



Cytokinetics Announces Continuation of COURAGE-ALS Following First Interim Analysis

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Phase 3 Clinical Trial to Proceed to Second Interim Analysis Expected to Occur in 2023

SOUTH SAN FRANCISCO, Calif., Oct. 10, 2022 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the Data Monitoring Committee (DMC) for COURAGE-ALS (Clinical Outcomes Using *reldesemtiv* on ALSFRS-R in a Global Evaluation in ALS), recently convened to conduct the first planned interim analysis of this ongoing Phase 3 clinical trial which assessed for the potential of futility. The DMC reviewed unblinded data from COURAGE-ALS and recommended that conduct of the clinical trial of *reldesemtiv* continue. *Reldesemtiv* is a fast skeletal muscle troponin activator (FSTA) in clinical development for the potential treatment of amyotrophic lateral sclerosis (ALS).

The first interim analysis was triggered 12 weeks after approximately one-third or more of the intended number of patients were randomized to participate in COURAGE-ALS. A second interim analysis, which is anticipated to occur in the first half of next year, will also assess for potential futility and will also allow for a fixed increase in total enrollment, if deemed necessary, to augment the statistical power of the trial.

COURAGE-ALS & COURAGE-ALS OLE: Trial Design

COURAGE-ALS, a Phase 3, multi-center, double-blind, randomized, placebo-controlled trial of *reldesemtiv*, is expected to enroll approximately 555 patients with ALS. Patients are randomized 2:1 to receive 300 mg of *reldesemtiv* or matching placebo dosed orally twice daily for 24 weeks, followed by a 24-week period in which all patients will receive 300 mg of *reldesemtiv* twice daily. Eligible patients are within the first two years of their first symptom of muscle weakness, have a vital capacity of $\geq 65\%$ predicted, and a screening ALS Functional Rating Scale – Revised (ALSFRS-R) ≤ 44 . Patients currently taking stable doses of Radicava® (*edaravone*) and/or Rilutek® (*riluzole*) are permitted to enroll, and randomization is stratified accordingly. The primary efficacy endpoint is change from baseline to 24 weeks in ALSFRS-R. Secondary endpoints include combined assessment of ALSFRS-R total score, time to onset of respiratory insufficiency and survival time up to week 24 using a joint rank test; change from baseline to 24 weeks for vital capacity; ALSAQ-40; and bilateral handgrip strength. Two unblinded interim analyses by the Data Monitoring Committee are planned. The first interim analysis assessed for futility, 12 weeks after approximately one-third or more of the planned sample size is randomized. A second interim analysis will also assess for futility and there will also be an option for a fixed increase in total enrollment, if deemed necessary, to augment the statistical power of the trial.

An open-label extension trial, COURAGE-ALS OLE, is open to people who have completed participation in COURAGE-ALS. Following enrollment in COURAGE-ALS OLE, participants continue to receive 300 mg of *reldesemtiv* dosed orally twice daily for 48 weeks after which they may transition into the Managed Access Program. The primary endpoint is the incidence of adverse events. Secondary endpoints include the time to the first occurrence of respiratory insufficiency or death, time to the first hospitalization, combined assessment of change in ALSFRS-R total score, time to onset of respiratory insufficiency, and survival time, changes in ALSFRS-R total score, and the slope of changes in ALSFRS-R total score. Additional information on COURAGE-ALS OLE can be found at www.clinicaltrials.gov.

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 the troponin complex, make the actin-myosin interaction dependent on changes in intracellular calcium levels. *Reldesemtiv* is an investigational, selective, small molecule fast skeletal muscle troponin activator (FSTA) arising from Cytokinetics' skeletal muscle contractility program. *Reldesemtiv* was designed to slow 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.

The development program for *reldesemtiv* is assessing its potential for the treatment of ALS and includes FORTITUDE-ALS, a completed Phase 2 trial, and COURAGE-ALS, the ongoing Phase 3 clinical trial designed to evaluate the effect of treatment with *reldesemtiv* compared to placebo on measures of disease progression, functional outcomes and survival.

About ALS

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that afflicts approximately 27,000 people in the United States and a comparable number of patients in Europe. Approximately 6,300 new cases of ALS are diagnosed each year in the United States. The average life expectancy of a person with ALS is approximately three to five years after diagnosis and only approximately 10 percent of people with ALS 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 Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and next-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised. 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 readying for the potential commercialization of *omecamtiv mecarbil*, its cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is also developing *aficamten*, a next-generation cardiac myosin inhibitor, currently the subject of SEQUOIA-HCM, the Phase 3 clinical trial of *aficamten* in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). *Aficamten* is also being evaluated in non-obstructive HCM in Cohort 4 of the Phase 2 clinical trial, REDWOOD-HCM. Cytokinetics is also developing *reldesemtiv*, an investigational fast skeletal muscle troponin activator, currently the subject of COURAGE-ALS, a Phase 3 clinical trial in patients with amyotrophic lateral sclerosis (ALS). Cytokinetics continues its over 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, express or implied, relating to the interim results of COURAGE-ALS as an indicator of any final results of COURAGE-ALS or statements relating to the potential efficacy or safety of *reldesemtiv*. 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; Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the FDA or foreign regulatory agencies may delay or limit Cytokinetics' ability to conduct clinical trials; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. 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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Contact:
Cytokinetics
Diane Weiser
Senior Vice President, Corporate Communications, Investor Relations
(415) 290-7757



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