



## Cytokinetics Announces Presentation of Additional Analyses from Clinical Trials of Tirasemtiv in Patients with Amyotrophic Lateral Sclerosis

December 7, 2012 12:30 PM EST

### *Pharmacokinetics of Tirasemtiv Are Dose Proportional*

### *Positive and Concentration Dependent Effects Were Observed on Multiple Functional Measures*

**South San Francisco, CA, December 7, 2012** - Cytokinetics, Incorporated (Nasdaq: CYTK) announced a platform presentation of pharmacokinetic data and pharmacokinetic/pharmacodynamic analyses from three previously-reported clinical trials of *tirasemtiv* in patients with amyotrophic lateral sclerosis (ALS) at the 23<sup>rd</sup> International Symposium on ALS and Motor Neurone Diseases (ALS/MND) in Chicago, IL. *Tirasemtiv* is the lead drug candidate that has emerged from the company's skeletal muscle contractility program. *Tirasemtiv* selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium, which increases skeletal muscle force in response to neuronal input. In preclinical studies, this mechanism has been shown to delay the onset and reduce the degree of muscle fatigue. *Tirasemtiv* is currently being evaluated in BENEFIT-ALS, 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.

### **Platform Presentation at the 23<sup>rd</sup> International Symposium on ALS/MND**

These analyses included data from three completed Phase II clinical trials and were presented in a platform presentation titled, "Pharmacokinetics and Interactive Effects of the Fast Skeletal Muscle Activator CK-2017357 and Riluzole," by Jeffrey M. Shefner, M.D., Ph.D., Professor and Chair, Department of Neurology at the Upstate Medical University, State University of New York, and Lead Investigator of BENEFIT-ALS. In this presentation, the authors concluded that the pharmacokinetic properties of *tirasemtiv* are predictable with linear kinetics and were not affected by the presence of *riluzole*. In addition, the authors concluded that *riluzole* exposure is approximately doubled in the presence of *tirasemtiv* so that reducing the *riluzole* dose to 50 mg once daily in the presence of *tirasemtiv* results in levels that are approximately the same as *riluzole* 50 mg twice daily in the absence of *tirasemtiv*.

Across all of these three clinical trials, *tirasemtiv* appeared to produce positive and concentration dependent positive effects on multiple functional measures, including maximum grip strength in the stronger hand ( $p=0.093$ ), handgrip fatigability (stronger hand,  $p=0.078$ ; weaker hand,  $p=0.039$ ), maximum voluntary ventilation ( $p=0.022$ ), maximal inspiratory pressure ( $p=0.0036$ ) and the ALS Functional Rating Scale - Revised (ALSFRS-R) ( $p=0.089$ ). These analyses, in conjunction with previously reported results showing potential benefit of *tirasemtiv* in single dose and multiple dose trials of up to three weeks in duration, support the further development of *tirasemtiv* in ALS.

"These analyses are encouraging regarding the potential of *tirasemtiv* to positively impact strength, endurance, respiratory function and overall functional status," stated Dr. Shefner. "Patients suffering from ALS are significantly limited in all of these functional areas and could benefit from a novel treatment."

"We are pleased to have these data presented in a platform presentation at the 23<sup>rd</sup> International Symposium on ALS/MND," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "These analyses contributed importantly to the design of our ongoing Phase IIb clinical trial, known as BENEFIT-ALS, in which we are evaluating three months of treatment with *tirasemtiv* in ALS patients to determine the safety, tolerability and possible efficacy of this novel therapy."

### **Development Status of Tirasemtiv**

*Tirasemtiv* (formerly CK-2017357) is currently being evaluated in BENEFIT-ALS, 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. *Tirasemtiv* has been granted orphan drug designation and fast track status by the United States Food and Drug Administration and orphan medicinal product designation by the European Medicines Agency for the potential treatment of ALS.

Data from two completed randomized, double-blind, placebo-controlled, multiple-dose, Phase II clinical trials of *tirasemtiv* in patients with ALS were presented at the April 2012 American Academy of Neurology Annual Meeting. In one of these trials, *tirasemtiv* appeared to be generally safe and well-tolerated when dosed daily for two weeks at 125 mg, 250 mg, or 375 mg, first in a cohort of patients not receiving *riluzole*, and then in a cohort of patients receiving *riluzole* at a reduced dose of 50 mg daily. Adverse events and clinical assessments during treatment with *tirasemtiv* appeared similar, with or without co-administration of *riluzole*. While the trial was not designed or powered to evaluate statistically the effects of *tirasemtiv* on the various outcome measures that were assessed during the study, a combined analysis of patients from two separate cohorts suggested encouraging trends in the ALSFRS-R and in MVV that appeared dose-related and potentially clinically meaningful in magnitude. In the other Phase II clinical trial, a twice-daily dose titration regimen of *tirasemtiv* also appeared to be generally safe and well-tolerated. The majority of patients in this trial were titrated successfully to a *tirasemtiv* dose level of 250 mg twice daily. While this trial also was not designed or powered to evaluate statistically the effects of *tirasemtiv* on the various outcome measures that were assessed during the study, increases were observed in ALSFRS-R that were similar in direction, and in MVV that were similar in direction and magnitude, to those observed in the aforementioned trial. In addition, in December 2010, data from a Phase IIa clinical trial evaluating single doses of *tirasemtiv* were presented at the 21<sup>st</sup> International Symposium on ALS and Motor Neurone Diseases. In all three of these Phase II clinical trials, *tirasemtiv* appeared to be safe and well-tolerated, and demonstrated encouraging trends to improvement in patients' functional abilities, and in measures of respiratory and skeletal muscle strength and endurance.

### **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 (excluding Japan) to develop and commercialize *omecamtiv mecarbil* and related compounds, subject to Cytokinetics' specified development and commercialization participation rights. Cytokinetics is independently developing *tirasemtiv*, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or 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 in which treatment with *tirasemtiv* produced potentially clinically relevant pharmacodynamic effects in Phase II trials. 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](http://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' research and development activities, including the progress, conduct, design and results of clinical trials and the significance and utility of clinical trial results; and the properties and potential benefits of tirasemtiv and Cytokinetics' other drug candidates and potential 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, Cytokinetics will require significant additional funding to conduct a registration program for tirasemtiv for the potential treatment of ALS and 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, and the U.S. Food and Drug Administration (FDA) or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil; Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics may incur unanticipated research and development and other costs; 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; regulatory authorities may not grant tirasemtiv orphan drug exclusivity in ALS even if it is approved for marketing; 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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