Cytokinetics Announces Start of FORTITUDE-ALS, a Phase 2 Clinical Trial of CK-2127107 in Patients With Amyotrophic Lateral Sclerosis

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SOUTH SAN FRANCISCO, Calif., July 27, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq:CYTK) today announced the start of FORTITUDE-ALS, **F**unctional **O**utcomes in a **R**andomized **T**rial of **I**nvestigational **T**reatment with CK-2127107 to **U**nderstand **D**ecline in **E**ndpoints – in ALS.

The Phase 2 clinical trial, now open to enrollment, is designed to assess the change from baseline in the percent predicted slow vital capacity (SVC) and other measures of skeletal muscle function after 12 weeks of treatment with CK-2127107. In collaboration with Astellas Pharma Inc. (TSE:4503) ("Astellas"), Cytokinetics is developing CK-2127107, a next-generation fast skeletal muscle troponin activator (FSTA), as a potential treatment for people living with debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue.

"Starting FORTITUDE-ALS reflects our increased commitment to explore the potential of our muscle-biology directed investigational therapies for the potential treatment of people with ALS," said Fady I. Malik, MD, PhD, Cytokinetics' Executive Vice President of Research & Development. "Under our collaboration with Astellas, we look forward to now exploring the potential of this next-generation FSTA in a fourth patient population in which it may alter the decline of muscle function and performance. This clinical trial offers an opportunity to assess exploratory measures of patient function that may also prove informative in further quantifying ALS disease progression."

Phase 2 Clinical Trial Design

FORTITUDE-ALS is a Phase 2, double-blind, randomized, placebo-controlled, parallel group, dose ranging study of CK-2127107 in patients with ALS. Approximately 450 eligible ALS patients from centers in the U.S. and Canada will be randomized (1:1:1:1) to receive either 150 mg, 300 mg or 450 mg of CK-2127107 dosed orally twice daily or placebo for 12 weeks. The primary efficacy endpoint is the change from baseline in the percent predicted SVC at 12 weeks. Secondary endpoints include slope of the change from baseline in the mega-score of muscle strength measured by hand held dynamometry (HHD) and handgrip dynamometry in patients on CK-2127107; change from baseline in the ALS Functional Rating Scale – Revised (ALSFRS-R); incidence and severity of treatment-emergent adverse events (TEAEs); and plasma concentrations of CK-2127107 at the sampled time points during the study.

In addition, exploratory endpoints will be measured including the effect of CK-2127107 versus placebo on self-assessments of respiratory function made at home by the patient with help as needed by the caregiver; disease progression through quantitative measurement of speech production characteristics over time; disease progression through quantitative measurement of handwriting abilities over time; and change from baseline in quality of life (as measured by the ALSAQ-5) in patients on CK-2127107.

Additional information about FORTITUDE-ALS can be found at clinicaltrials.gov.

About ALS

ALS is a progressive neurodegenerative disease that afflicts approximately 30,000 people in the United States and a comparable number of patients in Europe. Approximately 6,000 new cases of ALS are diagnosed each year in the United States. The average life expectancy of an ALS patient is approximately three to five years after diagnosis and only approximately 10 percent of patients survive for more than 10 years. Death is usually due to respiratory failure because of diminished strength in the skeletal muscles responsible for breathing. Few treatment options exist for these patients, resulting in a high unmet need for new therapies to address functional deficits and disease progression.

About Vital Capacity and Disease Progression in ALS

Vital capacity is a measure used in the management of ALS to assess the strength of respiratory muscles and, as a predictor of disease progression and survival, is used in clinical practice to make intervention decisions. Vital capacity can be measured via slow vital capacity (SVC) or forced vital capacity (FVC). SVC may be easier to perform in patients with bulbar and advanced disease. Vital capacity measures the amount of air expelled from the lungs after a maximum inhalation and is used to assess the strength of the skeletal muscles responsible for breathing (e.g., the diaphragm). Vital capacity is often expressed in terms of the percentage of the normal value predicted for the individual patient's sex, age, and height; i.e., percent predicted vital capacity. Percent predicted vital capacity declines an average of 2-3 percentage points per month in patients with ALS and is the most frequently monitored measure of respiratory function to measure disease progression. Vital capacity is also used to inform critical clinical decisions, such as initiation of non-invasive ventilation, feeding tube placement and palliative care.

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 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 next-generation fast skeletal muscle troponin activator (FSTA) 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 and power in response to neuronal input and delays in the onset and reductions in the degree of muscle fatigue. CK-2127107 has been granted orphan drug designation by the U.S. Food and Drug Administration (FDA) for the potential treatment of SMA. 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. In addition to the Phase 2 clinical trial in patients with ALS, Cytokinetics is conducting a Phase 2 clinical trial in patients with SMA and Astellas is conducting a Phase 2 clinical trial in patients with COPD, as well as a Phase 1b clinical 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' lead drug candidate is *tirasemtiv*, a fast skeletal muscle 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 for the potential treatment of ALS. Cytokinetics is preparing for the potential commercialization of *tirasemtiv* in North America and Europe and has granted an option to Astellas Pharma Inc. ("Astellas") for development and commercialization in other countries. Cytokinetics is collaborating with 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. An additional phase 1b clinical trial is being conducted in elderly subjects with limited mobility. 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. 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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