Cytokinetics Announces Start of Phase 3 Clinical Trial of Tirasemtiv in Patients With ALS

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VITALITY-ALS is Designed to Confirm and Extend Results Observed in Phase 2b Trial

SOUTH SAN FRANCISCO, Calif., July 14, 2015 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK), a leading muscle biology company, today announced the start of VITALITY-ALS (Ventilatory Investigation of *Tirasemtiv* and Assessment of Longitudinal Indices after Treatment for a Year in ALS), a Phase 3 clinical trial designed to assess the effects of *tirasemtiv* versus placebo on slow vital capacity (SVC) and other measures of respiratory function in patients with ALS.

“Beginning VITALITY-ALS is a significant milestone for our company and demonstrates our commitment to people living with ALS who desperately need new medicines,” said Robert I. Blum, Cytokinetics’ President and Chief Executive Officer. “We look forward to working closely with clinical trial investigators, study coordinators and the ALS community as we advance the development of *tirasemtiv,* the first muscle-based pharmaceutical therapy with the potential to impact muscle force and function.”

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. It has been shown to be an important predictor of disease progression and survival in previous clinical trials in patients with ALS who typically die of respiratory failure. 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. *Tirasemtiv*, a fast skeletal muscle troponin activator, demonstrated a statistically significant and potentially clinically meaningful effect on respiratory function (as assessed by SVC) and muscle strength in the Phase 2b clinical trial, BENEFIT-ALS.

“The start of VITALITY-ALS is a defining moment for the potential treatment of this devastating neuromuscular disease,” said Jeremy Shefner, M.D., Ph.D., Lead Investigator of VITALITY-ALS, Professor and Chair of Neurology at Barrow Neurological Institute, and Professor and Executive Chair of Neurology at University of Arizona, Phoenix. “Many key clinical decisions pivot on a patient’s breathing function, as typically measured by vital capacity. This clinical trial will determine the impact *tirasemtiv* may have on this critical measure and other clinically meaningful measures of respiratory function as well as on muscle strength and performance in patients with ALS.”

About VITALITY-ALS

VITALITY-ALS is a multi-national, randomized, double-blind, placebo-controlled trial that is designed to enroll 445 patients with possible, probable or definite ALS, diagnosed within 24 months, and with percent predicted SVC at baseline ≥ 70%. Patients may be enrolled whether or not they are on *riluzole* therapy. The primary endpoint of the trial will assess change from baseline in SVC, to be assessed after 24 weeks of double-blind, placebo-controlled treatment. Secondary endpoints, to be assessed at 48 weeks, include time to decline in any of the three respiratory domains of the ALSFRS-R or death; time to decline from baseline in percent predicted SVC by ≥ 20 percentage points or the onset of respiratory insufficiency or death; time to first occurrence of any use of assisted ventilation or death; time to decline from baseline in percent predicted SVC to ≤ 50 percent predicted or the onset of respiratory insufficiency or death; and change in the Mega-Score of muscle strength. Patients enrolled in VITALITY-ALS will receive two-weeks of open-label treatment with *tirasemtiv* administered at 250 mg/day. Patients will then be randomized into a double-blind treatment phase to placebo or one of three target *tirasemtiv* dose levels (250 mg/day, 375 mg/day, 500 mg/day) in a 3:2:2:2 ratio. After 48 weeks of randomized, double-blind, placebo-controlled treatment, patients will be re-randomized to continue the treatment they received for the past 48 weeks or to placebo for a four-week double-blind, *tirasemtiv* withdrawal phase. VITALITY-ALS is expected to be conducted in more than 75 centers in North America and Europe. For additional information, please visit www.clinicaltrials.gov.

About Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that afflicts approximately 25,000 people in the United States and a comparable number of patients in Europe. Approximately 5,600 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 10% 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 therapeutic options to address the symptoms and to modify the disease progression of this grievous illness.

About *Tirasemtiv*

Tirasemtiv, a novel skeletal muscle activator, selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium and, in preclinical studies and early clinical trials, demonstrated increases in skeletal muscle force in response to neuronal input and delays in the onset and reductions in the degree of muscle fatigue. *Tirasemtiv* has been studied in clinical trials that have enrolled over 1000 people internationally. In a recently completed Phase 2b clinical trial, *tirasemtiv* reduced the decline of slow vital capacity, a key measure of respiratory function in patients with ALS. *Tirasemtiv* is the subject of a Phase 3 clinical trial program designed to confirm and extend findings from prior studies.

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. With an unmatched understanding of muscle biology and 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 activator, for the potential treatment of 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 holds the exclusive right to develop and commercialize *tirasemtiv* throughout the world. Cytokinetics is collaborating with Amgen Inc. to develop *omecamtiv mecarbil*, a novel cardiac muscle activator, for the potential treatment of heart failure. Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a fast skeletal muscle activator, for the potential treatment of spinal muscular atrophy. Amgen holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and Astellas holds an exclusive license worldwide to develop and commercialize CK-2127107. Both licenses are subject to Cytokinetics' specified

development and commercialization participation 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, including the conduct, design, enrollment and progress of VITALITY-ALS and other clinical trials; the significance and utility of preclinical study and clinical trial results; and the properties and potential efficacy and safety profile of tirasemtiv 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, further clinical development of tirasemtiv in ALS patients will require significant additional funding, and Cytokinetics may be unable to obtain such additional funding on acceptable terms, if at all; the FDA and/or other regulatory authorities may not accept effects on slow vital capacity as a clinical endpoint to support registration of tirasemtiv for the treatment of ALS; 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 U.S. Food and Drug Administration 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; Amgen's and Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil and CK-2127107, respectively; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; Cytokinetics may be unable to enter into future collaboration agreements for its drug candidates and programs on acceptable terms, if at all; 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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