Cytokinetics Announces Positive Data From Phase I Clinical Trial of CK-2017357

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Statistically Significant Increases in Muscle Force Production Demonstrated During Treatment With Novel Skeletal Muscle Activator

SOUTH SAN FRANCISCO, CA, Jan 11, 2010 (MARKETWIRE via COMTEX) -- Cytokinetics, Incorporated (NASDAQ: CYTK) announced positive data from Part B of its Phase I, first-time-in-humans, randomized, double-blind, placebo-controlled, clinical trial of CK-2017357 in healthy volunteers.

Part B of this trial was designed to assess the pharmacodynamic effects of CK-2017357 on skeletal muscle function after single oral doses of 250, 500, and 1000 mg, and to assess the relationship of the effects observed to the associated plasma concentrations of CK-2017357. The company announced that CK-2017357 produced concentration-dependent, statistically significant increases versus placebo in the force developed by the tibialis anterior, the muscle evaluated in this trial, and that the doses administered were well tolerated by the healthy volunteers that participated.

Part A of this trial was designed to assess the safety, tolerability, and pharmacokinetic profile of increasing single doses of this drug candidate in healthy volunteers and to determine its maximum-tolerated dose and plasma concentration. The company announced that, to date, single doses up to 2000 mg have been administered without causing intolerable adverse events; accordingly, the maximum-tolerated dose has not yet been determined, and Cytokinetics continues to escalate the dose in this ongoing trial.

Part B Clinical Trial Results

In Part B of this clinical trial, CK-2017357 produced statistically significant, placebo-corrected increases in the force exerted by the tibialis anterior muscles of healthy male volunteers, as measured by a foot flexion device at each of several different nerve stimulation frequencies. These increases in skeletal muscle performance increased with both the dose and the plasma concentration of CK-2017357, and were most evident in the middle of the range of stimulation frequencies tested, consistent with preclinical observations. Compared to pre-dose measurements, statistically significant, placebo-corrected increases in skeletal muscle function were demonstrated at every time point tested after dosing.

At the higher doses and plasma concentrations and in association with mid-range stimulation frequencies, statistically significant mean percent increases from baseline versus placebo ranged up to 20.7%. For example, within the highest CK-2017357 plasma concentration range evaluated in the study (i.e., from > 12 mcg/mL up to 25.6 mcg/mL), the mean placebo-corrected percent increase in the peak force developed by the tibialis anterior muscle during stimulation at a frequency of 12.5 Hz was 13.7% ($p < 0.001$). The largest mean percent increase in peak force versus placebo, 20.7%, was observed during stimulation at 10 Hz, 5 hours after dosing with 1000 mg ($p = 0.02$).

CK-2017357 was well tolerated by the healthy volunteers in Part B of this trial. No serious adverse events were reported. Adverse events of dizziness and euphoric mood appeared to increase in frequency with increasing doses of CK-2017357; however, all these adverse events were characterized as mild in severity.

A more complete presentation of data from Part B of this trial is intended to be presented to the broader scientific community at an appropriate forum to be determined.

"These positive results are encouraging and consistent with data generated in our preclinical studies with this novel drug candidate. Importantly, the muscle we studied in this clinical trial, the tibialis anterior, has been reported to contain only about 20-30% fast fibers, so the effects of CK-2017357 may be even greater in muscles with a greater percentage of fast fibers," stated Andrew A. Wolff, MD, FACC, Cytokinetics' Senior Vice President of Clinical Research and Development and Chief Medical Officer. "These data from healthy volunteers bode well for successful demonstration of pharmacodynamic effects of CK-2017357 in our planned Evidence of Effect clinical trials in patients with impaired neuromuscular function."

"Results from this program are further validation of our leadership position in the emerging pharmacology of muscle function. With these promising data, our Research and Development teams have again successfully translated a first-in-class drug discovery program to demonstration of pharmacodynamic effects in humans," stated Robert I. Blum, Cytokinetics' President and CEO. "Progress in this program, which has potential applications in a wide array of conditions associated with impaired skeletal muscle function, nicely complements our development program directed to increasing cardiac muscle contractility for the potential treatment of heart failure."

