Cytokinetics Announces Cohort 3 of REDWOOD-HCM is Open to Enrollment

May 4, 2021 11:30 AM EDT

Next Cohort to Enroll Patients on Background Therapy of Disopyramide

SOUTH SAN FRANCISCO, Calif., May 04, 2021 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced the opening of enrollment in Cohort 3 of REDWOOD-HCM (**R**andomized **E**valuation of **D**osing **W**ith CK-274 in **O**bstructive **O**utflow **D**isease in **HCM**), an ongoing Phase 2 clinical trial of CK-3773274 (CK-274), a next-generation cardiac myosin inhibitor in development for the potential treatment of hypertrophic cardiomyopathy (HCM). Cohort 3 will enroll patients whose background therapy includes disopyramide.

"After completing enrollment in the first two cohorts in REDWOOD-HCM, we are pleased to now begin Cohort 3, which is enrolling patients who are being treated with disopyramide," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Given that disopyramide is often prescribed in patients with more severe HCM, the data from Cohort 3 may support the potential use of CK-274 in a broader population of patients with obstructive HCM. Importantly, we do not believe that Cohort 3 is required to refine the dosing strategy that we expect to use in Phase 3 but it will help inform the inclusion criteria for that potentially pivotal clinical trial which we are planning to begin later this year."

REDWOOD-HCM: Clinical Trial Design

REDWOOD-HCM is a multi-center, randomized, placebo-controlled, double-blind, dose finding clinical trial of CK-274 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 relationship of CK-274 on the resting and post-Valsalva left ventricular outflow tract gradient as measured by echocardiography during 10 weeks of treatment, to describe the dose response relationship of CK-274, and to evaluate the plasma concentrations of CK-274 in patients with oHCM.

The trial previously completed enrollment in Cohort 1 and Cohort 2, two sequential cohorts. Within each cohort, approximately 20 patients were randomized 2:1 to active or placebo treatment and received up to three escalating doses of CK-274 or placebo based on echocardiographic guidance. Patients received an echocardiogram after two weeks of treatment at each dose to determine whether they would be up-titrated. Overall, the treatment duration is 10 weeks with an echocardiogram to confirm reversibility of effect 2 weeks after the last dose. In Cohorts 1 and 2, patients continued taking background medications exclusive of disopyramide.

Cohort 3 will enroll, in an open label fashion, 8-12 patients whose background therapy includes disopyramide to assess the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of CK-274 in patients taking disopyramide. All patients will receive up to three escalating doses of CK-274, titrated based on echocardiographic guidance. Overall treatment duration will be 10 weeks with a 4-week follow up period after the last dose.

Interim analysis of data from Cohort 1 of REDWOOD-HCM showed patients experienced substantial reductions in the average resting left ventricular outflow tract gradient (LVOT-G) as well as the post-Valsalva LVOT-G (defined as resting gradient <30 mmHg and post-Valsalva gradient <50 mmHg). These clinically relevant decreases in pressure gradients were achieved with only modest decreases in average left ventricular ejection fraction (LVEF); there were no dose interruptions due to LVEF falling below 50%, the prespecified safety threshold. Pharmacokinetic data were similar to those observed in Phase 1 in healthy subjects. In addition, the safety and tolerability data were supportive of continued dose escalation with no serious adverse events attributed to study treatment reported by the investigators.

Results from REDWOOD-HCM, across both Cohort 1 and Cohort 2, are expected in mid-2021. Additional information about REDWOOD-HCM can be found on **clinicaltrials.gov/**.

About CK-274

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor arising 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, CK-274 reduced cardiac contractility in a predictable dose and exposure dependent fashion. In preclinical models of disease, CK-274 reduced compensatory cardiac hypertrophy and cardiac fibrosis. The preclinical pharmacokinetics of CK-274 were characterized, evaluated and optimized for potential ease of titration in the clinical setting.

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. There are no FDA approved 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 next-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 preparing for regulatory interactions for *omecamtiv mecarbil*, its novel cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is conducting METEORIC-HF, a second Phase 3 clinical trial of *omecamtiv mecarbil*. Cytokinetics is also developing CK-274, a next-generation cardiac myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies (HCM). Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical

trial of CK-274 in patients with obstructive HCM. Cytokinetics is also developing *reldesemtiv*, a fast skeletal muscle troponin activator for the potential treatment of ALS and other neuromuscular indications following conduct of FORTITUDE-ALS and other Phase 2 clinical trials. The company is preparing for the potential advancement of *reldesemtiv* to a Phase 3 clinical trial in ALS. 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' research and development activities; the timing of enrollment of patients in Cytokinetics' 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' 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.

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

Source: Cytokinetics, Incorporated