Cytokinetics Announces Publication of Results from Phase II Trials of Tirasemtiv in Patients with ALS

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Manuscripts Support the Design and Conduct of the Ongoing BENEFIT-ALS Trial

South San Francisco, CA, August 22, 2013 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced the publication of two manuscripts reporting data from two clinical trials of *tirasemtiv*, a novel mechanism fast skeletal muscle troponin activator, in patients with amyotrophic lateral sclerosis (ALS). These manuscripts are published in the journal *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration* and highlight results from Phase II clinical trials designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of two different dosing regimens of *tirasemtiv*.

"These manuscripts highlight encouraging results from two prior Phase II clinical trials of *tirasemtiv* in patients with ALS," stated Jeremy M. Shefner, M.D., Ph.D., Professor and Chair, Department of Neurology at the Upstate Medical University, State University of New York, and lead author of both publications. "Activation of skeletal muscle with *tirasemtiv*, as assessed under different dosing regimens in these studies, appears to be generally well-tolerated and to impact positively tests of strength, endurance and respiratory function that may be relevant to preserving the functional status of patients with ALS. I am looking forward to the availability of additional data from the continuing development of this promising compound."

"We are pleased to have these data published in a prestigious journal dedicated to reporting significant advances in the treatment of ALS," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "Results from these trials informed our design of BENEFIT-ALS, our ongoing Phase IIb clinical trial of *tirasemtiv*, which we hope may demonstrate longer term safety and the potential durability of clinically meaningful effects of this drug candidate in patients suffering from this grievous illness."

Manuscripts Published in *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*

One manuscript, titled "A Study to Evaluate Safety and Tolerability of Repeated Doses of *Tirasemtiv* in Patients with Amyotrophic Lateral Sclerosis," reports data from two Phase II clinical trials, designated as CY 4024 and CY 4025. In these trials, *tirasemtiv* appeared to be well-tolerated by patients with ALS, including when receiving a reduced dose of *riluzole*. The trials cited in this manuscript evaluated the tolerability of *tirasemtiv* at doses up to 500 mg daily for up to three weeks. In CY 4024, *tirasemtiv* was given in single daily doses of 125 mg, 250 mg, or 375 mg versus placebo for two weeks, in one cohort without concomitant *riluzole* and in a second cohort with *riluzole* administered at a reduced dose of 50 mg once daily. In CY 4025, the dose of *tirasemtiv* was titrated over three weeks of administration, beginning with 125 mg twice daily to a target of 250 mg twice daily. Safety and tolerability were assessed, as well as measures of function, muscle strength and endurance. Results showed that *tirasemtiv* was well-tolerated in these patients, with dizziness the most common adverse event. As predicted from earlier non-clinical and clinical studies, co-administration of *tirasemtiv* with *riluzole* approximately doubled the plasma concentration of *riluzole* compared to the administration of *riluzole* without *tirasemtiv*. Trends were noted for improvement in the ALS Functional Rating Scale-Revised (ALSFRS-R), Maximum Minute Ventilation, and Sniff Nasal Inspiratory Pressure. The authors concluded that positive trends in multiple exploratory outcome measures support the further study of this drug candidate for the potential treatment of ALS.

In the second manuscript, titled "The Relationship Between *Tirasemtiv* Serum Concentration and Functional Outcomes in Patients with ALS," the authors concluded that *tirasemtiv* appears to have concentration-dependent effects on both function and measures of strength and endurance when administered for up to 21 days, even when time is eliminated as a cofactor. In addition, they reported that both single and repeated dose studies suggested potentially beneficial effects on measures of function, muscle strength and endurance. Since the outcomes measured were identical in previous Phase II clinical trials of *tirasemtiv* in patients with ALS and the duration of all the trials was 21 days or less, the authors pooled data from all the trials and assessed the relationship between outcomes and plasma concentrations of *tirasemtiv* to assess consistency of observations and to increase sensitivity. The authors pooled data for ALSFRS-R, three pulmonary function measures, quantitative muscle strength, and submaximal handgrip endurance. Up to 855 values from 143 patients were plotted against concentrations of *tirasemtiv*. Linear associations between concentrations of *tirasemtiv* and changes from baseline of clinical measures were estimated using a repeated-measures mixed model. Statistically significant relationships between increases in these functional measures and increasing plasma concentration of *tirasemtiv* were observed for all measures except for vital capacity. The authors concluded that these findings support the development of this drug candidate for the potential treatment of ALS.

Development Status of *Tirasemtiv* in ALS

Tirasemtiv (formerly CK-2017357) is currently being evaluated in BENEFIT-ALS (**B**linded **E**valuation of **N**euromuscular **E**ffects and **F**unctional **I**mprovement with ***T****irasemtiv* in **ALS**). BENEFIT-ALS is an international, double-blind, randomized, placebo-controlled, Phase IIb clinical trial designed to evaluate the safety, tolerability and potential efficacy of this novel drug candidate in patients with ALS. BENEFIT-ALS is designed to enroll approximately 680 patients who will first complete one week of treatment with open-label *tirasemtiv* at 125 mg twice daily. Following completion of the open-label period, patients will be randomized to receive 12 weeks of double-blind treatment with twice-daily oral ascending doses of *tirasemtiv* beginning at 125 mg twice daily and increasing weekly up to 250 mg twice daily or a dummy dose titration with placebo. Clinical assessments will take place monthly during the course of treatment; patients will also participate in follow-up evaluations one and four weeks after their final dose. The primary efficacy analysis of BENEFIT-ALS will compare the mean change from baseline in the ALS Functional Rating Scale in its revised form (ALSFRS-R) on *tirasemtiv* versus placebo. Secondary endpoints will include Maximum Voluntary Ventilation (MVV) and other measures of respiratory and skeletal muscle function. Patients taking *riluzole* at the time of enrollment and who are randomized to receive *tirasemtiv* will receive *riluzole* at a reduced dose of 50 mg daily.

About Cytokinetics

Cytokinetics is a clinical-stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions. Cytokinetics' lead drug candidate from its cardiac muscle contractility program, *omecamtiv mecarbil*, is in Phase II clinical development for the potential treatment of heart failure. Amgen Inc. holds an exclusive license worldwide to develop and commercialize *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing *tirasemtiv*, a fast skeletal muscle activator, as a potential treatment for diseases and medical conditions associated with neuromuscular dysfunction. *Tirasemtiv* is currently the subject of a Phase II

clinical trials program and 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 amyotrophic lateral sclerosis, a debilitating disease of neuromuscular impairment. Cytokinetics is collaborating with Astellas Pharma Inc. to develop CK-2127107, a skeletal muscle activator structurally distinct from *tirasemtiv*, for non-neuromuscular indications. All of these drug candidates have arisen from Cytokinetics' muscle biology focused research activities and are directed towards the cytoskeleton. The cytoskeleton is a complex biological infrastructure that plays a fundamental role within every human cell. Additional information about Cytokinetics can be obtained at www.cytokinetics.com.

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, progress, completion and results of clinical trials, and the significance and utility of clinical trial results; and the properties and potential benefits of tirasemtiv and Cytokinetics' drug candidates, including the potential benefits of tirasemtiv in treating patients with ALS. 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, Cytokinetics anticipates that it will be required to conduct at least one confirmatory Phase III clinical trial of tirasemtiv in ALS patients which will require significant additional funding, and it may be unable to obtain such additional funding on acceptable terms, if at all; 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 trials 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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