NEWS RELEASE

Cytokinetics Presents New Data Related to Aficamten at the HFSA Annual Scientific Meeting 2025

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Additional Data from MAPLE-HCM Show Aficamten Significantly Improves Measures of Maximal and Submaximal Exercise Capacity and Recovery Compared to Metoprolol

96-Week Analyses from FOREST-HCM Support Long-Term Efficacy and Tolerability of Aficamten in Patients with Non-Obstructive HCM

SOUTH SAN FRANCISCO, Calif., Sept. 29, 2025 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data related to *aficamten* were presented in a Late Breaking Clinical Research session at the Heart Failure Society of America (HFSA) Annual Scientific Meeting 2025 in Minneapolis, MN. The first presentation was a pre-specified analysis of the effect of *aficamten* compared to *metoprolol* on exercise performance in obstructive HCM (oHCM) in MAPLE-HCM (***M****etoprolol* vs ***A****ficamten* in **P**atients with **L**VOT Obstruction on **E**xercise Capacity in **HCM**), and the second was an analysis from FOREST-HCM (**F**ollow-up, **O**pen-Label, **R**esearch **E**valuation of **S**ustained **T**reatment with *Aficamten* in **HCM**) on the efficacy and tolerability of long-term treatment of *aficamten* in patients with non-obstructive hypertrophic cardiomyopathy (nHCM), simultaneously published in the *Journal of Cardiac Failure*.[1]

“The additional data from MAPLE-HCM expands our understanding of *aficamten* across several measures of exercise performance, with effects observed not only in peak exercise capacity, but also in submaximal exercise and recovery from exercise,” said Fady I. Malik, M.D., Ph.D., Cytokinetics’ Executive Vice President of Research & Development. “Additionally, the long-term data from FOREST-HCM in patients with nHCM show sustained improvements in both patient symptom burden and cardiac biomarkers associated with *aficamten*. Most patients achieved the highest doses available without any early treatment discontinuations, giving us confidence in the dosing strategy and the potential of *aficamten* to benefit patients with nHCM, as is being assessed in the ongoing Phase 3 clinical trial, ACACIA-HCM.”

Pre-Specified Analysis of Supplemental Endpoints from MAPLE-HCM Shows *Aficamten* Improves Measures of Submaximal and Maximal Exercise Performance and Post-Exercise Recovery Compared to *Metoprolol*

Gregory Lewis, M.D., Jeffrey and Mary Ellen Jay Chair and Section Head, Heart Failure Medical Director, Cardiopulmonary Exercise Testing (CPET) Laboratory, Professor of Medicine, Harvard Medical School presented pre-specified supplemental analyses of the impact of treatment with *aficamten* relative to *metoprolol* on CPET measures of exercise performance from onset through post-exercise recovery in MAPLE-HCM. The primary result of MAPLE-HCM demonstrated the superiority of *aficamten* to *metoprolol* on peak oxygen uptake (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). In these new analyses, *aficamten* compared to *metoprolol* was also shown to nominally significantly improve measures of submaximal exercise performance, including anaerobic threshold, aerobic efficiency (VO_2/work), ventilatory efficiency (pre-anaerobic threshold and VE/VCO_2 slope), and other key measures of maximal exercise performance, including peak workload, peak heart rate, exercise duration and heart rate reserve (Table 1). Additionally, the speed of VO_2 recovery, a sensitive measure of cardiometabolic resilience, increased with *aficamten* and slowed with *metoprolol*. A responder analysis showed that any improvement in pVO_2 was observed more commonly with *aficamten* compared to *metoprolol*, while any worsening was more frequent in the *metoprolol* group.

Table 1		
Submaximal Exercise Response Variables		
CPET variable	LSM (95% CI)*	*P*-value**
Anaerobic threshold, mL	+76 (41, 111)	<0.001
Aerobic efficiency (VO_2/work), mL/min/watt	+0.8 (0.2, 1.3)	0.004
Ventilatory efficiency (pre-anaerobic threshold)	−1.3 (−2.3, −0.3)	0.013
Ventilatory efficiency (VE/VCO_2 slope)	−2.8 (−4.0, −1.5)	<0.001
Maximal Exercise Response Variables		
Peak workload, watt	+8 (3, 13)	0.003
Peak heart rate, bpm	+28 (24, 32)	<0.001
Exercise duration, min	+0.6 (0.2, 1.0)	0.002
Heart rate reserve, bpm	+12 (8, 16)	<0.001
* LSM (95% CI) = change from baseline to Week 24 least squares mean treatment difference between *aficamten* and *metoprolol*, 95% confidence interval ** All p-values are nominal and not controlled for multiple comparisons		

New Data from FOREST-HCM Support the Efficacy and Tolerability of Long-Term Treatment with *Aficamten* in Patients with Non-Obstructive HCM

Ahmad Masri, M.D., MS, Director of the Hypertrophic Cardiomyopathy Center at Oregon Health & Science University, presented new data related to the safety and long-term use of *aficamten* in patients with nHCM in FOREST-HCM.

These analyses included 34 patients with nHCM who enrolled in FOREST-HCM, the open-label extension study, after completion of Cohort 4 of the Phase 2 clinical trial REDWOOD-HCM. Patients were followed for at least 96 weeks of treatment. At the end of titration (Week 6), 82.4% of patients were on the highest available doses of 15 mg and 20 mg. Through 96 weeks of treatment, there were no early treatment discontinuations and *aficamten* demonstrated sustained reductions in symptom burden. At Week 96, 27 of the 34 patients (79%) improved by at least one NYHA Functional Class,

including 20 (74%) who became asymptomatic (NYHA Functional Class 1). Patients also experienced a mean increase in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) of 11.2 points (±14.3 points). *Aficamten* also improved cardiac biomarkers, with both NT-proBNP and high-sensitivity cardiac troponin I rapidly declining by Week 12 and remaining low through Week 96. There was a modest reduction in left ventricular ejection fraction (LVEF) from hyperdynamic at baseline to within normal range at Week 12 (-6.2%; p<0.0001). Over the treatment period, four patients had LVEF <50% (5.4 per 100 patient-years) which were reversible after down titration or a short treatment interruption. Only one instance of LVEF <50% was corroborated by the core lab.

The efficacy and safety of *aficamten* in non-obstructive HCM is being investigated in an ongoing Phase 3 clinical trial.

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.[1] *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 HFSA Annual Scientific Meeting 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.[2,3,4] 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.[5] 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.[6] 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

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