Cytokinetics Announces Receipt of FDA Feedback Regarding Reldesemtiv in Patients With SMA

January 22, 2019 12:30 PM EST

Six Minute Walk Test Acceptable as Primary Efficacy Endpoint for Potential Registration Program

SOUTH SAN FRANCISCO, Calif., Jan. 22, 2019 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that it has received feedback from the U.S. Food and Drug Administration (FDA) that the Six Minute Walk Test (6MWT) is an acceptable primary efficacy endpoint for a potential registration program for *reldesemtiv* in patients with spinal muscular atrophy (SMA) who have maintained ambulatory function. The FDA also recommended adding a global function scale as a secondary endpoint, such as the Hammersmith Functional Motor Scale – Expanded (HFMSE). In collaboration with Astellas, Cytokinetics is developing *reldesemtiv* as a potential treatment for people with SMA and certain other debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue. The companies are discussing potential next steps regarding the ongoing development program for *reldesemtiv* in this patient population.

Results from a Phase 2 clinical study of *reldesemtiv* in patients with SMA showed a statistically significant exposure-response relationship in changes from baseline in Six Minute Walk Distance (6MWD), a sub-maximal exercise test of aerobic capacity and endurance. The study also showed statistically significant increases for Maximal Expiratory Pressure (MEP), a measure of strength of respiratory muscles. Other assessments, including the HFMSE, did not demonstrate differences between *reldesemtiv* versus placebo. Adverse events in the Phase 2 study in patients with SMA were similar between treatment groups receiving *reldesemtiv* and placebo.

Cytokinetics is preparing to conduct an additional Phase 1 study of *reldesemtiv* in healthy volunteers designed to assess whether higher doses than were evaluated in the Phase 2 study of patients with SMA may result in higher plasma concentrations. This study is expected to begin in the first quarter.

Cytokinetics recently announced the completion of patient enrollment in 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**), a Phase 2 clinical trial 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 *reldesemtiv* (formerly CK-2127107). Results are expected in the first half of 2019.

About *Reldesemtiv*

Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction and 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. *Reldesemtiv*, 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. *Reldesemtiv* 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. *Reldesemtiv* 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 study in patients with SMA, Cytokinetics is conducting FORTITUDE-ALS, a Phase 2 clinical trial of *reldesemtiv* in patients with ALS.

About SMA

SMA is a severe, genetic neuromuscular disease that leads to debilitating muscle function and progressive, often fatal, muscle weakness. It occurs in 1 in 6,000 to 10,000 live births each year and is one of the most common potentially 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 1 (Infantile), Type 2 (Intermediate), Type 3 (Juvenile) and Type 4 (Adult onset). Of the prevalent population, approximately 80% of the patients are characterized as Type 2 and Type 3. 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 two years; Type 2 patients have delayed motor milestones with the most advanced milestone normally achieved being sitting unsupported; Type 3 patients can usually stand and walk but have increasingly limited mobility as their abilities regress as they age; Type 4 patients may have a normal life span but eventually suffer gradual weakness in the proximal muscles of the extremities, eventually resulting in mobility issues. With the recent introduction of gene modifying therapies, it is expected that patients may live longer but will still have a significant need to address ongoing disabilities related to respiration and mobility. Approximately 50% of Type 3 patients with SMA are believed to maintain ambulatory function today and an increasing number of Type 2 patients with SMA are expected to remain ambulatory with the advent of complementary new therapies that can enable motor milestones. Over the next 5 years, the prevalence of ambulatory adolescents and adults with SMA may exceed 5-10,000 patients in the United States alone.

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 *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA), in non-neuromuscular indications. In 2014, Astellas and Cytokinetics agreed to expand the collaboration to include certain neuromuscular indications, including SMA, and to advance *reldesemtiv* into Phase 2 clinical development, initially in SMA. Under the agreement as further amended in 2016, Astellas has exclusive rights to co-develop and commercialize *reldesemtiv* 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 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 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 Cytokinetics' and its partners' research and development activities, including the Phase 2 clinical study of *reldesemtiv* in patients with SMA and its potentially beneficial effects; 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; Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*; 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.

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

Source: Cytokinetics, Incorporated