New Publication Summarizes Phase 1 Studies of CK-2127107 Showing Tolerability and Amplification of Skeletal Muscle Response to Nerve Activation

November 30, 2017 12:30 PM EST

Next Generation Fast Skeletal Muscle Activator Appears Promising Compared to *Tirasemtiv* in Studies of Healthy Volunteers

SOUTH SAN FRANCISCO, Calif., Nov. 30, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq:CYTK) today announced the publication of results from three double-blind, randomized, placebo-controlled Phase 1 clinical studies that evaluated safety, tolerability, pharmacokinetics, and pharmacodynamics of CK-2127107, an investigational next-generation fast skeletal muscle troponin activator (FSTA). The results showed that CK-2127107 increased the force generated by the tibialis anterior muscle versus placebo in response to nerve stimulation in a dose, plasma concentration, and frequency-dependent manner. Single doses of CK-2127107 were well-tolerated in healthy volunteers at doses up to 4000 mg. No serious adverse effects (SAEs) were reported and adverse effects (AEs) were all mild or moderate. Additionally, the results showed that CK-2127107 appeared more potent and produced a larger increase in force than *tirasemtiv* which was evaluated in a comparable study.[1] The publication, titled "CK-2127107 Amplifies Skeletal Muscle Response to Nerve Activation in Humans," is published online in *Muscle & Nerve.*[2]

"These published results reinforce CK-2127107 as a promising drug candidate with potential advantages relative to *tirasemtiv* that may include tolerability and potency," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President of Research & Development. "We look forward to the results from four ongoing mid-stage clinical trials of CK-2127107 anticipated in 2018."

CY 5011 was a single ascending dose crossover clinical trial that evaluated the safety, tolerability and pharmacokinetics of single doses of CK-2127107 in 35 healthy male participants. Participants received two ascending, active doses and one placebo dose, one in each of three treatment periods. CK-2127107 was well tolerated at all dose levels ranging from 30 mg to 4000 mg. A maximum tolerated dose was not achieved. All AEs were mild or moderate, and no clinically meaningful changes from baseline were observed in the neurological examination, walk test, laboratory values, vital signs, ECG parameters or pulse oximetry. Exposure to CK-2127107 increased approximately dose proportionally.

CY 5012 was a multiple ascending dose, parallel group clinical trial that evaluated the safety, tolerability and pharmacokinetics of CK-2127107 in male and female healthy volunteers. The clinical trial enrolled 59 young (aged 18-55) and elderly (aged 65-85) participants. Three cohorts enrolled young participants and two enrolled elderly participants; four cohorts received 300 mg or 500 mg for 10 days and one cohort received 500 mg for 17 days. CK-2127107 was generally well-tolerated at all doses administered, and all AEs were mild or moderate. No other clinically meaningful changes from baseline were observed in other laboratory values, neurological examination, vital signs, or ECG parameters, and there were no clinically meaningful differences in pharmacokinetics of CK-2127107 between young and elderly participants. Steady state was achieved in elderly participants dosed with 300 mg for 10 days and young participants taking 500 mg for 17 days.

CY 5013 was a single-dose, four-period crossover clinical trial of CK-2127107 in 16 healthy male participants that evaluated the change in the force-frequency profile of the tibialis anterior muscle during transcutaneous stimulation of the deep fibular nerve and its relationship to dose and plasma concentrations of CK-2127107. Participants received placebo, 300 mg, 1000 mg and 3000 mg single doses in random order administered one week apart. Single doses were well-tolerated and all AEs were mild or moderate. CK-2127107 increased the response of the tibialis anterior muscle to neuronal input as dose and plasma concentration increased. The overall largest increase from baseline in peak force, compared to placebo, was 58.7 (10.2)% (least-squares mean [SE]) occurring at a stimulation frequency of 10 Hz. For comparison, the largest response *tirasemtiv* produced in a comparable study was a 24.5 (3.1)% increase in peak force at 10 Hz.[1] The effect of CK-2127107 on the force-frequency relationship was also related to the stimulation frequency, being greatest at approximately the rate that motor units typically discharge during daily physical activity.

