Cytokinetics Announces Presentation of Results From VITALITY-ALS at 28th International Symposium on ALS/MND

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Previously Announced Results from Phase 3 Clinical Trial of Tirasemtiv Shared with ALS Community

VITALITY-ALS Did Not Meet Primary or Secondary Endpoints

Trial Informs Development of Next Generation Drug Candidate

SOUTH SAN FRANCISCO, Calif., Dec. 08, 2017 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq:CYTK) today announced the presentation of results from VITALITY-ALS (**V**entilatory **I**nvestigation of ***T****irasemtiv* and **A**ssessment of **L**ongitudinal **I**ndices after **T**reatment for a **Y**ear in **ALS**), the international Phase 3 clinical trial of *tirasemtiv* in patients with amyotrophic lateral sclerosis (ALS), at the 28th International Symposium on ALS and Motor Neurone Disease (MND) in Boston. This presentation follows a prior announcement that the trial did not meet the primary endpoint of change from baseline in slow vital capacity (SVC) which was evaluated at 24 weeks following randomization or any of the secondary endpoints in the trial which were evaluated at 48 weeks. The results were presented by 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.

"Although we are profoundly disappointed with these results, we believe that data from VITALITY-ALS provide validation for the mechanism of action of fast skeletal muscle troponin activation. The effects of *tirasemtiv* observed in patients with ALS support the future development of CK-2127107, our next-generation fast skeletal muscle troponin activator which is the subject of FORTITUDE-ALS, our ongoing Phase 2 clinical trial in patients with ALS," said Robert I. Blum, Cytokinetics' President and CEO. "As recently published Phase 1 studies demonstrate, CK-2127107 may be more effective and better tolerated than *tirasemtiv*. We are humbled by the outpouring of support we have received from the ALS community and will continue our search for a potential therapy to slow the progressive respiratory decline and muscle weakness which characterize this dreadful disease."

"VITALITY-ALS did not achieve our pre-specified objectives which included improving tolerability in ALS patients by altering the dosing of *tirasemtiv*," said Dr. Shefner. "The increased numbers of non-serious adverse effects and drop-outs in patients who received *tirasemtiv* confound our ability to evaluate efficacy and safety in the primary analyses of VITALITY-ALS. Additional analyses of patients able to tolerate *tirasemtiv* suggest slowing of the decline in SVC, providing support for the continued investigation of fast skeletal muscle troponin activators in patients with ALS."

VITALITY-ALS randomized patients to placebo and three target doses of *tirasemtiv* (250, 375, and 500 mg/day) in a 3:2:2:2 ratio. The primary analysis was an intent to treat analysis of the dose groups of *tirasemtiv* pooled together and compared to placebo. The least squares mean change from baseline in percent predicted SVC was -13.4 percentage points in the patients randomized to *tirasemtiv* compared to -14.4 percentage points in those randomized to placebo. The least squares mean difference from baseline to 24 weeks between *tirasemtiv* and placebo was 0.92 percentage points (p=0.5552). In a pre-specified analysis of the average daily maintenance dose of *tirasemtiv* actually taken (rather than as randomized), patients who completed VITALITY-ALS at the highest average daily dose of *tirasemtiv* (> 437.5 mg/day), experienced the largest difference from placebo in change from baseline to 24 weeks in percent predicted SVC, although the difference was not statistically significant (least squares mean difference from placebo: 4.57, p=0.107). VITALITY-ALS did not meet any of the pre-specified secondary endpoints which were evaluated at 48 weeks.

Of the 565 randomized patients who received double-blind treatment in the trial, 188 received placebo and 377 received *tirasemtiv*. 165 (87.8 percent) of patients on placebo completed 24 weeks of treatment, while 248 (65.8 percent) of patients on *tirasemtiv* completed 24 weeks of treatment.

Serious adverse events in patients receiving *tirasemtiv* were consistent with disease progression of ALS with no meaningful differences from placebo. Mortality was also similar in patients receiving *tirasemtiv* and placebo. No new safety or tolerability findings related to *tirasemtiv* were identified in VITALITY-ALS. The adverse events with the greatest differences in frequency between patients receiving *tirasemtiv* and those on placebo were dizziness, weight decrease, insomnia, fatigue and nausea, consistent with the adverse event profile of *tirasemtiv* observed in Phase 2.

About VITALITY-ALS and VIGOR-ALS

VITALITY-ALS was a multi-national, randomized, double-blind, placebo-controlled trial in patients with possible, probable or definite ALS, diagnosed within 24 months, and with SVC at baseline ≥ 70 percent predicted. The primary endpoint of the trial assessed change from baseline in SVC after 24 weeks of double-blind, placebo-controlled treatment. Secondary endpoints, assessed at 48 weeks, included change from baseline in the score of the three respiratory items of the ALSFRS-R (i.e., the sum of items 10, 11 and 12) at 48 weeks; slope of the mega-score of muscle strength at 48 weeks; time to the first occurrence of a decline from baseline in percent predicted SVC ≥20 percentage points or the onset of respiratory insufficiency or death through 48 weeks; time to the first occurrence of a decline in SVC to ≤50 percent predicted or the onset of respiratory insufficiency or death through 48 weeks; change from baseline in the ALSFRS-R total score at 48 weeks; and time to the first use of mechanical ventilatory assistance or death through 48 weeks. Patients enrolled in VITALITY-ALS received two-weeks of open-label treatment with *tirasemtiv* administered at 250 mg/day. Patients were then 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 who received *tirasemtiv* during those 48 weeks of double-blind treatment were randomized to continue the dose of *tirasemtiv* at which they completed the 48 weeks of double-blind treatment or to placebo for a four-week double-blind, *tirasemtiv* withdrawal phase. Patients who received placebo during the 48 weeks of double-blind treatment continued to receive placebo during the double-blind, *tirasemtiv* withdrawal phase.

Following their participation in VITALITY-ALS, patients were eligible to participate in an open-label extension study of *tirasemtiv*, VIGOR-ALS (**V**entilatory **I**nvestigations in **G**lobal **O**pen-label **R**esearch in **ALS**), designed to assess the long-term safety and tolerability of *tirasemtiv* in patients with ALS. Cytokinetics will seek advice from the academic leadership of VITALITY-ALS and its clinical investigators, regulatory authorities and other consultants before making decisions about continuing treatment with *tirasemtiv* in VIGOR-ALS.

About ALS

Amyotrophic lateral sclerosis (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 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 *Tirasemtiv* and CK-2127107

Tirasemtiv is a fast skeletal muscle troponin activator (FSTA) that 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 1500 people internationally.

CK-2127107 is a next-generation FSTA 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*. 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 SMA, ALS, or COPD, as well as a Phase 1b trial in elderly subjects with limited mobility.

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 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 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. 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 including FORTITUDE-ALS; 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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