Cytokinetics Highlights Progress in Cardiac Myosin Modulation Programs and Global Commercial Launch Readiness at Investor & Analyst Day

October 16, 2024 11:30 AM EDT

NDA for Aficamten Submitted to FDA in Q3

COMET-HF, Confirmatory Phase 3 Clinical Trial of Omecamtiv Mecarbil, and AMBER-HFpEF, Phase 2 Clinical Trial of CK-586, Expected to Begin in Q4

Global Commercial Launch Preparations Underway for First Potential Approval Towards Building Specialty Cardiovascular Franchise

Company Recently Launched Unbranded Disease Awareness Campaign "HCM Beyond The Heart" for Health Care Professionals

SOUTH SAN FRANCISCO, Calif., Oct. 16, 2024 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) will provide an update on the company's cardiac myosin modulation programs and global commercial launch readiness for *aficamten* at its Investor and Analyst Day, "Heart Forward: Advancing Cardiac Myosin Modulation," today at 8:30 AM Eastern Time in New York and streamed live online. The Company plans to synthesize recent updates from clinical trials relating to *aficamten*, a next-in-class cardiac myosin inhibitor, as well as share the design of COMET-HF, a confirmatory Phase 3 clinical trial of *omecamtiv mecarbil*, a cardiac myosin activator being developed for the potential treatment of patients with symptomatic heart failure (HF) and severely reduced ejection fraction, and the design of AMBER-HFpEF, a Phase 2 clinical trial of CK-4021586 (CK-586), another cardiac myosin inhibitor being developed for the potential treatment of patients with symptomatic heart failure with preserved ejection fraction (HFpEF) and hypercontractility. Today's event will also feature perspectives from leading expert clinicians on the evolving landscape for the treatment of hypertrophic cardiomyopathy (HCM) and heart failure.

"Our pioneering science relating to the mechanics of cardiac muscle function continues to be the engine empowering Cytokinetics as we advance our specialty cardiology franchise focused on myosin modulation to address unmet patient needs in HCM as well as those patients with heart failure whose disease is characterized by irregularities in cardiac muscle contractility," said Robert I. Blum, Cytokinetics' President and Chief Executive Officer. "We are pleased to announce that we recently submitted the New Drug Application for *aficamten* to FDA, as we have continued to advance our later-stage development programs. As we approach the potential commercial launch of *aficamten*, we believe our bespoke commercial planning positions us well to deliver on our specialty cardiology franchise business objectives and, as bolstered by a strong balance sheet and available access to additional long-term capital, our corporate development strategies."

COMET-HF: Confirmatory Phase 3 Clinical Trial of *Omecamtiv Mecarbil*

Today, Cytokinetics will present the design of COMET-HF (**C**onfirmation of ***O****mecamtiv* ***M****ecarbil* **E**fficacy **T**rial in **H**eart **F**ailure), a Phase 3 multi-center, double-blind, randomized, placebo-controlled trial to assess the efficacy and safety of *omecamtiv mecarbil* in patients with symptomatic HF with severely reduced ejection fraction.

Omecamtiv mecarbil was previously the subject of GALACTIC-HF, a Phase 3 clinical trial of *omecamtiv mecarbil* in over 8,000 patients with heart failure with reduced ejection fraction (HFrEF) which showed a statistically significant risk reduction of heart failure outcomes with *omecamtiv mecarbil* on top of standard of care. The magnitude of the treatment effect in the pre-specified subgroup of more than 4,000 patients with heart failure with severely reduced ejection fraction (<30%) was observed to be greater than in the overall drug treated population of GALACTIC-HF. The treatment benefit in this subgroup was observed to increase further in patients with recent heart failure hospitalizations, higher NT-proBNP and lower blood pressure. Given the greater observed treatment benefit and high unmet need in the subgroup of patients with HF and severely reduced ejection fraction, the company plans to seek regulatory approval of *omecamtiv mecarbil* for use in this population if the results are confirmed by COMET-HF.

