiac remodeling. These results were also simultaneously published in the *Journal of the American College of Cardiology.*[1]

After 24 weeks of treatment, *aficamten* was associated with greater improvements than *metoprolol* in

all outcome measures (all p<0.001) (Figure 1). Additionally, the proportion of patients who had a positive response (improvement in three or four clinical parameters) or a complete response (improvement in all five clinical parameters) was 78% in those receiving *aficamten* vs. 3% for those receiving *metoprolol* (p<0.001).




*KCCQ, Kansas City Cardiomyopathy Questionnaire; LAVI, left atrial volume index; LVOT-G, left ventricular outflow tract gradient; NNT, number needed to treat; NT-proBNP, N-terminal pro–B-type natriuretic peptide; NYHA, New York Heart Association*

As previously disclosed, in MAPLE-HCM the rate of adverse events (AEs) was similar between groups. At least one treatment-emergent AE was reported by 65 (73.9%) and 66 (75.9%) patients treated with *aficamten* and *metoprolol*, respectively. The most common AE reported in the *aficamten* group in excess of the comparator (>5%) was hypertension (9 [10.2%] patients on *aficamten* compared to 2 [2.3%] patients on *metoprolol*) and the most common AE reported in the *metoprolol* group in excess of the comparator was dizziness (15 [17.2%] patients on *metoprolol* compared to 5 [5.7%] patients on *aficamten*).

**Analysis of Patient Reported Outcomes Expands on Effect of *Aficamten* on Patient Symptom Burden**

Michael E. Nassif, M.D., Cardiologist, Saint Luke's Mid America Heart Institute, Associate Professor of Medicine, University of Missouri Kansas City presented results from a pre-specified sub-study of two patient reported outcome instruments in MAPLE-HCM: the Kansas City Cardiomyopathy Questionnaire (KCCQ) and Seattle Angina Questionnaire Summary Score (SAQ). The results from this analysis were also simultaneously published in the *Journal of the American College of Cardiology*.[2]

At 24 weeks, treatment with *aficamten* resulted in significantly greater improvements than *metoprolol* in both KCCQ Overall Summary Score (KCCQ-OSS) (16.6 points vs. 8.9 points, respectively; between-

group difference = 7.8 points [95% CI: 3.3 to 12.3; p=0.001]) and KCCQ Clinical Summary Score (KCCQ-CSS) (15.8 points vs. 8.7 points, respectively; between-group difference = 6.9 points [95% CI: 2.6 to 11.2; p=0.002]).

*Aficamten* was also associated with statistically significant improvements across all KCCQ domains (p<0.05). Patients on *aficamten* more frequently reported very large improvements in KCCQ-OSS, defined as ≥20-point improvement (38.6% vs. 18.4%; number needed to treat (NNT)=4.9), and were significantly less likely to experience a worsening in KCCQ-OSS than those treated with *metoprolol* (6.8% vs 18.4%; number needed to harm (NNH)=8.6).

A non-statistically significant trend for greater improvement in SAQ-SS was observed with *aficamten* (13.9 vs. 8.4 [adjusted between-group difference = 4.6 points; 95% CI: -0.3 to 9.5; p=0.063]), driven by a large and statistically significant improvement in the SAQ Physical Limitation Domain, where patients on *aficamten* improved by a mean of 18.7 points compared with 6.9 points for those on *metoprolol* (between-group difference = 10.1 points; 95% CI: 3.9 to 16.2; p=0.001). Changes in the SAQ Angina Frequency and Quality of Life Domains were similar between treatment groups.

