Cytokinetics Announces COURAGE-ALS Met Criteria for Futility at Second Interim Analysis

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Company Plans to Discontinue the Phase 3 Clinical Trial of Reldesemtiv
After Data Monitoring Committee Found No Effect on Primary or Key Secondary Endpoints

Cytokinetics to Host Conference Call and Webcast Today at 8:30 am Eastern Time

SOUTH SAN FRANCISCO, Calif., March 31, 2023 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the Data Monitoring Committee (DMC) for COURAGE-ALS (**C**linical **O**utcomes **U**sing ***R**eldesemtiv* on **A**LSFRS-R in a **G**lobal **E**valuation in **ALS**), recently convened to conduct the second planned interim analysis of this Phase 3 clinical trial.

The DMC reviewed unblinded data from COURAGE-ALS and recommended the discontinuation of the clinical trial due to futility, as it found no evidence of effect in patients treated with *reldesemtiv* relative to placebo on the primary endpoint of change from baseline to 24 weeks in ALSFRS-R or in key secondary endpoints. Given these results, study conduct in COURAGE-ALS will be concluding. In addition, Cytokinetics plans to discontinue treatment with *reldesemtiv* in all patients including those in the open-label extension study, COURAGE-ALS OLE.

"We are extremely disappointed with this outcome and would like to thank the people with ALS, caregivers, investigators and clinical trial staff for their participation in COURAGE-ALS," said Robert I. Blum, Cytokinetics' CEO and President. "Cytokinetics has been committed to the ALS community for more than a decade and recognizes the urgency to bring new potential medicines to the forefront for this grievous disease. In the coming months, we will assess next steps relating to our neuromuscular development programs."

The second interim analysis was triggered 24 weeks after at least one third of the planned sample size was randomized in COURAGE-ALS. At the interim analysis, approximately 460 patients had been randomized and over 200 had reached the 24-week assessment of the trial endpoints. This interim analysis assessed the primary and key secondary endpoints for potential futility as well as provided for a potential fixed increase in total enrollment, if it had been deemed necessary to augment the statistical power of the trial, or to continue the trial to its conclusion as planned. Cytokinetics intends to notify all regulatory agencies and clinical trial investigators involved in COURAGE-ALS of these interim findings. The full data set from this trial is being analyzed and more details will be presented at an upcoming medical meeting.

Conference Call and Webcast

Cytokinetics will host a conference call today, March 31, 2023 at 8:30 AM Eastern Time that will be simultaneously webcast and can be accessed from the homepage and in the Investors & Media section of Cytokinetics' website at www.cytokinetics.com. The live audio of the event can also be accessed by telephone by registering in advance at the following link: **COURAGE-ALS Update Call**. Upon registration, participants will receive a dial-in number and a unique passcode to access the call.

COURAGE-ALS & COURAGE-ALS OLE: Trial Design

COURAGE-ALS was a Phase 3, multi-center, double-blind, randomized, placebo-controlled trial of *reldesemtiv* designed to enroll approximately 555 patients with ALS. Patients were 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 received 300 mg of *reldesemtiv* twice daily. Eligible patients were within the first two years of their first symptom of muscle weakness, had a vital capacity of ≥65% predicted, and a screening ALS Functional Rating Scale – Revised (ALSFRS-R) ≤44. Patients taking stable doses of *edaravone* and/or *riluzole* were permitted to enroll, and randomization was stratified accordingly. The primary efficacy endpoint was change from baseline to 24 weeks in ALSFRS-R. Secondary endpoints included 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. The trial included two planned unblinded interim analyses conducted by the Data Monitoring Committee. The first interim analysis assessed for futility, 12 weeks after approximately one-third or more of the planned sample size were randomized. The second interim analysis assessed for futility with the option for a fixed increase in total enrollment, if it had been deemed necessary, to augment the statistical power of the trial.

An open-label extension trial, COURAGE-ALS OLE, has enrolled people who completed participation in COURAGE-ALS. In COURAGE-ALS OLE, participants received 300 mg of *reldesemtiv* dosed orally twice daily for 48 weeks after which they were eligible to transition into the Managed Access Program, a program designed to provide access to *reldesemtiv* for patients diagnosed with ALS who have completed a prior Cytokinetics clinical trial with *reldesemtiv* or *tirasemtiv*.

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* assessed its potential for the treatment of ALS and includes FORTITUDE-ALS, a completed Phase 2 trial, and COURAGE-ALS, the 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 two to four years 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 developing *aficamten*, a next-in-class 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 and the company plans to begin a Phase 3 trial later this year. Cytokinetics is also developing *omecamtiv mecarbil*, a cardiac muscle activator in patients with heart failure. In 2023, Cytokinetics is celebrating its 25-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 our future plans for our neuromuscular development programs. 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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