The primary endpoint of COMET-HF is the time to first event in the primary composite endpoint of cardiovascular death, first heart failure event, left ventricular assist device (LVAD) implantation or cardiac transplantation, or stroke. COMET-HF is expected to enroll approximately 1,800 patients randomized on a 1:1 basis to receive *omecamtiv mecarbil* or placebo. Patients randomized to *omecamtiv mecarbil* will receive up to a maximum dose of 50 mg twice daily based on the plasma concentration of *omecamtiv mecarbil* during a run-in period. Patients will continue to receive *omecamtiv mecarbil* or placebo twice daily until approximately 850 primary composite endpoint events have occurred. Cytokinetics expects to begin COMET-HF in Q4 2024.

AMBER-HFpEF: Phase 2 Clinical Trial of CK-586

Cytokinetics will also today present the design of AMBER-HFpEF (**A**ssessment of CK-586 in a **M**ulti-Center, **B**linded **E**valuation of Safety and Tolerability **R**esults in **HFpEF**), a Phase 2 randomized, placebo-controlled, double-blind, multi-center, dose-finding clinical trial in patients with symptomatic HFpEF with left ventricular ejection fraction (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, its pharmacokinetics, and its pharmacokinetic/pharmacodynamic relationship. Cytokinetics expects to begin AMBER-HFpEF in Q4 2024.

Perspectives from Expert Clinicians

Today's event will feature the following expert clinicians:

- **Mariko Harper, M.D., MS, FACC,** Medical Director, The Hypertrophic Cardiomyopathy Center, Virginia Mason Franciscan Health
- **Shepard D. Weiner, M.D.,** Medical Director, Hypertrophic Cardiomyopathy Center and Associate and Professor of Medicine, Columbia University Medical Center
- **G. Michael Felker, M.D., MHS, FACC, FAHA, FHFSA,** Professor of Medicine, Division of Cardiology, Duke Clinical Research Institute,

Principal Investigator of COMET-HF, the Confirmatory Phase 3 Clinical Trial of *Omecamtiv Mecarbil*

Global Commercial Launch Readiness for *Aficamten*

Cytokinetics commercial leaders will provide an update on the company's global launch preparations for *aficamten*. In Q3 the company submitted a New Drug Application (NDA) for *aficamten* to the U.S. Food and Drug Administration (FDA) and advanced its commercial planning initiatives in anticipation of a potential approval and launch in the U.S. in 2025. The company's go-to-market strategies are anchored in differentiated market access and patient experience as key priorities. Activities supportive of launch include ongoing payer engagement, and publication of health economics and outcomes research. Market research and real-world feedback from payors, cardiologists, nurses and patients has informed the development of "HCM Beyond the Heart," an unbranded disease awareness campaign for healthcare professionals which the Company recently launched to illuminate the multidimensional struggle and daily burden faced by people living with HCM.

Cytokinetics also continues to publish a substantial volume of clinical data in peer-reviewed publications to build an evidence base supportive of a potential launch and is supporting independent Continuing Medical Education (CME) to help educate physicians about HCM.

The Company also will provide updates today relating to earlier commercial readiness activities in Europe with the hiring of its leadership team, design of the planned distribution model and development of regulatory and labeling strategies. The company plans to submit a Marketing Authorization Application (MAA) for *aficamten* to the European Medicines Agency (EMA) in Q4. The Company is engaging European payers, key opinion leaders, Health Technology Assessment (HTA) organizations and patient advocacy groups in preparation for the potential approval and launch of *aficamten* with go-to-market strategies in Europe designed to prioritize major markets and gate capital deployment alongside regulatory and reimbursement milestones.

Access to Virtual Event

This event is intended for investor audiences. Interested parties must register online at https://cytokinetics-2024-analyst-and-investor-day.open-exchange.net/. Registered attendees may access the live virtual event platform by visiting the Investor & Media section of the Cytokinetics website at www.cytokinetics.com. A link to the webcast replay will be archived on the Cytokinetics website until April 16, 2025.

