Cytokinetics Announces Data and Trial Design Presented at the International Symposium on ALS/MND

December 14, 2020 12:30 PM EST

Additional Data from FORTITUDE-ALS Support Rationale and Design for COURAGE-ALS, A Planned Phase 3 Clinical Trial of Reldesemtiv in Patients with ALS

SOUTH SAN FRANCISCO, Calif., Dec. 14, 2020 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that additional data relating to the impact of patient characteristics on treatment effect in FORTITUDE-ALS, the Phase 2 clinical trial of *reldesemtiv* in patients with amyotrophic lateral sclerosis (ALS), were presented at the 31st International Symposium on ALS/MND. Additionally, the company announced that the design of COURAGE-ALS (**C**linical **O**utcomes **U**sing ***R**eldesemtiv* on **A**LSFRS-R in a **G**lobal **E**valuation in **ALS**), a planned Phase 3 clinical trial of *reldesemtiv* in patients with ALS and an update on the IMPACT ALS Europe survey, a patient and caregiver survey funded in part by Cytokinetics, were also presented.

"FORTITUDE-ALS provided important insights into patient characteristics that may yield a greater potential treatment effect, namely that faster progressing patients who received *reldesemtiv* in the Phase 2 trial experienced larger reductions in disease progression," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "These additional data have informed the design of COURAGE-ALS which we hope to open to enrollment in 2021."

FORTITUDE-ALS: Effect of *Reldesemtiv* More Apparent in Faster Progressing Patients

Jeremy Shefner, M.D., Ph.D., Lead Investigator of COURAGE-ALS, Professor and Chair of Neurology at Barrow Neurological Institute, and Professor and Executive Chair of Neurology at the University of Arizona, Phoenix, presented additional post-hoc analyses from FORTITUDE-ALS, the Phase 2 clinical trial of *reldesemtiv* in patients with ALS, evaluating how baseline patient characteristics impacted the effect of treatment with *reldesemtiv* versus placebo. When patients were divided into faster, middle and slower progressing tertiles based on pre-study ALSFRS-R progression rates, the middle and fastest progressing tertiles of patients combined showed a 27% difference at 12 weeks between patients receiving *reldesemtiv* versus placebo (1.15 ALSFRS-R points, p=0.011), compared to 18% (0.4 points; p=0.43) in the slowest progressing tertile. In general, patients with a longer symptom duration were slower progressors; 59% of those with SD >24 months were in the slowest tertile. Most patients who were minimally affected with an ALSFRS-R ≥45 at baseline were also slow progressors. In comparing the treatment effect of slow progressing patients with symptoms ≤24 months and a baseline ALSFRS-R score of ≤44 to the original primary analysis population, the effect size and statistical significance increased, despite reducing the number of analyzed patients. In an analysis of the total study population (n=458), combining all patients who received *reldesemtiv* and comparing to those who received placebo, the change from baseline to week 12 in the ALSFRS-R total score showed a least square mean (LSM) difference of 0.87 (p=0.013). However, limiting the analysis population to patients with symptoms ≤24 months and a baseline ALSFRS-R score of ≤44 (n=272), the LSM difference was 1.84 (p=0.0002). Together, these post-hoc analyses indicate that the impact of treatment with *reldesemtiv* was more apparent in patients with faster pre-study rates of progression, which include patients with short symptom duration and lower baseline ALSFRS-R scores.

COURAGE-ALS: Planned Phase 3 Clinical Trial of *Reldesemtiv* in Patients with ALS

The design of COURAGE-ALS (**C**linical **O**utcomes **U**sing ***R**eldesemtiv* on **A**LSFRS-R in a **G**lobal **E**valuation in **ALS**) was also presented by Dr. Jeremy Shefner. This planned Phase 3, multi-center, double-blind, randomized, placebo-controlled clinical trial of *reldesemtiv* is expected to enroll approximately 555 patients with ALS. Patients will be 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 will be within the first two years of their first symptom of muscle weakness, have a vital capacity of ≥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)* will be permitted and randomization stratified accordingly. The primary efficacy endpoint will be 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 will assess 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 be an option for a fixed increase in total enrollment if necessary to augment the statistical power of the trial. This Phase 3 clinical trial design builds on insights gained from FORTITUDE-ALS, the Phase 2 clinical trial of *reldesemtiv* in patients with ALS, further exploring the hypothesis that fast skeletal muscle activation with *reldesemtiv* may be an important therapeutic strategy in ALS.

IMPACT ALS: European Survey of ALS Patient and Caregiver Perspectives

An overview of the ongoing IMPACT ALS Europe survey of patients and caregivers was also presented by Miriam Galvin, Ph.D., Department of Neurology, Trinity College Dublin. The survey includes patients with ALS and caregivers from nine European countries and gathered perspectives on the burden of disease and disease progression, as well as input on the drug development process. Recruitment of patients and caregivers was conducted in partnership with the European Network for the Cure of ALS (ENCALS) and advocacy groups in each country, and survey materials were adapted from materials used in the United States for a similar survey. Upon completion, statistical analysis of the data, as well as a free text analysis of open-ended responses will be conducted. The results will also be compared to the results from the survey conducted in the United States in 2017. The data from this survey will provide valuable information characterizing the patient and caregiver experience and may help inform global drug development in ALS.

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 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 preparing for regulatory interactions for *omecamtiv mecarbil*, its novel cardiac muscle activator, following positive results from GALACTIC-HF, a large, international Phase 3 clinical trial in patients with heart failure. Cytokinetics is conducting METEORIC-HF, a second Phase 3 clinical trial of *omecamtiv mecarbil*. Cytokinetics is also developing CK-274, a next- generation cardiac

myosin inhibitor, for the potential treatment of hypertrophic cardiomyopathies (HCM). Cytokinetics is conducting REDWOOD-HCM, a Phase 2 clinical trial of CK-274 in patients with obstructive HCM. Cytokinetics is also developing *reldesemtiv*, a fast skeletal muscle troponin activator for the potential treatment of ALS and other neuromuscular indications following conduct of FORTITUDE-ALS and other Phase 2 clinical trials. The company is considering potential advancement of *reldesemtiv* to Phase 3 pending ongoing regulatory interactions. 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 relating to the potential benefits of *reldesemtiv*; Cytokinetics' continued evaluation of *reldesemtiv* as a treatment for patients with ALS; and the properties and potential benefits of 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; 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
Senior Vice President, Corporate Communications, Investor Relations
(415) 290-7757

Source: Cytokinetics, Incorporated