Cytokinetics Announces Preclinical Data for CK-2127107 Presented at MDA Scientific Conference

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Next-Generation Fast Skeletal Troponin Activator Improves Muscle Function in Mouse Models of Spinal Muscular Atrophy

SOUTH SAN FRANCISCO, Calif., March 22, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) today announced that preclinical data for CK-2127107 were presented at the MDA Scientific Conference in Arlington, VA, showing that this next-generation fast skeletal troponin activator (FSTA) improves muscle function in mouse models of spinal muscular atrophy (SMA). In collaboration with Astellas Pharma Inc. (TSE:4503) ("Astellas"), Cytokinetics is developing CK-2127107 as a potential treatment for people living with SMA and certain other debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue.

"These data support our ongoing Phase 2 clinical trial of CK-2127107 in adolescent and adult patients with SMA," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President, Research and Development. "The increased muscle force at sub-maximal nerve stimulation frequencies in mice inform the potential for CK-2127107 to increase muscle function in patients living with motor neuron dysfunction."

Preclinical Study Design and Results
The objective of this study was to investigate the effect of CK-2127107 on skeletal muscle function in two mouse models of SMA with varying levels of disease severity. The study evaluated CK-2127107 in 2B/2B-Neo Intermediate SMA mice (similar to Type II SMA), in collaboration with Lurie Children's Hospital and Hung Li SMA mice (similar to Types III and IV SMA). These mouse models exhibit significant nerve dysfunction and/or muscle atrophy and a decrease in maximum muscle force production. Muscle force production was assessed by electrical stimulation of the sciatic nerve and plantar flexor force was measured in response to a range of stimulation frequencies (10-200Hz).

Single doses of CK-2127107 increased isometric force *in situ* in response to sub-tetanic nerve stimulation in both mouse models. In the 2B/2B-Neo SMA mice, force output at a physiologically relevant sub-tetanic stimulation frequency (30Hz) was significantly increased following dosing of CK-2127107 at 10 mg/kg ($p<0.01$) and 30 mg/kg ($p<0.001$). In the Hung Li SMA mice, force output at sub-tetanic (30Hz) nerve stimulation increased with 30 mg/kg of CK-2127107 to levels higher than wild-type control mice ($p<0.001$). In both the 2B/2B Neo and Hung Li SMA mouse models there was a leftward shift of the force-frequency response curve indicating a calcium sensitizing effect of CK-2127107 in the skeletal muscle of these mouse models of SMA with nerve dysfunction and muscle atrophy. These results suggest that CK-2127107 and other FSTAs may be viable therapeutics for improving muscle function in SMA.

About SMA
SMA is a severe neuromuscular disease that occurs in 1 in every 6,000 to 10,000 live births each year and is one of the most common fatal genetic disorders. Spinal muscular atrophy manifests in various degrees of severity as progressive muscle weakness resulting in respiratory and mobility impairment. There are four types of SMA, named for age of initial onset of muscle weakness and related symptoms: Type I (Infantile), Type II (Intermediate), Type III (Juvenile) and Type IV (Adult onset). Life expectancy and disease severity vary by type of SMA. Type I patients have the worst prognosis, with a life expectancy of no more than 2 years; Type IV patients have a normal life span but eventually suffer gradual weakness in the proximal muscles of the extremities resulting in mobility issues. Few treatment options exist for these patients, resulting in a high unmet need for new therapeutic options to address symptoms and modify disease progression.

About CK-2127107
Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction. It is a highly ordered cytoskeletal structure composed of several key proteins. Skeletal muscle myosin is the cytoskeletal motor protein that converts chemical energy into mechanical force through its interaction with actin. A set of regulatory proteins, which includes tropomyosin and several types of troponin, make the actin-myosin interaction dependent on changes in intracellular calcium levels. CK-2127107, a novel skeletal muscle activator arising from Cytokinetics' skeletal muscle contractility program, slows the rate of calcium release from the regulatory troponin complex of fast skeletal muscle fibers, which sensitizes the sarcomere to calcium, leading to an increase in skeletal muscle contractility. CK-2127107 has demonstrated pharmacological activity that may lead to new therapeutic options for diseases associated with muscle weakness and fatigue. In non-clinical models of SMA, a skeletal muscle activator has demonstrated increases in submaximal skeletal muscle force in response to neuronal input and delays in the onset and reductions in the degree of muscle fatigue. CK-2127107 has been the subject of five completed Phase 1 clinical trials in healthy volunteers, which evaluated safety, tolerability, bioavailability, pharmacokinetics and pharmacodynamics. In addition to the Phase 2 clinical trial in patients with SMA, Cytokinetics is collaborating with Astellas on the conduct of a Phase 2 clinical trial in patients with chronic obstructive pulmonary disease. Two additional clinical trials of CK-2127107 are planned to begin in 2017, one in patients with ALS and one in elderly subjects with limited mobility.

About Cytokinetics and Astellas Collaboration
In 2013, Astellas and Cytokinetics formed a partnership focused on the research, development, and commercialization of skeletal muscle activators. The primary objective of the collaboration is to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness. Under the collaboration, Cytokinetics exclusively licensed to Astellas rights to co-develop and potentially co-commercialize CK-2127107, a FSTA, in non-neuromuscular indications. In 2014, Astellas and Cytokinetics agreed to expand the collaboration to include certain neuromuscular indications, including spinal muscular atrophy (SMA), and to advance CK-2127107 into Phase 2 clinical development, initially in SMA. The agreement was further amended in 2016 to provide Astellas exclusive rights to co-develop and commercialize CK-2127107 and other FSTAs in non-neuromuscular indications and certain neuromuscular indications (including SMA and ALS) and other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics' development and commercialization rights; Cytokinetics may co-promote and conduct certain commercial activities in North America and Europe under agreed scenarios.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators 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 increase muscle function and contractility. Cytokinetics' lead drug candidate is *tirasemtiv*, a fast skeletal troponin activator (FSTA). *Tirasemtiv* is the subject of VITALITY-ALS, an international Phase 3 clinical trial in patients with ALS. *Tirasemtiv* has been granted orphan drug designation and fast track status by the U.S. Food

and Drug Administration and orphan medicinal product designation by the European Medicines Agency. Cytokinetics is preparing for the potential commercialization of *tirasemtiv* in North America and Europe and has granted an option to Astellas Pharma Inc. for development and commercialization in other countries. Cytokinetics is collaborating with Astellas to develop CK-2127107, a next-generation fast skeletal muscle activator. CK-2127107 is the subject of two ongoing Phase 2 clinical trials enrolling patients with spinal muscular atrophy and chronic obstructive pulmonary disease. Cytokinetics is collaborating with Amgen Inc. 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. Astellas holds an exclusive worldwide license to develop and commercialize CK-2127107. Licenses held by Amgen and Astellas are subject to Cytokinetics' specified co-development and co-commercialization rights. For additional information about Cytokinetics, visit http://www.cytokinetics.com/.

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 Cytokinetics' and its partners' research and development activities; the design, results, significance and utility of preclinical study 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, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results, 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, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for CK-2127107; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; 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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