Cytokinetics Announces Start of MAPLE-HCM, a Phase 3 Clinical Trial of Aficamten Compared to Metoprolol in Patients With Symptomatic Obstructive Hypertrophic Cardiomyopathy

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First Phase 3 Trial Evaluating Monotherapy with a Cardiac Myosin Inhibitor Compared to Monotherapy with a Beta Blocker in Adults with Symptomatic Obstructive Hypertrophic Cardiomyopathy

SOUTH SAN FRANCISCO, Calif., June 20, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that MAPLE-HCM (***M****etoprolol* vs ***A****ficamten* in **P**atients with **L**VOT Obstruction on **E**xercise Capacity in **HCM)**, a Phase 3 clinical trial comparing *aficamten* as monotherapy to *metoprolol* as monotherapy in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM), is open to enrollment. *Aficamten* is a next-in-class cardiac myosin inhibitor in development for the potential treatment of HCM.

"We are pleased to further expand the development program for *aficamten* with the start of MAPLE-HCM, a Phase 3 trial assessing for the potential superiority of *aficamten* compared to a commonly prescribed beta blocker, *metoprolol*," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "MAPLE-HCM is, to date, the first and only clinical trial directly comparing a cardiac myosin inhibitor to what is considered the standard of care therapy in patients with HCM. While beta-blockers like *metoprolol* can reduce the left ventricular outflow tract gradient (LVOT-G) and improve patient symptoms, they are often associated with undesirable side effects and have not been shown to improve exercise capacity, a desired treatment outcome for patients suffering from HCM. We hope that MAPLE-HCM will generate evidence showing treatment with *aficamten* as first-line monotherapy is superior to monotherapy with *metoprolol*, which may help offer a simplified treatment approach in HCM."

MAPLE-HCM: Clinical Trial Design

MAPLE-HCM is a Phase 3, multi-center, randomized, double-blind active-comparator clinical trial of *aficamten* compared to *metoprolol* in patients with symptomatic obstructive HCM. The primary endpoint is 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 is expected to enroll 170 patients, randomized on a 1:1 basis to receive *aficamten* or *metoprolol*. Randomization will be stratified by CPET exercise modality (treadmill or bicycle) and recently diagnosed versus chronic obstructive HCM. At screening, patients enrolled in MAPLE-HCM must have 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 pVO_2 <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 will undergo a washout period of up to 14 days of weaning from SOC therapy, followed by an additional 7 days with no SOC therapy prior to the second screening visit. Each patient will receive up to four escalating doses of *aficamten* or *metoprolol* based on echocardiographic guidance. Patients receiving *aficamten* will begin with 5 mg dosed once daily. At weeks 2, 4 and 6 patients will receive an echocardiogram to determine if they will be up-titrated to escalating doses of 10, 15 or 20 mg. Patients receiving *metoprolol* will begin with 50 mg dosed once daily. At weeks 2, 4 and 6 patients will receive an echocardiogram to determine if they will be up-titrated to escalating doses of 100, 150 or 200 mg. Patients who complete MAPLE-HCM will be eligible to participate in the open-label extension clinical study, FOREST-HCM (**F**ollow-Up, **O**pen-Label, **R**esearch **E**valuation of **S**ustained **T**reatment with *Aficamten* in **HCM**). Additional information can be found on www.clinicaltrials.gov.

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 in clinical development. *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 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* is currently the subject of SEQUOIA-HCM (**S**afety, **E**fficacy, and **Q**uantitative **U**nderstanding of **O**bstruction **I**mpact of ***A****ficamten* in **HCM**), the pivotal Phase 3 clinical trial in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). Results from SEQUOIA-HCM are expected in the fourth quarter of 2023. *Aficamten* received Breakthrough Therapy Designation for the treatment of symptomatic obstructive HCM from the U.S. Food & Drug Administration (FDA) as well as the National Medical Products Administration (NMPA) in China.

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 symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. A subset of patients with HCM are at high risk of progressive disease which can lead to atrial fibrillation, stroke and death due to arrhythmias.

About Cytokinetics

Cytokinetics is a late-stage, specialty cardiovascular biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors 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. *Aficamten* is a next-in-class cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM).

Aficamten is also being evaluated in non-obstructive HCM and the company plans to begin a Phase 3 trial later this year. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator in patients with heart failure. Additionally, Cytokinetics is developing CK-136, a cardiac troponin activator for the potential treatment HFrEF and other types of heart failure, such as right ventricular failure, resulting from impaired cardiac contractility, and CK-586, a cardiac myosin inhibitor with a mechanism of action distinct from *aficamten*. In 2023, Cytokinetics is celebrating its 25-year history of pioneering innovation in muscle biology and related pharmacology focused to diseases of muscle dysfunction and conditions of muscle weakness.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on Twitter, 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* or any of our other drug candidates, our ability to publish the results of SEQUOIA-HCM or any of our other clinical trials by any particular date, if at all, and the likelihood or timing of regulatory approval for *aficamten* or any of our 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 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.

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

Source: Cytokinetics, Incorporated