



Cytokinetics Announces Positive Results From Phase II Clinical Trial Evaluating CK-2017357 in Patients With Amyotrophic Lateral Sclerosis

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CK-2017357 Demonstrated to Be Well-Tolerated in First Cohort of Ongoing Clinical Trial

SOUTH SAN FRANCISCO, CA, Nov 30, 2011 (MARKETWIRE via COMTEX) --

Cytokinetics, Incorporated (NASDAQ: CYTK) announced today positive results from the first cohort, or Part A, of a continuing Phase II clinical trial of CK-2017357 in patients with amyotrophic lateral sclerosis (ALS). Data were presented at the 22nd International Symposium on ALS/MND in Sydney, Australia.

A poster titled "A Study to Evaluate Safety, Tolerability and Clinical Outcomes Following Repeated Doses of CK-2017357 in Patients with Amyotrophic Lateral Sclerosis" was presented by Jeremy M. Shefner, MD, PhD, Professor and Chair of the Department of Neurology at the Upstate Medical University at the State University of New York. The poster summarized data from Part A of this ongoing Phase II clinical trial. CK-2017357 selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium, which increases skeletal muscle force in response to neuronal input and delays the onset and reduces the degree of muscle fatigue. CK-2017357 is the lead drug candidate from the company's skeletal muscle contractility program.

"The objective of Part A of this Phase II clinical trial was to evaluate the tolerability of a range of doses of CK-2017357 when administered over a two-week period to ALS patients not currently taking riluzole. We are pleased that Part A of this clinical trial successfully achieved its primary objective in demonstrating that CK-2017357 was well-tolerated when dosed daily in these patients with ALS and provides encouraging information with respect to a key question regarding the abatement of dizziness with continued dosing," stated Jesse M. Cedarbaum, MD, Cytokinetics' Vice President of Clinical Research and Operations, Neuroscience and Neuromuscular Disorders. "The majority of adverse events observed in Part A of this trial were mild; in particular, episodes of dizziness reported by patients while receiving CK-2017357 were mostly mild and generally abated as dosing continued over the course of the two-week dosing period."

"These positive multi-dose tolerability data will help guide the continuing development of CK-2017357 and also inform ongoing discussions with potential partners and regulatory authorities as we continue planning a registration strategy directed towards the potential treatment of patients with ALS," stated Robert I. Blum, Cytokinetics' President and CEO. "Advancing CK-2017357 into later-stage development remains an important corporate priority and we look forward to seeing the results from our other ongoing Phase II clinical trials that may also guide our preparations."

Phase II Clinical Trial Results From Part A

Part A of this Phase II clinical trial successfully met its primary objective of defining the tolerability and pharmacokinetic profile of CK-2017357 during two weeks of daily dosing in 24 ALS patients who were not taking riluzole concurrently. CK-2017357 was well-tolerated as a single agent at all dose levels from 125 mg daily to 375 mg daily for two weeks in these patients.

In Part A of this trial, 83% of patients in the combined CK-2017357 dose groups reported at least one treatment-emergent adverse event, compared with 67% of the patients receiving placebo. In the combined dose groups receiving CK-2017357, the most common and dose-related side effect reported was dizziness, observed in no patients receiving placebo and 8 of the 18 patients receiving CK-2017357. The dizziness did not persist beyond the second day of dosing in all but one of the patients studied. A total of 14 episodes of dizziness were reported, 12 of which were mild in severity. The incidence of dizziness appeared dose-related and self-limiting in all patients who completed study drug treatment except for one patient in whom it was mild in severity. Two patients withdrew early, both due to treatment-emergent dizziness. No serious adverse events were reported.