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 and as may translate into next-in-class potential. *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 hypertrophic cardiomyopathy (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 into a force producing state.

The development program for *aficamten* is assessing its potential as a treatment that improves exercise capacity and relieves symptoms in patients with HCM as well as its potential long-term effects on cardiac structure and function. *Aficamten* was evaluated in SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A****ficamten* in **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) as well as the National Medical Products Administration (NMPA) in China.

Aficamten is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, 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 obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM.

About *Omecamtiv Mecarbil*

Omecamtiv mecarbil is an investigational, selective, small molecule cardiac myosin activator, the first of a novel class of myotropes[1] designed to directly target the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. *Omecamtiv mecarbil* is designed to increase the number of active actin-myosin cross bridges during each cardiac cycle and consequently augment the impaired contractility that is associated with heart failure with reduced ejection fraction (HFrEF). Preclinical research has shown that *omecamtiv mecarbil* increases cardiac contractility without increasing intracellular myocyte calcium concentrations or myocardial oxygen consumption.[2-4]

The development program for *omecamtiv mecarbil* assessed its potential for the treatment of HFrEF. Positive results from GALACTIC-HF demonstrated a statistically significant effect of treatment with *omecamtiv mecarbil* to reduce risk of the primary composite endpoint of cardiovascular (CV) death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care. Adverse events and treatment discontinuation of study drug were balanced between the treatment arms.

About CK-4021586 (CK-586)

CK-4021586 (CK-586) is 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 selectively inhibits the ATPase of intact cardiac myosin but does not inhibit the ATPase of subfragment-1 of myosin (S1) as does *aficamten*, a cardiac myosin inhibitor also developed by the Company. Unlike *aficamten*, 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.

Lending support for investigating this mechanism of action in HFpEF, a subset of patients with HFpEF resemble patients with non-obstructive hypertrophic cardiomyopathy (HCM) 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* in patients with non-obstructive HCM show that *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. Cytokinetics is planning to start AMBER-HFpEF, a Phase 2 clinical trial of CK-586 in a subgroup of patients with symptomatic HFpEF with hypercontractility and ventricular hypertrophy, in Q4 2024.

About Cytokinetics

Cytokinetics is a late-stage, specialty cardiovascular biopharmaceutical company focused on discovering, developing and commercializing muscle

biology-directed drug candidates as potential treatments for debilitating diseases in which cardiac muscle performance is compromised. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to impact myocardial muscle function and contractility. Cytokinetics is preparing for regulatory submissions for *aficamten*, its next-in-class cardiac myosin inhibitor, following positive results from SEQUOIA-HCM, the pivotal Phase 3 clinical trial in obstructive hypertrophic cardiomyopathy which were published in the *New England Journal of Medicine*. *Aficamten* is also currently being evaluated in MAPLE-HCM, a Phase 3 clinical trial of *aficamten* as monotherapy compared to metoprolol as monotherapy in patients with obstructive HCM, 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 obstructive HCM, and FOREST-HCM, an open-label extension clinical study of *aficamten* in patients with HCM. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator, in patients with heart failure with severely reduced ejection fraction (HFrEF). Additionally, Cytokinetics is developing 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).

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 properties or potential benefits of *aficamten*, *omecamtiv mecarbil*, CK-586 or any of our other drug candidates, our ability to commence AMBER-HFpEF by the end of 2024, our ability to approval of our new drug application or other marketing authorization application for *aficamten* in oHCM or nHCM or commercially launch *aficamten* in the United States or any other jurisdiction. 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 the risks related to Cytokinetics' business outlines in Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and Cytokinetics' actual results of operations, financial condition and liquidity, and the development of the industry in which it operates, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that Cytokinetics makes in this press release speak only as of the date of this press release. Cytokinetics assumes no obligation to update its forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Source: Cytokinetics, Incorporated