Cytokinetics Announces Data From Phase 1 Study of CK-3773274 at the HFSA 23rd Annual Scientific Meeting

September 16, 2019 11:30 AM EDT

Pharmacokinetic/Pharmacodynamic Relationship in Humans Similar to Preclinical Findings

Data Support Progression to Phase 2 Clinical Trial in Patients with Obstructive Hypertrophic Cardiomyopathy to Begin in Q4 2019

SOUTH SAN FRANCISCO, Calif., Sept. 16, 2019 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced data from the Phase 1 study of CK-3773274 (CK-274) were presented in a poster session at the HFSA 23rd Annual Scientific Meeting in Philadelphia. The study met its primary and secondary objectives to assess the safety and tolerability of single and multiple oral doses of CK-274, describe the pharmacokinetics (PK) of CK-274 and its pharmacodynamic effects (PD) as measured by echocardiography, as well as to characterize the PK/PD relationship with regards to cardiac function. These data support the advancement of CK-274 into a Phase 2 clinical trial in patients with obstructive hypertrophic cardiomyopathy which is expected to begin in Q4 2019. CK-274 is a novel selective cardiac myosin inhibitor, discovered by company scientists, in development for the potential treatment of hypertrophic cardiomyopathy (HCM).

Phase 1 Design and Key Findings

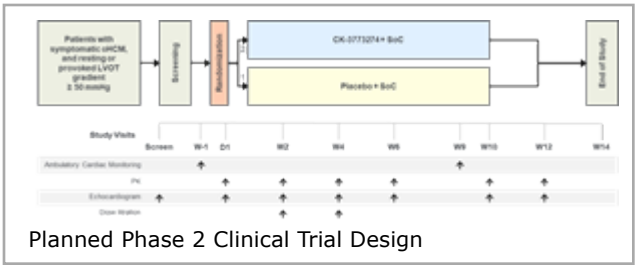
The primary objective of this Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose study was to assess the safety and tolerability of CK-274 in healthy volunteers. The study design included single ascending dose cohorts and multiple ascending dose cohorts, with eight healthy subjects per cohort. Additional objectives included to describe the PK of CK-274 and its PD effects as measured by echocardiography, as well as to characterize the relationship between the two with regards to cardiac function. This study was not designed to identify a maximum tolerated dose of CK-274.

The study demonstrated that CK-274 was safe and well tolerated in healthy participants. No serious adverse events and no clinically meaningful changes in vital signs, ECGs or laboratory tests were observed. Stopping criteria for continued dose escalation were reached after a single dose of 75 mg and after 14 days of a daily of 10 mg dose. Decreases in ejection fraction below 50% were readily reversible within six hours following single doses and within 24-48 hours following 14 days of dosing. 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.

“Our scientists originally pioneered this emerging area of muscle pharmacology and we have now advanced a potential next-in-class drug candidate that was optimized for its pharmacokinetic properties and therapeutic index, both of which are evident in this study,” said Fady I. Malik, MD, PhD, Cytokinetics’ Executive Vice President, Research and Development. “Importantly, steady state was achieved within two weeks of daily dosing and reversibility of drug effect within 24-48 hours following 14 days of dosing. These properties enable two-week dose titration in the planned Phase 2 trial and may translate to rapid onset, ease of titration and rapid symptom relief in the clinical setting.”

Planned Phase 2 Clinical Trial Design

Cytokinetics expects to begin a randomized, placebo-controlled Phase 2 trial of CK-274 in patients with symptomatic obstructive HCM later this year. The primary objective of the planned trial is to assess the safety and tolerability of CK-274 in these patients. Secondary objectives are to assess the PK and PD of CK-274 in these patents, guided by echocardiography, with two-week dose titration. CK-274 will be added to stable background medical therapy.



Planned Phase 2 Clinical Trial Design

About CK-274

CK-274 is a novel, selective, 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 purposely 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.

The preclinical pharmacokinetics of CK-274 were evaluated and optimized for potential rapid onset, ease of titration, individualized dosing and rapid symptom relief in the clinical setting. The initial focus of the development program for CK-274 will include an extensive characterization of its PK/PD

relationship as has been a hallmark of Cytokinetics' industry-leading development programs in muscle pharmacology. The overall development program will assess the potential of CK-274 to improve exercise capacity and relieve symptoms in patients with hypercontractile ventricular function 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. 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 1 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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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/5a6efc9d-d14e-4a7b-9ffe-4ab4de674521

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