Plasma concentrations of CK-2017357 increased with escalating doses; however, there was considerable overlap between the dose groups in the range of observed plasma levels. As expected, due to the small sample size of 24 patients, the large inter-patient variability and the short, two-week duration, Part A of this trial lacked the statistical power to detect significant differences in clinical outcome measures. However, trends to improved clinical outcome measures were observed, especially at the highest CK-2017357 dose of 375 mg daily. Four of five patients who completed treatment in this dose group reported improvement in their Global Assessments and three of these five patients improved at least 1 point on the ALS Functional Rating Scale-Revised (ALSFRRS-R). The changes observed in Maximum Voluntary Ventilation (MVV) after two weeks of dosing at 375 mg compare favorably to improvements observed at 24 hours after a single 500 mg dose of CK-2017357 in the prior Phase IIa Evidence of Effect clinical trial in ALS patients. Additional analyses from this ongoing clinical trial, including results from efficacy outcome measures, are expected to be presented at a later date.

Phase II Clinical Trial Design

This ongoing Phase II clinical trial is a double-blind, randomized, placebo-controlled trial designed to evaluate the safety and tolerability of multiple doses of CK-2017357 in patients with ALS. In Part A, 24 ALS patients who were not currently taking riluzole were randomized to one of four different treatment groups to receive daily oral doses of placebo or 125 mg, 250 mg, or 375 mg of CK-2017357, respectively, for two weeks. Clinical assessments took place at pre-determined times during the course of treatment. Patients also participated in follow-up evaluations one week after their final dose. Cytokinetics recently announced the initiation of a second cohort, or Part B, of this trial in 24 patients with ALS who are receiving riluzole.

The primary objective of this clinical trial is to assess the safety and tolerability of CK-2017357, after multiple oral doses to steady state plasma concentrations, in patients with ALS. A secondary objective of this clinical trial is to evaluate the ALSFRS-R, other measures of pulmonary function, muscle strength and fatigue, and physician and patient global assessments in these patients while receiving two weeks of treatment with CK-2017357 at the indicated doses or placebo.

Additional Poster Presentation at the 22nd International Symposium on ALS/MND

In addition, a second poster presentation titled "The ALSFRS @ 20: Evolution of the ALSFRS-R, History, Clinimetric Properties and Future Directions,"

was presented by Dr. Cedarbaum at the 22nd International Symposium on ALS/MND. In the 20 years since its creation, the ALSFRS, now in its revised version as the ALSFRS-R, has become the most frequently used assessment of activities of daily living in ALS trials. The authors of this poster, all of whom were involved in the original development of the assessment, highlighted that the ALSFRS and the ALSFRS-R are reliable and reproducible scales with good clinimetric properties. Both scales are easy to standardize for use by patients and caregivers and have been translated and validated in multiple languages for use in worldwide clinical studies. The authors concluded that the ALSFRS, as it has evolved into the ALSFRS-R, continues to be a valuable tool in ALS clinical and drug development research, and has become a template for assessing functional changes in ALS patients and other patients with other neuromuscular diseases.

Development Status of CK-2017357 in ALS

Cytokinetics is developing CK-2017357, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. CK-2017357 is currently the subject of a Phase II clinical trials program and has been granted orphan-drug designation by the U.S. Food and Drug Administration for the potential treatment of ALS, a debilitating disease of neuromuscular impairment. In addition to the above-mentioned ongoing Phase II clinical trial of CK-2017357, the company also recently announced the opening of another Phase II clinical trial of CK-2017357, which is designed to evaluate the safety and tolerability of an ascending dose-titration regimen of CK-2017357.

CK-2017357 previously demonstrated potentially clinically relevant pharmacodynamic effects in a completed Phase IIa Evidence of Effect clinical trial in ALS patients. In that trial, the single doses of CK-2017357 evaluated appeared generally well-tolerated. In addition, both patients and investigators perceived a positive change in the patients' overall status, in a dose-dependent fashion, at 6 hours after dosing with CK-2017357, based on a Global Assessment in which the patient and the investigator each independently assessed patients' status compared to prior to dosing. Furthermore, there was a clear relationship between improvements in Global Assessments and the CK-2017357 plasma concentration. Also at this 6-hour time point, there was a trend towards decreased muscle fatigability, as evidenced by data from a test of sub-maximal hand-grip endurance. Data from that clinical trial also demonstrated a statistically significant increase in the maximum volume of air patients could inhale and exhale in ten seconds (Maximum Voluntary Ventilation) at both 6 and 24 hours after 500 mg of CK-2017357, as well as small but statistically significant increases in maximum strength of certain muscle groups tested.