Clinical Trial Design

In the ongoing Part A of this clinical trial, initiated in June 2009, healthy male volunteers participate in two dosing sessions separated by an adequate washout period. Volunteers are randomized (3:1) at the start of each dosing session to receive active study drug or placebo, respectively.

Part B of this trial, initiated in November 2009, was a double-blind, randomized, placebo-controlled, crossover study in healthy, male volunteers of single oral doses of CK-2017357 that were tolerated in Part A. The volunteers in Part B received each of three single oral doses of 250, 500, and 1000 mg of CK-2017357 and oral placebo treatment in a 4-period crossover design; doses were separated by an adequate washout period. In order to assess the effects of CK-2017357 on skeletal muscle function, the force generated by the tibialis anterior muscle was measured during external nerve stimulation across a range of frequencies. Using these data, curves were constructed to describe the relationship between the force produced by the muscle and the frequency at which it was stimulated; i.e., the force-frequency relationship. The force-frequency relationship was characterized before each dose of double-blind study medication, and at 1, 3, 5, and 7 hours after dosing.

In preclinical studies characterizing the force-frequency relationship, CK-2017357 appeared to shift the curve upward and to the left, with more force being produced at lower to mid-range nerve stimulation frequencies, which are the physiologic frequencies at which motor neurons stimulate skeletal muscle during normal function. Part B of this ongoing trial was designed to assess if these effects of CK-2017357 could be recapitulated in humans.

Additional Phase I Clinical Trial of CK-2017357

In November 2009, the company announced the initiation of a second Phase I clinical trial to investigate the safety, tolerability and pharmacokinetic profile of CK-2017357 after multiple oral doses to steady state in healthy male volunteers. Data from this trial are anticipated to be available in the first quarter of 2010.

Background on CK-2017357 and Skeletal Muscle Activators

CK-2017357 is a fast skeletal muscle troponin activator and is the lead drug candidate from the company's skeletal sarcomere activator program. CK-2017357 selectively activates the fast skeletal troponin complex and increases 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. It is a highly ordered cytoskeletal structure composed of skeletal muscle myosin, the cytoskeletal motor that is directly responsible for converting chemical energy into the mechanical force, 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 Phase II clinical development as a potential treatment for heart failure. Skeletal sarcomere activators have demonstrated pharmacological activity 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.

Market Potential for CK-2017357 and Skeletal Muscle Activators

The conditions that could benefit from a skeletal muscle activator are grievous and severe. Amyotrophic lateral sclerosis (ALS) afflicts between 20,000 and 30,000 people in the United States and is associated with a 3-year mortality rate of 50%. In addition, few options exist for the treatment of other neuromuscular disorders, such as myasthenia gravis, a chronic disease characterized by a defect in the transmission of nerve impulses to skeletal muscles, which afflicts approximately 60,000 patients in the United States. Patients with disorders and conditions with a higher prevalence could also benefit from enhanced skeletal muscle functional performance, including patients with cachexia, intermittent claudication and sarcopenia. Cachexia, a syndrome characterized by a drastic and unintentional loss of body mass, is estimated to be prevalent in 15%-35% of heart failure patients and in approximately 50% of cancer patients. Intermittent claudication, which usually refers to cramping pains in the legs caused by peripheral arterial disease, is a condition that impacts between 1 million and 3 million people in the United States each year. Sarcopenia, which is an age-related loss of muscle mass, strength, and function, is estimated to impact the lives of over 25-30% of the U.S. population over the age of 65 and can result in additional injuries and medical conditions due to limited mobility.

About Cytokinetics

Cytokinetics is a clinical-stage biopharmaceutical company focused on the discovery and development of 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 (formerly CK-1827452), is in Phase II 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. Cytokinetics is also conducting non-clinical development of compounds that inhibit smooth muscle contractility and which may be useful as potential treatments for diseases and conditions such as systemic hypertension, pulmonary arterial hypertension or bronchoconstriction In addition, prior Cytokinetics' research generated three anti-cancer drug candidates in Phase I 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 the design, focus, scope and conduct of clinical trials relating to CK-2017357, the significance and utility of the results from such clinical trials and the availability of such results, and the planned Evidence of Effect clinical trials for CK-2017357; the market potential for skeletal muscle activators such as 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 effects in muscles with a high percentage of fast fibers. 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 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 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; 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; and others may develop competitive products or alternative therapies for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target. 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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