



Cytokinetics Announces Additional Results from BENEFIT-ALS

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First Clinical Trial in Patients with ALS to Show a Significant Reduction in Decline of Slow Vital Capacity

Adverse Events on Tirasemtiv May Have Confounded Primary Efficacy Results and Warrant Additional Analyses to Inform Potential Continued Development

SOUTH SAN FRANCISCO, CA, April 29, 2014 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced today additional results from BENEFIT-ALS (Blinded Evaluation of Neuromuscular Effects and Functional Improvement with *Tirasemtiv* in **ALS**), which will be presented later today during the 66th Annual Meeting of the American Academy of Neurology at the Pennsylvania Convention Center in Philadelphia by Jeremy M. Shefner, M.D., Ph.D., Professor and Chair, Department of Neurology at the Upstate Medical University, State University of New York and the Lead Investigator for BENEFIT-ALS.

In BENEFIT-ALS, 711 patients with amyotrophic lateral sclerosis (ALS) were enrolled into the open-label phase; subsequently 605 patients were randomized 1:1 to double-blind treatment with either *tirasemtiv* or placebo for 12 weeks. As previously announced, 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). Secondary endpoints evaluated measures of respiratory performance and other measures of skeletal muscle function and fatigability.

Treatment with *tirasemtiv* resulted in a statistically significant and potentially clinically meaningful reduction in the decline of Slow Vital Capacity (SVC, 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. This pre-specified secondary efficacy endpoint also declined less on *tirasemtiv* than on placebo at each assessment time point.

Slow Vital Capacity	Placebo (n = 210)	<i>Tirasemtiv</i> (n = 178)	All (N = 388)
Baseline (% Predicted, mean ± SD)	89.7 (17.2)	85.7 (19.3)	87.8 (18.3)
Time Point	Changes from Baseline (Least Square Mean ± Standard Error)	p-value	
Week 4	-3.89 (0.62)	-0.99 (0.68)	0.001
Week 8	-5.81 (0.68)	-2.85 (0.77)	0.004
Week 12	-8.66 (0.80)	-3.12 (0.90)	<0.0001
	Slope of decline (Percentage Points per day)		
Week 0 to Week 12	-0.0905	-0.0394	0.0006

The analyses of other pre-specified secondary efficacy endpoints in BENEFIT-ALS produced mixed results. The Muscle Strength Mega-Score, a measure of strength combining the data from several muscle groups in each patient, declined more slowly on *tirasemtiv* versus placebo ($p = 0.016$ for the difference in slope of decline); however, there were no differences at any time point that reached statistical significance. The rate of decline for Sniff Nasal Inspiratory Pressure (SNIP) was not statistically significant different ($p = 0.21$); however, SNIP decreased more on *tirasemtiv* compared with placebo in a statistically significant manner at 4 and 12 weeks (p values at 4, 8, and 12 weeks were 0.012, 0.066, 0.050, respectively). No differences in Maximum Voluntary Ventilation and Hand Grip Fatigue were observed on *tirasemtiv* versus placebo.

"I am pleased to present the results of BENEFIT-ALS at the American Academy of Neurology," stated Dr. Shefner. "While this clinical trial did not meet its primary efficacy endpoint, it is the first clinical trial in patients with ALS to demonstrate a positive and potentially clinically meaningful effect on Slow Vital Capacity, an important measure of disease progression and predictor of survival. In addition, muscle strength appeared to decline more slowly on *tirasemtiv* versus placebo. The results of BENEFIT-ALS support continued investigation into the role *tirasemtiv* may play in the treatment of patients with ALS."

Serious adverse events (SAE) during double-blind treatment were more frequent on *tirasemtiv* than on placebo (9.0% vs. 5.4%). The most common SAE was respiratory failure which occurred in 1 patient on *tirasemtiv* and 3 patients on placebo, while confusional state and delirium occurred in 2 patients on *tirasemtiv* and no patients on placebo. More patients on *tirasemtiv* withdrew from the trial following randomization than on placebo (99 vs. 33 patients, respectively). Adverse events more common on *tirasemtiv* than on placebo (>10% difference) were dizziness (50.8% vs. 19.7%), fatigue (33.2% vs. 14.2%), and nausea (21.9% vs. 7.8%).

Patients on *tirasemtiv* lost more weight than patients on placebo (change from baseline to Week 12: -1.70 kg vs. -0.79 kg; $p = 0.006$). Weight loss was significantly greater in patients with gastrointestinal adverse events (e.g. nausea and decreased appetite) which occurred more frequently on *tirasemtiv* than on placebo (43.5% vs. 25.8%). The weight loss on *tirasemtiv* appeared to negatively impact the effect of *tirasemtiv* on the ALSFRS-R when compared to placebo (p value for weight change-by-treatment interaction = 0.052). ALSFRS-R declined less on *tirasemtiv* than on placebo in those patients treated with *tirasemtiv* who lost less weight.

"On behalf of Cytokinetics, I want to extend our gratitude to the patients and investigators who participated in BENEFIT-ALS. We are pleased that BENEFIT-ALS provides the first evidence that fast skeletal muscle troponin activation with *tirasemtiv* may slow the progression of skeletal muscle weakness in patients with ALS," stated Andrew A. Wolff, M.D., F.A.C.C., Cytokinetics' Chief Medical Officer and Senior Vice President of Clinical Research and Development. "Adverse events on *tirasemtiv* in BENEFIT-ALS may have confounded certain results of the trial. We will continue to analyze the results of BENEFIT-ALS to understand how to approach the potential further development of *tirasemtiv*."

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 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.

About BENEFIT-ALS

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 patients in 73 centers in 8 countries. Patients enrolled in BENEFIT-ALS began treatment with open-label *tirasemtiv* at 125 mg twice daily. Patients who tolerated this open-label treatment for one week were randomized to receive 12 weeks of double-blind treatment with twice-daily oral ascending doses of *tirasemtiv* or placebo, beginning at 125 mg twice daily and increasing weekly up to 250 mg twice daily (or a dummy dose titration with placebo). Clinical assessments occurred every four weeks during double-blind treatment; patients also returned for follow-up evaluations at one and four weeks after their final dose of double-blind study medication. The primary efficacy analysis of BENEFIT-ALS compared the mean change from baseline in the ALS Functional Rating Scale in its revised form (ALSFRS-R) to the average of the scores obtained after 8 and 12 weeks of double-blind treatment on *tirasemtiv* versus placebo. Secondary endpoints evaluated measures of respiratory performance and other measures of skeletal muscle function and fatigability.

About Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis 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 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*; 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) 624-3060