



## Cytokinetics Announces Presentations Relating to Tirasemtiv and Effects on Respiratory Muscle Function at International Symposium on ALS/MND

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**South San Francisco, CA, December 5, 2014** - Cytokinetics, (Nasdaq: CYTK) announced today that an oral presentation and four poster presentations relating to *tirasemtiv* were presented at the 25<sup>th</sup> International Symposium on ALS/MND held at the Square Brussels Meeting Centre in Brussels, Belgium.

"We are pleased to present clinical and preclinical data relating to *tirasemtiv*, as well as other related analyses, at this important annual meeting of the ALS community," stated Fady I. Malik, M.D., Ph.D., Cytokinetics' Senior Vice President, Research and Development. "We believe that the effects of *tirasemtiv* on Slow Vital Capacity in patients treated with *tirasemtiv* in BENEFIT-ALS are consistent with its novel mechanism of action and therapeutic rationale for use in patients with ALS. Potentially clinically meaningful effects of *tirasemtiv* on this key measure of respiratory function merit further investigation in a trial of longer duration."

### Oral Presentation at the 25th International Symposium on ALS/MND

An oral presentation titled "The Effects of *Tirasemtiv* on Measures of Respiratory Function in Amyotrophic Lateral Sclerosis" was presented by Jinsy Andrews, MD, MSc, Director, Clinical Research and Development at Cytokinetics. Dr. Andrews summarized results on measures of respiratory function from BENEFIT-ALS and concluded that *tirasemtiv* may have had cumulative, longer term pharmacologic effects on Slow Vital Capacity (SVC) and that the effect of *tirasemtiv* on SVC appeared robust. In BENEFIT-ALS, the effect of *tirasemtiv* on SVC was similar in magnitude across all subgroups evaluated and was statistically significant within the majority of subgroups evaluated. Dr. Andrews observed that vital capacity is a clinically meaningful measure of disease progression and prognosis and is used to determine major clinical decisions in the treatment of patients with ALS.

### Poster Presentations at the 25th International Symposium on ALS/MND

A poster titled "Relationships between *Riluzole* and *Tirasemtiv* Levels on Outcomes in the BENEFIT-ALS Trial" was presented by Jeremy M. Shefner, MD, PhD, Professor & Chair of Neurology, Barrow Neurological Institute and Lead Investigator for BENEFIT-ALS. The authors concluded that in this trial, *tirasemtiv* reduced the slope of the decline in SVC by approximately 50%; effects on SVC were observed at all doses studied and the concentration-response relationship was flat. In addition, *tirasemtiv* reduced the decline in muscle strength measured by hand-held dynamometry; the effect was only evident in the lower two quartiles of plasma concentrations of *tirasemtiv*. There was no effect of *tirasemtiv* on ALSFRS-R in any plasma concentration quartile. *Riluzole* did not increase plasma concentrations of *tirasemtiv* nor did *riluzole* impact the tolerability of *tirasemtiv*. The effect of *tirasemtiv* to reduce the decline in SVC was observed in patients on and off *riluzole*. The effects of *tirasemtiv* on SVC and muscle strength in BENEFIT-ALS suggest that a lower target dose of *tirasemtiv* than was studied in the trial may warrant further evaluation.

A poster titled "Effect of *Tirasemtiv* on Submaximal Rodent Diaphragm Strength and Respiratory Function" was presented by Darren T. Hwee, PhD, Scientist at Cytokinetics. The authors noted that pathological conditions that lead to diaphragm weakness can have severe consequences, ranging from dyspnea and reduced quality of life to respiratory failure and death. The authors concluded that *tirasemtiv* increased rat diaphragm fiber calcium sensitivity in a concentration-dependent manner, increased mouse diaphragm submaximal force production *ex vivo* and increased tidal volume *in vivo* in a mouse model of ALS. These results suggest that *tirasemtiv* and other fast skeletal muscle troponin activators may be viable for improving respiratory muscle function.

A poster titled "Fast Skeletal Muscle Troponin Activator *Tirasemtiv* Increases Muscle Function and Performance in Mouse Models of Spinal Muscular Atrophy" was presented by Darren T. Hwee, PhD, Scientist at Cytokinetics. The authors concluded that "intermediate-severity" and "adult-onset" spinal muscle atrophy (SMA) mice exhibited nerve dysfunction, muscle atrophy, and weakness. Single doses of *tirasemtiv* significantly increased submaximal muscle force and fatigue resistance *in situ* in both SMA mouse models. The authors also concluded that *tirasemtiv* improved grip strength *in vivo* in "intermediate-severity" mice and inverted grid hang time *in vivo* in "adult-onset" mice. These results suggest that *tirasemtiv* and other fast skeletal muscle troponin activators may be viable therapeutics for improving muscle function in SMA.

A poster titled "Profile of Medical Care Costs in Patients with Amyotrophic Lateral Sclerosis in the Medicare Program and under Commercial Insurance" was presented by Lisa Meng, PhD, Director of Biometrics at Cytokinetics. The authors concluded that medical costs in the month of ALS diagnosis were significantly higher than in other months of treatment and that costs started to increase exponentially within about eight months before the month of diagnosis for both Medicare and commercial cases. In addition, costs in the month following diagnosis increased on average every month following diagnosis. For patients with commercial insurance coverage, eligibility for Medicare coverage increased the total insurance coverage by 50% but no trends were observed during the coverage transition to Medicare. Approximately 30% of ALS patients were receiving supportive services for disabilities at the time of diagnosis and their medical care costs increased rapidly and substantially with each disability milestone.

### About *Tirasemtiv* and BENEFIT-ALS

*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 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.

BENEFIT-ALS was a Phase IIb, multi-national, double-blind, randomized, placebo-controlled, clinical trial designed to evaluate the safety, tolerability and efficacy of *tirasemtiv* in patients with ALS. BENEFIT-ALS enrolled 711 patients from 73 centers in 8 countries; 605 patients were subsequently randomized 1:1 to double-blind treatment with either *tirasemtiv* or placebo for 12 weeks. The primary outcome measure, the ALS Functional Rating Scale in its revised form (ALSFRS-R), and secondary outcome measures of respiratory performance and other measures of skeletal muscle function and fatigability were assessed after 4, 8, and 12 weeks of double-blind treatment, and again at 1 and 4 weeks after the last dose of double-blind treatment.

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 the treatment groups. Treatment with *tirasemtiv* in BENEFIT-ALS resulted in a statistically significant and potentially clinically meaningful slowing of the rate of decline of SVC versus placebo; the reduction from baseline in SVC was statistically significantly smaller on *tirasemtiv* versus placebo at each time point 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 medication. Effects of *tirasemtiv* on SVC appeared to be consistent across patient subgroups.

### About Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that afflicts approximately 25,000 people in the United States and a comparable number of patients in Europe. Approximately 5,600 new cases of ALS are diagnosed each year in the United States. The average life expectancy of an ALS patient is approximately three to five years after diagnosis and only 10% of patients survive for more than 10 years. Death is usually due to respiratory failure because of diminished strength in the skeletal muscles responsible for breathing. Few treatment options exist for these patients, resulting in a high unmet need for new therapeutic options to address the symptoms and modify the disease progression of this grievous illness.

### 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 <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' research and development activities, including the potential significance and utility of the results from BENEFIT-ALS and other studies of *tirasemtiv*; the potential further development of *tirasemtiv*; the potential size of markets for *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, 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 slow vital capacity 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 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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