**_Aficamten_ Associated with Statistically Significant Improvement in Cardiac Biomarkers Compared to _Metoprolol_**

Neal K. Lakdawala, M.D., Cardiovascular Medicine, Brigham and Women's Hospital, Harvard Medical School presented a pre-specified supplemental analysis from MAPLE-HCM of the impact of treatment with *aficamten* compared to *metoprolol* on the cardiac biomarkers NT-proBNP and high sensitivity cardiac troponin I (hs-cTnI). At baseline, high NT-proBNP and high hs-cTnI, indicative of cardiac wall stress and myocardial injury, respectively, were strongly correlated and generally associated with worse diastolic dysfunction. After treatment for 24 weeks, *aficamten* was associated with a 73% reduction (p<0.001) from baseline in NT-proBNP compared to an increase of 42% observed in patients receiving *metoprolol* (-81% treatment effect, p<0.001). Similarly, *aficamten* was associated with a 43% reduction in hs-cTnI, compared to a 17% decrease for *metoprolol* (-28% treatment effect, p=0.001). Patients with the greatest reductions in NT-proBNP experienced greater improvements in peak oxygen uptake ($pVO_2$) and ventilatory efficiency ($VE/VCO_2$). Additionally, changes in NT-proBNP were correlated with reductions of left ventricular outflow tract gradients (LVOT-G) and improved health status (KCCQ-OSS).

**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.[3] *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 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 as measured by peak oxygen uptake ($pVO_2$) and relieves symptoms in patients with HCM. *Aficamten* was evaluated in SEQUOIA-HCM, a positive pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic HCM from the U.S. Food & Drug Administration (FDA) and for the treatment of symptomatic obstructive HCM from the National Medical Products Administration (NMPA) in China.

*Aficamten* is also currently being evaluated in ACACIA-HCM, a Phase 3 clinical trial of *aficamten* in patients with non-obstructive HCM; CEDAR-HCM, a clinical trial of *aficamten* in a pediatric population with oHCM; and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM.

**Disclaimer**

This communication contains a summary of new data related to the clinical development of *aficamten* presented at the Hypertrophic Cardiomyopathy Medical Society Scientific Sessions and the American Heart Association Scientific Sessions 2025. *Aficamten* is an investigational drug and is not approved by any regulatory agency. Its safety and efficacy have not been established. *Aficamten* is currently under regulatory review in the U.S, where the FDA is reviewing a New Drug Application (NDA) for *aficamten* with a Prescription Drug User Fee Act (PDUFA) target action date of December 26, 2025. Additionally, the European Medicines Agency (EMA) is reviewing a Marketing Authorization Application (MAA) for *aficamten*, and The Center for Drug Evaluation (CDE) of the China National Medical Products Administration (NMPA) is reviewing an NDA for *aficamten* with Priority Review.

**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 reduced exercise capacity and symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. HCM is the most common monogenic inherited cardiovascular disorder, with approximately 280,000 patients diagnosed, however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed in the U.S.[4,5,6] Two-thirds of patients with HCM have obstructive HCM (oHCM), where the thickening of the cardiac muscle leads to left ventricular outflow tract (LVOT) obstruction, while one-third have non-obstructive HCM (nHCM), where blood flow isn't impacted, but the heart muscle is still thickened. People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease.[7] 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.[8] 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 is readying for potential regulatory approvals and commercialization of *aficamten*, a cardiac myosin inhibitor, following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in patients with obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in additional clinical trials enrolling patients with obstructive and non-obstructive HCM. In addition, Cytokinetics is developing *omecamtiv mecarbil*, a cardiac myosin activator, in patients with heart failure with severely reduced ejection fraction (HFrEF), *ulacamten*, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten*, for the potential treatment of heart failure with preserved ejection fraction (HFpEF) and CK-089, a fast skeletal muscle troponin activator with potential therapeutic application to a specific type of muscular dystrophy and other conditions of impaired skeletal muscle function.

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 any of our clinical trials, statements relating to the potential benefits of *aficamten* or any of our other drug candidates, or our ability to obtain regulatory approval for *aficamten* in any jurisdiction by any particular date, if ever. Cytokinetics' research and development activities; the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics' other drug candidates. 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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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/8de3104b-50ad-4620-849f-73bfa6212075

Figure 1: Effect of Aficamten Monotherapy vs Metoprolol Monotherapy on Clinical Efficacy Outcomes

Responder Analysis from MAPLE-HCM
Source: Cytokinetics, Incorporated