Cytokinetics recently met with the U.S. Food and Drug Administration's Division of Neurology Products to discuss its progress in the development of CK-2017357 as a potential treatment for patients with ALS and the company's plans for its further development, including potential registration strategies. Based on this discussion, Cytokinetics is assessing options that may enable the initiation of a clinical trial of CK-2017357 in ALS patients that could potentially serve as a pivotal trial for global registration purposes.

Background on Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that afflicts 20,000 to 30,000 people in the United States. Approximately 5,600 new cases of ALS are diagnosed each year. The average life expectancy of an ALS patient is approximately three to five years 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.

Background on Cytokinetics Skeletal Muscle Contractility Program

CK-2017357, a fast skeletal muscle troponin activator, is the lead drug candidate from the company's skeletal muscle contractility program. CK-2017357 selectively activates the fast skeletal muscle troponin complex by increasing its sensitivity to calcium, leading to an increase in skeletal muscle force. This mechanism of action has demonstrated encouraging pharmacological activity in preclinical models that may relate to the potential treatment of diseases associated with aging, muscle wasting or neuromuscular dysfunction. Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction. The sarcomere is a highly ordered cytoskeletal structure composed of skeletal muscle myosin, the cytoskeletal motor that is directly responsible for converting chemical energy into mechanical force, as well as actin, and a set of regulatory proteins, troponins and tropomyosin, which make the actin-myosin interaction dependent on changes in intracellular calcium levels. Cytokinetics' skeletal muscle contractility program is focused to the discovery and development of small molecule skeletal sarcomere activators and leverages Cytokinetics' expertise developed in its ongoing discovery and development of cardiac sarcomere activators, including the cardiac myosin activator omecamtiv mecarbil, now in clinical development as a potential treatment for heart failure. Skeletal sarcomere activators have demonstrated pharmacological activity in preclinical models that may lead to new therapeutic options for diseases associated with aging, muscle wasting and neuromuscular dysfunction. The clinical effects of muscle wasting, fatigue and loss of mobility can range from decreased quality of life to, in some instances, life-threatening complications. By directly improving skeletal muscle function, a small molecule activator of the skeletal sarcomere may potentially enhance physical performance and quality of life in aging 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 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 CK-2017357, a skeletal muscle activator, as a potential treatment for diseases and conditions associated with aging, muscle wasting or neuromuscular dysfunction. CK-2017357 is currently the subject of a Phase II clinical trials program and has been granted orphan-drug designation by the U.S. Food and Drug Administration for the potential treatment of amyotrophic lateral sclerosis, a debilitating disease of neuromuscular impairment in which CK-2017357 demonstrated potentially clinically relevant pharmacodynamic effects in a Phase IIa trial. Cytokinetics is also conducting research and non-clinical development of compounds that inhibit smooth muscle contractility and which may be useful as potential treatments for diseases and conditions associated with excessive smooth muscle contraction, such as bronchoconstriction associated with asthma and chronic obstructive pulmonary disorder (COPD). In addition, prior Cytokinetics' research generated three anti-cancer drug candidates that have progressed into clinical development: ispinesib, SB-743921 and GSK-923295. All of these drug candidates and potential drug candidates have arisen from Cytokinetics' 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.

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' and its partners' research and development activities, including plans for and the initiation, conduct, design and results of clinical trials for CK-2017357, and the significance and utility of clinical trial results for CK-2017357; the potential size of markets for CK-2017357, and the properties and potential benefits of CK-2017357 and Cytokinetics' other drug candidates and potential drug candidates, including CK-2017357's potential utility in the treatment of patients with ALS.

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, 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 (FDA) or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, the FDA may not grant CK-2017357 orphan drug exclusivity in ALS even if it is approved for marketing, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for omecamtiv mecarbil; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products on acceptable terms, if at all; funding from the National Institute of Neurological Disorders and Stroke may not be available in future periods; 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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