NEWS RELEASE

Cytokinetics Announces Start of AMBER-HFpEF, a Phase 2 Clinical Trial of CK-586 in Patients With Symptomatic Heart Failure With Preserved Ejection Fraction

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SOUTH SAN FRANCISCO, Calif., Jan. 21, 2025 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that AMBER-HFpEF (**A**ssessment of CK-586 in a **M**ulti-Center, **B**linded **E**valuation of Safety and Tolerability **R**esults in **HFpEF**) is open to enrollment. AMBER-HFpEF is a Phase 2 randomized, placebo-controlled, double-blind, multi-center, dose-finding clinical trial of CK-4021586 (CK-586) in patients with symptomatic heart failure with preserved ejection fraction (HFpEF) with left ventricular ejection fraction (LVEF) ≥60%. CK-586 is a cardiac myosin inhibitor in development for the potential treatment of a subgroup of with symptomatic HFpEF patients with hypercontractility and ventricular hypertrophy.

“We are pleased to be advancing CK-586 into a Phase 2 trial in a subset of patients with symptomatic HFpEF,” said Stuart Kupfer, M.D., Senior Vice President, Chief Medical Officer. “Despite recent advances in available treatments, patients with heart failure with supranormal ejection fraction continue to have a poor prognosis following hospitalization. Evaluating CK-586 in this Phase 2 trial further extends the potential of our cardiac myosin directed development platform focused to specialty cardiology indications.”

Approximately half of patients with heart failure have HFpEF, characterized by an ejection fraction of at least 50%, impaired diastolic function and elevated NTpro-BNP, which can lead to poor ventricular compliance and reduced cardiac output. A subset of patients with HFpEF resemble patients with non-obstructive hypertrophic cardiomyopathy (nHCM) in that those patients have higher ejection fractions and thickened walls of their heart in association with elevated cardiac biomarkers and symptoms of heart failure. The evaluation of CK-586 in HFpEF builds on the similarity of these conditions and the data accumulated to date with *aficamten* in nHCM.

About AMBER-HFpEF

AMBER-HFpEF is a Phase 2 randomized, placebo-controlled, double-blind, multi-center, dose-finding clinical trial in patients with symptomatic HFpEF with LVEF ≥60%. The primary objective is to evaluate the safety and tolerability profile of CK-586 compared to placebo. The secondary objectives include

assessing the effect of CK-586 on LVEF and NT-proBNP, and determining both its pharmacokinetics and its pharmacokinetic/pharmacodynamic relationship. A number of exploratory endpoints will evaluate the effect of CK-586 on patient function, symptoms, and measures of cardiac function.

AMBER-HFpEF is planned to enroll approximately 60 patients randomized on a 3:1 basis to receive CK-586 or placebo in three dose escalation cohorts. Patients will receive up to two escalating doses of CK-586 over 12 weeks or placebo. An echocardiogram at Week 6 will determine whether patients will be up-titrated to the higher dose. Once-daily doses of 150 mg and 300 mg are planned in Cohort 1, 300 mg and 450 mg in Cohort 2 and 450 mg and 600 mg in Cohort 3. At screening, patients enrolled in AMBER-HFpEF must have LVEF ≥60%, NT-proBNP ≥300 pg/mL for participants in sinus rhythm and ≥900 pg/mL for participants with atrial fibrillation or flutter (AFF), and be New York Heart Association (NYHA) Functional Class II or III. Additional information can be found on www.clinicaltrials.gov.

About CK-4021586 (CK-586)

CK-4021586 (CK-586) is designed to be a novel, selective, oral, small molecule cardiac myosin inhibitor designed to reduce the hypercontractility associated with heart failure with preserved ejection fraction (HFpEF). CK-586 was designed to selectively inhibit the ATPase of intact cardiac myosin but does not inhibit the ATPase of subfragment-1 of myosin (S1). The inhibitory effect of CK-586 requires the presence of the regulatory light chain (RLC) of myosin in the context of the intact myosin dimer (heavy meromyosin or HMM). In preclinical models, CK-586 reduced cardiac hypercontractility by decreasing the number of active myosin cross-bridges during cardiac contraction thereby reducing the contractile force, without effect on calcium transients. In engineered human HCM heart tissues, CK-586 demonstrated shallow force-concentration response and improved lusitropy.

A subset of patients with HFpEF resemble patients with non-obstructive hypertrophic cardiomyopathy (nHCM) in that those patients have higher ejection fractions, thickened walls of their heart, elevated biomarkers, and symptoms of heart failure. Data from a Phase 2 clinical trial of *aficamten,* another investigational cardiac myosin inhibitor being developed by Cytokinetics, showed that in patients with nHCM *aficamten* was well tolerated, improved patient reported outcomes (Kansas City Cardiomyopathy Questionnaire (KCCQ) and New York Heart Association (NYHA) Functional Class) and biomarkers, measures that are also relevant to HFpEF. *Aficamten* was also well-tolerated with no drug discontinuations due to adverse events and no adverse events of heart failure. These data provide support for investigating this mechanism of action in HFpEF.

About Heart Failure with Preserved Ejection Fraction

Heart failure is a grievous condition that affects more than 64 million people worldwide.[1] Approximately 6.7 million Americans have heart failure, which is expected to increase to over 8.5 million Americans by 2030.[2] Approximately half of patients with heart failure have heart failure with preserved ejection fraction (HFpEF)[3], and the prevalence of HFpEF is increasing.[2,4] Approximately 75% of patients with HFpEF will die within five years of initial hospitalization, and 84% will be rehospitalized.[2] Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is poor.[5] A subset of HFpEF patients with hypercontractility, ventricular hypertrophy, elevated biomarkers and symptoms of heart failure may benefit from treatment with a cardiac sarcomere inhibitor.

About Cytokinetics

Cytokinetics is a late-stage, muscle biology specialty biopharmaceutical company focused on

discovering, developing and commercializing muscle biology-directed drug candidates as potential treatments for debilitating diseases in which muscle performance is compromised. As a leader in muscle biology and the mechanics of muscle performance, Cytokinetics is intent on meaningfully improving the lives of patients through global access to innovative medicines. Cytokinetics is readying for potential regulatory approvals and commercialization of *aficamten,* a potential next-in-class 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. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac myosin activator, in patients with heart failure with severely reduced ejection fraction (HFrEF), CK-586, 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, express or implied, relating to the Company's development plans for CK-586 in the United States, including its ability to full enroll AMBER-HFpEF by any particular date, if at all. 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.

References:

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Contact:
Cytokinetics
Diane Weiser
Senior Vice President, Corporate Affairs
(415) 290-7757

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