These results suggest that by directly increasing skeletal muscle force production, with maximal effects in the middle of the 5 to 15 Hz range where most normal daily human muscle activity occurs[3,4], CK-2127107 may have an effect on physical performance in patients with neuromuscular and non-neuromuscular diseases in which weakness and fatigue are the result of reduced skeletal muscle force production. Furthermore, the results show that compared to the first-generation FSTA *tirasemtiv,* CK-2127107 may be more potent and produce larger increases in force.

About CK-2127107

CK-2127107 is an investigational next-generation FSTA arising from Cytokinetics' skeletal muscle contractility program. CK-2127107 was derived from a different chemical structural class and was designed to have certain advantages relative to *tirasemtiv*. CK-2127107 appears to be more potent than *tirasemtiv* in preclinical models and in humans and appears better tolerated compared to *tirasemtiv* in comparable Phase 1 studies. CK-2127107 has demonstrated pharmacological activity that CK-2127107 has demonstrated pharmacological activity that may lead to new therapeutic options for diseases associated with muscle weakness and fatigue. CK-2127107 has been the subject of five completed Phase 1 clinical trials in healthy volunteers, which evaluated the safety, tolerability, bioavailability, pharmacokinetics and pharmacodynamics of the drug candidate. CK-2127107 is the subject of an ongoing clinical development program in neuromuscular and non-neuromuscular diseases and conditions associated with muscle dysfunction and weakness, including three Phase 2 trials currently underway in patients with each of spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), or chronic obstructive pulmonary disease (COPD), as well as a Phase 1b trial in elderly subjects with limited mobility.

About Cytokinetics and Astellas Collaboration

Cytokinetics and Astellas collaborate 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. Cytokinetics has licensed to Astellas exclusive rights to 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 is collaborating with Astellas Pharma Inc. ("Astellas") to develop CK-2127107, a next-generation FSTA. CK-2127107 has been granted orphan drug designation by the FDA for the potential treatment of SMA. CK-2127107 is the subject of three ongoing Phase 2 clinical trials enrolling patients with spinal muscular atrophy, chronic obstructive pulmonary disease and ALS. Astellas is also conducting a Phase 1b clinical trial of CK-2127107 in elderly adults with limited mobility. Astellas holds an exclusive worldwide license to develop and commercialize CK-2127107. 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. Licenses held by Amgen and Astellas are subject to Cytokinetics' specified co-development and co-commercialization rights. For additional information about Cytokinetics, visit 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, including our continuing review and assessment related to the results from VITALITY-ALS, our evaluation, in consultation with the FDA and other regulatory authorities of future development plans for *tirasemtiv* and the process and timing of anticipated future development of *tirasemtiv*; the design, results, significance and utility of preclinical study results; and the properties and potential benefits of CK-2127107 and Cytokinetics' other 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.

References

1. Hansen R, Saikali KG, Chou W, Russell AJ, Chen MM, Vijayakumar V, Stoltz RR, Baudry S, Enoka RM, Morgans DJ, Wolff AA, Malik FI. *Tirasemtiv* amplifies skeletal muscle response to nerve activation in humans. Muscle & Nerve. 2014 Dec;50(6):925-31.
2. Andrews JA, Miller TM, Vijayakumar V, Stoltz R, James JK, Meng L, Wolff AA, Malik FI. CK-2127107 amplifies skeletal muscle response to nerve activation in humans. Muscle & Nerve. 2017 Nov 18.
3. Person RS, Kudina LP. Discharge frequency and discharge pattern of human motor units during voluntary contraction of muscle. Electroencephalography and clinical neurophysiology. 1972;32(5):471-483.
4. Tanji J, Kato M. Firing rate of individual motor units in voluntary contraction of abductor digiti minimi muscle in man. Experimental neurology. 1973;40(3):771-783.

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

Cytokinetics

Source: Cytokinetics, Incorporated