Cytokinetics Announced Additional Results Relating to Tirasemtiv from Pre-Specificed Subgroup Analyses of BENEFIT-ALS

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Effects of Tirasemtiv on Slow Vital Capacity During 12 Weeks of Double-Blind Treatment Were Observed Consistently Across Patient Subgroups

SOUTH SAN FRANCISCO, CA, July 10, 2014 - Cytokinetics, Incorporated (Nasdaq: CYTK) announced that additional results from BENEFIT-ALS (**B**linded **E**valuation of **N**euromuscular **E**ffects and **F**unctional **I**mprovement with ***T****irasemtiv* in **ALS**) were presented today during a poster presentation at the 13th International Congress on Neuromuscular Diseases in Nice, France. The results from pre-specified subgroup analyses of BENEFIT-ALS were presented by Andrew A. Wolff, M.D., F.A.C.C., Senior Vice President, Clinical Research and Development, and Chief Medical Officer of Cytokinetics. These results indicate that the reduced decline in Slow Vital Capacity (SVC) on *tirasemtiv* versus placebo in BENEFIT-ALS were observed consistently across all subgroups of patients with amyotrophic lateral sclerosis (ALS).

The effects of *tirasemtiv* versus placebo on the changes from baseline to the average score after 8 and 12 weeks of treatment for the primary and secondary endpoints were evaluated in pre-specified analyses of subgroups based on age, sex, geography, *riluzole* use, onset of disease, weight, body-mass index (BMI) and baseline respiratory function. Based on these results, the authors concluded that *tirasemtiv* reduced the decline in SVC versus placebo by a similar magnitude regardless of age (≥65 versus <65), sex, geographic region (Europe versus North America), *riluzole* use, site of ALS onset (bulbar versus limb), baseline pulmonary function, baseline weight, and baseline BMI. The reduced decline in SVC versus placebo was statistically significant within each subgroup examined except patients enrolled in Europe, those with bulbar onset, and those with a percent predicted SVC less the median at baseline. The authors concluded that *tirasemtiv* may have both immediate and longer term pharmacologic effects, especially on SVC, and that the potentially beneficial effects of *tirasemtiv* on measures of respiratory function and other assessments of skeletal muscle performance observed in BENEFIT-ALS merit further investigation.

"The consistent effects of *tirasemtiv* across pre-specified subgroups on the clinically meaningful measure of SVC corroborate our prior observations across the total population studied in BENEFIT-ALS," stated Dr. Wolff. "We believe that *tirasemtiv* is the first drug candidate to reduce the decline in SVC in ALS patients so consistently, regardless of age, sex, geographic region, *riluzole* use, site of disease onset, baseline pulmonary function and baseline weight and BMI. We are encouraged by these results as we continue to analyze data from BENEFIT-ALS to inform the potential further development of *tirasemtiv* in patients with ALS."

In addition, analyses presented today indicated that *tirasemtiv* had no effect on Maximum Voluntary Ventilation (MVV) in any subgroup examined; however, a trend toward an increase in MVV on *tirasemtiv* versus placebo in patients with bulbar onset approached statistical significance. Overall, Sniff Nasal Inspiratory Pressure (SNIP) was reduced on *tirasemtiv* versus placebo and the magnitude of this effect was similar across all subgroups except in patients older than 65 years, in whom a marginal increase was observed. Conversely, the only subgroup in which the reduction of SNIP on *tirasemtiv* versus placebo was statistically significant was in patients less than 65 years old. In these subgroup analyses, *tirasemtiv* had no effect on the changes in muscle strength and in handgrip fatigue from baseline to the average after 8 and 12 weeks, neither overall nor within any of the subgroups.

About *Tirasemtiv* and BENEFIT-ALS

Tirasemtiv 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, increased skeletal muscle force in response to neuronal input and delayed the onset and reduced 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. In BENEFIT-ALS, patients with ALS were randomized 1:1 to 12 weeks of double-blind treatment with *tirasemtiv* or placebo. 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 results from double-blind treatment during BENEFIT-ALS were presented in April 2014 at the Annual Meeting of the American Academy of Neurology in Philadelphia. In June 2014, at the Joint Congress of European Neurology in Istanbul, outcome measures obtained at 1 and 4 weeks after the last dose of double-blind study medication were presented.

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. Secondary endpoints included measures of respiratory function (specifically SVC, MVV, and SNIP) and other assessments of skeletal muscle performance, specifically muscle strength Mega-Score and handgrip fatigue. Treatment with *tirasemtiv* resulted in a statistically significant and potentially clinically meaningful slowing of the rate of decline of SVC versus placebo; in addition, the reduction from baseline in SVC was statistically significantly smaller on *tirasemtiv* versus placebo at each time point it was 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 study medication.

Tirasemtiv also significantly slowed the rate of decline in the muscle strength Mega-Score (a measure of strength combining the data from several muscle groups in each patient) versus placebo; however, there were no differences in the changes from baseline at any time point that reached statistical significance. The rate of decline for SNIP was not statistically significant different; however, SNIP decreased more on *tirasemtiv* compared with placebo in a statistically significant manner at 4 and 12 weeks. The difference in SNIP between *tirasemtiv* and placebo observed after 12 weeks of double-blind treatment in BENEFIT-ALS was similar in magnitude at 1 week and at 4 weeks after discontinuation of treatment but was statistically significant only at 1 week. There were no statistically significant differences between treatment groups in the rates of decline for the remaining secondary endpoints. No differences in MVV and hand grip fatigue were observed on *tirasemtiv* versus placebo during double-blind treatment nor through 4 weeks after the last double-blind dose.

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; 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, 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.

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