



## Cytokinetics Announces Data Relating to Tirasemtiv Presented at the 2014 Annual Spinal Muscular Atrophy Conference

June 13, 2014 8:00 PM EDT

### *Tirasemtiv Demonstrates Improvements in Muscle Force, Grip Strength and Resistance to Fatigue in Preclinical Models*

**South San Francisco, CA, June 13, 2014-** Cytokinetics, Incorporated (Nasdaq: CYTK) announced that data from preclinical research relating to *tirasemtiv* in mouse models of spinal muscular atrophy (SMA) were presented today at the 2014 Annual Spinal Muscular Atrophy Conference in National Harbor, Maryland. In these models, *tirasemtiv* increased muscle force and improved grip strength, grid hang time, and resistance to fatigue. These studies were supported in part by a grant from the Families of Spinal Muscle Atrophy.

In both an oral presentation entitled "Small Molecule *Tirasemtiv* Improves Muscle Function in Two Mouse Models of SMA" and a poster entitled "*Tirasemtiv* Increases Skeletal Muscle Performance in SMA Mice" Cytokinetics' scientists shared data from research performed in collaboration with Christine DiDonato, Ph.D., Associate Professor at the Feinberg School of Medicine at Northwestern University and colleagues at the Manne Children's Research Institute, affiliated with Ann & Robert H. Lurie Children's Hospital of Chicago and W. David Arnold, MD, Assistant Professor at The Ohio State University. The objective of the research was to examine the effect of *tirasemtiv* on measures of muscle function in two mouse models of SMA that were generated in the DiDonato laboratory and exhibit mild to moderate neuromuscular dysfunction. In these models, isometric ankle plantarflexor force was measured following sciatic nerve stimulation and muscle fatigability was assessed by repeated sciatic nerve stimulation. Grip strength was assessed with a pull bar assembly connected to a force measurement gauge and grid hang time was measured by placing the mice on a grid and inverting it. The first model evaluated mild-severity "adult-onset" SMA mice and the second model evaluated "intermediate-severity" SMA mice.

In the "adult-onset" SMA mice, the authors noted that, in response to subtetanic nerve stimulation, mice treated with *tirasemtiv* produced increases in submaximal isometric force compared to vehicle-treated mice. In addition, treatment with *tirasemtiv* significantly improved resistance to muscle fatigue. In particular, grid hang time (mean  $\pm$  sem) increased ( $138 \pm 18$  vs.  $192 \pm 34$  seconds for vehicle and *tirasemtiv* treated mice respectively,  $p = 0.048$ ) to levels similar to that of wild-type mice ( $197 \pm 23$  seconds). In the "intermediate-severity" SMA mice in which the authors noted that muscle weakness was more pronounced than in the "adult-onset" SMA mice, treatment with *tirasemtiv* also produced more force than vehicle-treated controls in response to subtetanic nerve stimulation. In addition, treatment with *tirasemtiv* improved forelimb grip strength in these mice ( $43 \pm 4$  vs.  $52 \pm 4$  grams for vehicle and *tirasemtiv* treated mice respectively,  $p = 0.01$ ) although it was not feasible to normalize grip strength to that of wild-type mice ( $95 \pm 4$  grams) in this more severely affected model. The authors concluded that in these animal models of SMA, *tirasemtiv* increased submaximal muscle force *in situ*, improved fatigue resistance *in situ*, improved grip strength *in vivo* in the "intermediate-severity" mouse model and improved grid hang time *in vivo* in the "adult-onset" mouse model.

"We are pleased to share results from our research performed with *tirasemtiv* in preclinical models of Spinal Muscular Atrophy," stated Fady I. Malik, M.D., Ph.D., Cytokinetics' Senior Vice President, Research and Early Development. "We believe these data lend support to the translation of *tirasemtiv* as a potential treatment for neuromuscular diseases such as SMA and we continue to evaluate opportunities to expand the development for this novel mechanism drug candidate. We would like to thank the Families of Spinal Muscular Atrophy for their support of our research."

#### **About Tirasemtiv**

*Tirasemtiv*, a novel skeletal muscle activator, is the lead drug candidate from Cytokinetics' skeletal muscle contractility program. *Tirasemtiv* selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium and, in preclinical studies, 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* was the subject of BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with *Tirasemtiv* in ALS), a recently completed Phase IIb clinical trial. BENEFIT-ALS was a multi-national, double-blind, randomized, placebo-controlled, clinical trial designed to evaluate the safety, tolerability and efficacy of *tirasemtiv* in patients with amyotrophic lateral sclerosis (ALS). BENEFIT-ALS did not achieve its primary efficacy endpoint, the mean change from baseline in the ALS Functional Rating Scale in its revised form (ALSFRS-R). Treatment with *tirasemtiv* resulted in a statistically significant and potentially clinically meaningful reduction in the decline of Slow Vital Capacity (SVC), a pre-specified secondary efficacy endpoint and a measure of the strength of the skeletal muscles responsible for breathing that has been shown to be an important predictor of disease progression and survival in prior trials of patients with ALS. The analyses of other pre-specified secondary efficacy endpoints produced mixed results. Results from BENEFIT-ALS were presented at the 66th Annual Meeting of the American Academy of Neurology on April 29, 2014 and at the Joint Congress of European Neurology on June 1, 2014. Cytokinetics expects to continue to analyze the data from BENEFIT-ALS to inform the potential further development of *tirasemtiv* in patients living with ALS.

#### **About Families of Spinal Muscular Atrophy**

Families of Spinal Muscular Atrophy is the world's leading organization focused on funding Spinal Muscular Atrophy (SMA) research to develop a treatment and cure for the disease. The successful results and progress that the organization has delivered, from basic research to drug discovery to clinical trials, provide real hope for families and patients impacted by the disease. The charity has invested over \$55 million in research and has been involved in funding half of all the ongoing novel drug programs for SMA. Families of SMA is a nonprofit 501(c)3 organization, with 31 Chapters and 90,000 members and supporters throughout the United States. The organization's work has produced major discoveries, including identification of the underlying cause and a back-up gene for the disease, which provides a clearly defined target for disease altering therapies. The organization is also dedicated to supporting SMA families through networking, information and services and to improving care for all SMA patients.

#### **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 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 (ALS). 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](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 potential significance and utility of the results from BENEFIT-ALS and other clinical and pre-clinical studies of tirasemtiv; planned further analyses of the results from BENEFIT-ALS and the potential outcomes of such analyses; potential further development of tirasemtiv; and the properties and potential benefits 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, the results of BENEFIT-ALS may not support further clinical development of tirasemtiv; further clinical development of tirasemtiv in ALS patients, if supported by the BENEFIT-ALS data, will require significant additional funding, and Cytokinetics 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.*

**Contact:**

Joanna L. Goldstein  
Manager, Investor Relations & Corporate Communications  
(650) 624-3000