Cytokinetics Announces Start of REDWOOD-HCM, a Phase 2 Clinical Trial of CK-3773274

January 6, 2020 12:30 PM EST

Next-Generation Cardiac Myosin Inhibitor Advances In Clinical Trial Designed to Assess Effects Using Two-Week Dose Titration Schedule

SOUTH SAN FRANCISCO, Calif., Jan. 06, 2020 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that REDWOOD-HCM (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM**) has opened to enrollment. REDWOOD-HCM is a Phase 2 clinical trial of CK-3773274 (CK-274), a next-generation cardiac myosin inhibitor discovered by company scientists, which Cytokinetics is developing for the potential treatment of hypertrophic cardiomyopathy (HCM).

"Our ability to quickly begin REDWOOD-HCM following the recently announced and encouraging Phase 1 data is a result of the enthusiasm of our clinical trial sites and participating investigators working in partnership with our dedicated team here at our company," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Our Phase 1 study showed CK-274 achieved the intended pharmacodynamic effect and exposure-response relationship reaching steady state pharmacokinetics levels within 14 days, thereby enabling a dose titration regimen at two-week intervals. REDWOOD-HCM is designed to evaluate translation of a flexible dose optimization schedule with CK-274 to therapeutic window and echocardiographic parameters associated with clinical outcomes in patients with HCM."

"Patients suffering from HCM experience daily limiting symptoms that significantly decrease their overall quality of life. What they may benefit from is an alternative therapy designed to optimally treat the underlying cause of their disease," said Marty Maron, M.D., Director, Hypertrophic Cardiomyopathy Center; Director, Cardiac CT and MRI; Tufts University School of Medicine, and Principal Investigator of REDWOOD-HCM. "Investigating CK-274 in this Phase 2 trial is an important step toward a potential new treatment option for HCM patients."

REDWOOD-HCM: Clinical Trial Design

REDWOOD-HCM is a multi-center, randomized, placebo-controlled, double-blind, dose-finding clinical trial in patients with symptomatic, obstructive HCM (oHCM). The primary objective of the trial is to determine the safety and tolerability of CK-274. The secondary objectives are to describe the concentration-response and dose-response relationship of CK-274 on the resting and post-Valsalva left ventricular outflow tract gradient as measured by echocardiography during 10 weeks of treatment. Additionally, the trial will evaluate the plasma concentrations of CK-274 in patients with oHCM in relationship to dose. Exploratory objectives include the effect of CK-274 on N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and New York Heart Association (NYHA) Functional Classification.

The trial will enroll two sequential cohorts of patients, with an option for a third cohort. Within each cohort, 18 patients will be randomized 2:1 to active or placebo treatment and receive up to three escalating doses of CK-274 or placebo based on echocardiographic guidance. Patients will receive an echocardiogram after two weeks of treatment at each dose to determine whether they will be up-titrated to the next higher dose. Cohort 1 will employ doses of 5, 10 and 15 mg, once daily. The doses in Cohort 2 will be determined following a review of the data from Cohort 1. Overall, the treatment duration will be 10 weeks with an echocardiogram to confirm reversibility of effect two weeks after the last dose. REDWOOD-HCM is expected to enroll patients in approximately 20 investigative sites in North America and Europe. All patients will be eligible to participate in an open label extension study of CK-274. Additional information can be found on www.clinicaltrials.gov.

About CK-274

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor that company scientists discovered independent of its collaborations. CK-274 arose from an extensive chemical optimization program conducted with careful attention to therapeutic index and pharmacokinetic properties that may translate into next-in-class potential in clinical development. CK-274 was designed to reduce the hypercontractility that is associated with hypertrophic cardiomyopathy (HCM). In preclinical models, CK-274 reduces 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. CK-274 reduces the number of active actin-myosin cross bridges during each cardiac cycle and consequently reduces myocardial contractility. This mechanism of action may be therapeutically effective in conditions characterized by excessive hypercontractility, such as HCM.

In preclinical models of cardiac function, both in normal models of cardiac function and mouse models of HCM, CK-274 reduced cardiac contractility in a predictable dose and exposure dependent fashion. The preclinical pharmacokinetics of CK-274 were characterized, evaluated and optimized for potential ease-of-use in the clinical setting. A Phase 1 study demonstrated that CK-274 was safe and well tolerated in healthy participants. The pharmacokinetics of CK-274 were generally dose linear, and steady-state appeared evident within 14 days of dosing. Left ventricular ejection fraction decreased in an exposure dependent manner and the PK/PD relationship for CK-274 observed in humans was similar to that observed preclinically when adjusted for differences in protein binding. Specifically, the shallow exposure-response relationship observed preclinically appears to translate to humans and thereby may enable flexible dose optimization in humans.

The overall development program will assess the potential of CK-274 to improve exercise capacity and relieve symptoms in patients with hyperdynamic ventricular contraction due to HCM.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is an inherited cardiovascular disorder 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. In the majority of patients, thickening of the heart muscle in the left ventricular outflow tract obstructs the flow of blood out of the heart. 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 ventricular arrhythmias, atrial fibrillation, stroke, heart failure and sudden cardiac death. There are no current medical treatments that directly address the hypercontractility that underlies HCM.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and

best-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to impact muscle function and contractility. Cytokinetics is collaborating with Amgen Inc. (Amgen) to develop *omecamtiv mecarbil*, a novel cardiac muscle activator. *Omecamtiv mecarbil* is the subject of an international clinical trials program in patients with heart failure including GALACTIC-HF and METEORIC-HF. Amgen holds an exclusive worldwide license to develop and commercialize *omecamtiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is collaborating with Astellas Pharma Inc. (Astellas) to develop *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA) for diseases of neuromuscular dysfunction, including SMA and ALS. Astellas holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. Licenses held by Amgen and Astellas are subject to specified co-development and co-commercialization rights of Cytokinetics. Cytokinetics is also developing CK-274, a novel cardiac myosin inhibitor that company scientists discovered independent of its collaborations, for the potential treatment of hypertrophic cardiomyopathies. Cytokinetics continues its over 20-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 relating to the timing, design and results of Cytokinetics' Phase 2 clinical trial of CK-274; the potential benefits of CK-274; Cytokinetics’ and its partners’ research and development activities; the timing of enrollment of patients in Cytokinetics’ and its partners’ clinical trials; the design, timing, results, significance and utility of preclinical and clinical results; and the properties and potential benefits of Cytokinetics’ 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; patient enrollment for or conduct of clinical trials may be difficult or delayed; Cytokinetics’ drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics’ or its partners’ ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics’ partners decisions with respect to research and development activities; standards of care may change, rendering Cytokinetics’ drug candidates obsolete; competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics’ drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics’ collaboration agreements with such partners. 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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Source: Cytokinetics, Incorporated