Cytokinetics Announces Initiation of Phase 1 Clinical Trial of CK-3773274, a Cardiac Myosin Inhibitor

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SOUTH SAN FRANCISCO, Calif., Dec. 05, 2018 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced the first subject has been dosed in a Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose clinical trial of CK-3773274 (CK-274) in healthy adult subjects. CK-274 is a novel cardiac myosin inhibitor, discovered by company scientists, in development for the potential treatment of hypertrophic cardiomyopathy (HCM).

"The start of clinical trials for CK-274 marks an important milestone in our continuing innovation of potential sarcomere-directed medicines," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Our scientists pioneered this emerging area of muscle pharmacology and have now advanced a next-generation drug candidate that was optimized for pharmacokinetic properties and therapeutic index. This first trial will elaborate on CK-274 and its potential to be best-in-class and we look forward to reporting data in 2019."

Phase 1 Clinical Trial Design

The primary objective of this Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose trial is to assess the safety and tolerability of single and multiple oral doses of CK-274. The study design includes eight single ascending dose cohorts and three multiple ascending dose cohorts, with eight healthy subjects per cohort. Additional objectives include describing the pharmacokinetics (PK) of CK-274 and its pharmacodynamic effects (PD) as measured by echocardiography, as well as characterizing the relationship between the two with regards to cardiac function. 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 best-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-use 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 hyperdynamic ventricular contraction due to HCM.

About Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiovascular disorder, affecting approximately 1 in 500 individuals worldwide. 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 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 GALACTIC-HF, an international Phase 3 clinical trial in patients with heart failure. 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 also collaborating with Amgen to develop AMG 594, a first-in-class cardiac troponin activator, discovered under the companies' joint research program. Further development of AMG 594 is subject to the collaboration agreement between Amgen and Cytokinetics. Cytokinetics is collaborating with Astellas Pharma Inc. ("Astellas") to develop *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA). *Reldesemtiv* has been granted orphan drug designation by the FDA for the potential treatment of spinal muscular atrophy. *Reldesemtiv* was the subject of a positive Phase 2 clinical study in patients with spinal muscular atrophy which showed increases in measures of endurance and stamina consistent with the mechanism of action. *Reldesemtiv* is currently the subject of FORTITUDE-ALS, a Phase 2 clinical trial in patients with amyotrophic lateral sclerosis. Cytokinetics is also advancing CK-601, a next-generation FSTA into IND-enabling studies under the collaboration with Astellas. 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 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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