Cytokinetics Presents Analyses Demonstrating Predictive Value of Slow Vital Capacity for Clinical Outcomes in ALS

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SOUTH SAN FRANCISCO, Calif., Jan. 10, 2016 (GLOBE NEWSWIRE) -- Cytokinetics, Inc. (Nasdaq:CYTK) today announced the presentation of exploratory analyses of data from EMPOWER, a Phase 3 clinical trial of dexpramipexole in patients with ALS, which demonstrated the rate of decline of slow vital capacity (SVC) predicts the risk of meaningful clinical events, including a decline in the three respiratory questions of the ALSFRS-R, as well as the time to the first occurrence of respiratory insufficiency, tracheostomy or death. Data from placebo-treated patients in EMPOWER were provided to Cytokinetics by Knopp Biosciences. The analyses were presented recently at the 6th Annual California ALS Research Summit in La Jolla, California.

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 2.5-3 percentage points per month in patients with ALS and is the most frequently monitored measure of respiratory function to measure disease progression.

To better understand the relationship of decline in SVC to the decline in other measures of respiratory function in ALS, investigators analyzed data from placebo-treated patients in EMPOWER, one of the largest clinical trials conducted in ALS. The objective of the study was to investigate the natural history of SVC decline to determine what demographic variables impact decline in SVC and how changes in SVC predict other clinically meaningful events in ALS.

Key findings from the analyses of data from EMPOWER include:

- The overall slope of decline in percent predicted SVC from baseline through the follow-up period of 1.5 years was -0.090 percentage points per day (2.73 percentage points per month)
- Older subjects (greater than 65) had a steeper slope of decline in SVC (-0.12 percentage points per day), as did subjects with baseline ALSFRS-R less than 39 (-0.10 percentage points per day).
- A slowing in the decline in SVC by 0.05 percentage points per day from baseline to the month 6 visit predicted reduction in risk by 19% of any decline in the respiratory subdomain of ALSFRS-R or death; by 22% for the first onset of respiratory insufficiency or death; by 23% for first occurrence of tracheostomy or death; and by 23% for death at any time after the month 6 visit ($p < 0.0001$ for all).

"These findings, derived from the placebo group of a large and well-conducted clinical trial, are consistent with prior studies and suggest there is predictive value in the rate of decline of SVC for the occurrence of clinically meaningful outcomes in ALS," said Jinsy Andrews, M.D., Cytokinetics' Senior Director, Clinical Research and Development and Head of Neuromuscular Therapeutics. "We look forward to the results of VITALITY-ALS which we hope may confirm and extend findings from BENEFIT-ALS as well as further explore a relationship between the decline of SVC and the time to clinically meaningful events associated with the loss of respiratory function in patients with ALS."

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. *Tirasemtiv* was the subject of BENEFIT-ALS a Phase 2b, multi-national, double-blind, randomized, placebo-controlled, clinical trial which enrolled 711 patients from 73 centers in 8 countries. The primary efficacy endpoint in BENEFIT-ALS, the change from baseline to the average of the ALSFRS-R total scores obtained after 8 and 12 weeks of double-blind treatment, was not statistically different between patients treated with *tirasemtiv* or placebo. Treatment with *tirasemtiv* in BENEFIT-ALS did result in a statistically significant and potentially clinically meaningful slowing of the rate of decline of SVC versus placebo; in addition, the reduction from baseline in SVC was statistically significantly smaller on *tirasemtiv* versus placebo at each time point it was assessed. The difference in the reduction from baseline in SVC in patients treated with *tirasemtiv* versus those on placebo persisted for at least four weeks following the last dose of double-blind study medication. *Tirasemtiv* is the subject of VITALITY-ALS, an ongoing Phase 3 clinical trial designed to confirm and extend findings from prior clinical trials.

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' lead drug candidate is *tirasemtiv*, a fast skeletal muscle troponin 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 retains the right to develop and commercialize *tirasemtiv*. 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, including those of EMPOWER; the acceptance by regulatory authorities of the effects of *tirasemtiv* on respiratory function, including SVC; 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 SVC 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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