

## PRESS RELEASE

### CYTOKINETICS ANNOUNCES DATA FROM PHASE 2 CLINICAL STUDY OF RELDESEMTIV IN PATIENTS WITH SPINAL MUSCULAR ATROPHY PRESENTED AT THE 2018 ANNUAL CURE SMA CONFERENCE

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#### **First Study of Muscle-Directed Therapy in Patients with SMA Showed Potentially Clinically Meaningful Effects on Six Minute Walk Distance and Maximal Expiratory Pressure**

SOUTH SAN FRANCISCO, Calif., June 16, 2018 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq:CYTK) today announced data from the Phase 2 clinical study of *reldesemtiv* in patients with spinal muscular atrophy (SMA) were presented in an oral presentation by John W. Day, M.D., Ph.D., Professor of Neurology and Pediatrics (Genetics), Stanford University, at the 2018 Annual Cure SMA Conference in Dallas. This hypothesis-generating study met its primary objective to determine potential pharmacodynamic effects of *reldesemtiv* after multiple oral doses in patients with SMA, and secondary objectives to evaluate the safety, tolerability and pharmacokinetics of *reldesemtiv*. In collaboration with Astellas, Cytokinetics is developing *reldesemtiv* as a potential treatment for people with SMA and certain other debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue.

The study showed dose- and concentration-dependent increases in time to muscle fatigue as measured by changes from baseline in Six Minute Walk Distance (6MWD), a sub-maximal exercise test of aerobic capacity and endurance, and Maximal Expiratory Pressure (MEP), a measure of strength of respiratory muscles, after eight weeks of treatment with *reldesemtiv*.

The study, which examined two dose levels of *reldesemtiv*, 150 mg or 450 mg twice daily, demonstrated dose-dependent increases in 6MWD in ambulatory patients as measured at both post-baseline time points, week four and week eight. In the 150 mg twice daily group, the increase vs. placebo was 10.86 meters ( $p=0.2531$ ) after four weeks of treatment with *reldesemtiv* and 7.72 meters ( $p=0.4684$ ) after eight weeks of treatment. In the 450 mg twice daily group, the increase vs. placebo was 35.63 meters ( $p= 0.0037$ ) at week four and 24.89 meters ( $p= 0.0584$ ) at week eight. There was also a statistically significant correlation between  $C_{max}$ , or peak concentration of *reldesemtiv*, and change from baseline in 6MWD, with a slope estimate of 9.53 meters/ $(\mu\text{g}/\text{mL})$ . ( $p=0.0086$ ).

The study also showed increases vs. placebo in MEP. In the 150 mg twice daily group, the increase in MEP was 5.95 cm H<sub>2</sub>O ( $p=0.2276$ ) after four weeks of treatment with *reldesemtiv* and 11.69 cm H<sub>2</sub>O ( $p=0.0378$ ) after eight weeks of treatment. In the 450 mg twice daily group, the increase in MEP compared to placebo was 9.17 cm H<sub>2</sub>O ( $p=0.0855$ ) after four weeks of

treatment with *reldesemtiv* and 13.15 cm H<sub>2</sub>O (p=0.0298) after eight weeks of treatment. Other assessments in the study, including the Hammersmith Functional Motor Score - Extended, Revised Upper Limb Module, Timed Up-and-Go and Forced Vital Capacity did not demonstrate meaningful differences between *reldesemtiv* versus placebo.

Adverse events were similar between groups receiving *reldesemtiv* and placebo. The most commonly observed adverse effects were headache, constipation and nausea. Four patients had serious adverse events reported that resulted in early termination of study drug treatment, all considered to be unrelated to *reldesemtiv*.

“This hypothesis-generating study provides the first data indicating that a muscle-directed therapy, namely a fast skeletal muscle troponin activator, may be clinically beneficial in patients with SMA,” said Dr. Day. “These data are especially encouraging given the unmet need among those adolescent and adult individuals with SMA who have persistent muscle weakness, fatigue and functional impairment.”

“We are pleased that treatment with *reldesemtiv* showed potentially clinically beneficial effects in adolescent and adult patients with SMA as evidenced by dose-dependent increases vs. placebo in Six Minute Walk and Maximal Expiratory Pressure,” said Fady I. Malik, M.D., Ph.D., Cytokinetics’ Executive Vice President of Research and Development. “We believe that these data support the evaluation of higher doses of *reldesemtiv* in future clinical trials in SMA given the absence of an efficacy plateau and no dose-limiting safety or tolerability issues. We look forward to working with Astellas, investigators and regulatory authorities to further review the data and consider a potential path forward.”

### **Clinical Study Design**

The primary objective of this Phase 2, double-blind, randomized, placebo-controlled clinical study was to determine the potential pharmacodynamic effects of a suspension formulation of *reldesemtiv* following multiple oral doses in patients with Type II, Type III, or Type IV SMA. Secondary objectives were to evaluate the safety, tolerability and pharmacokinetics of *reldesemtiv*. There was no single primary endpoint in this early, Phase 2, hypothesis-generating study.

The study enrolled 70 patients, 39 in Cohort 1 and 31 in Cohort 2. Ambulatory and non-ambulatory (Type II or Type III) patients 12 years of age and older were randomized 2:1, stratified by ambulatory ability, to receive *reldesemtiv* or placebo dosed twice daily for eight weeks. The first cohort of patients received 150 mg of *reldesemtiv* or placebo and the second cohort received 450 mg of *reldesemtiv* or placebo twice daily. Enrollment in this study was stopped short of the targeted 72 patients after blinded analyses of the variability around the changes from baseline of several efficacy measures demonstrated that the study had sufficient statistical power to detect clinically relevant differences versus placebo in efficacy endpoints with the 70 patients already enrolled.

Multiple assessments of skeletal muscle function and fatigability were performed in the study, including respiratory assessments, upper limb strength and functionality for non-ambulatory

patients, as well as Six Minute Walk Distance and Timed Up-and-Go for ambulatory patients. In this hypothesis-generating study, all endpoints were evaluated using nominal p-values without adjusting for multiple comparisons. Patients enrolled in the second cohort were also assessed with the SMA Health Index, a patient reported outcome measure. Additional information regarding the study can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **About *Reldesemtiv***

Skeletal muscle contractility is driven by the sarcomere, the fundamental unit of skeletal muscle contraction and a highly ordered cytoskeletal structure composed of several key proteins. Skeletal muscle myosin is the motor protein that converts chemical energy into mechanical force through its interaction with actin. A set of regulatory proteins, which includes tropomyosin and several types of troponin, make the actin-myosin interaction dependent on changes in intracellular calcium levels. *Reldesemtiv*, a next-generation fast skeletal muscle troponin activator (FSTA) arising from Cytokinetics' skeletal muscle contractility program, slows the rate of calcium release from the regulatory troponin complex of fast skeletal muscle fibers, which sensitizes the sarcomere to calcium, leading to an increase in skeletal muscle contractility. *Reldesemtiv* has demonstrated pharmacological activity that may lead to new therapeutic options for diseases associated with muscle weakness and fatigue. In non-clinical models of SMA, a skeletal muscle activator has demonstrated increases in submaximal skeletal muscle force and power in response to neuronal input and delays in the onset and reductions in the degree of muscle fatigue. *Reldesemtiv* has been the subject of five completed Phase 1 clinical trials in healthy volunteers, which evaluated the safety, tolerability, bioavailability, pharmacokinetics and pharmacodynamics of the drug candidate. In addition to the Phase 2 clinical study in patients with SMA, Cytokinetics is collaborating with Astellas on the conduct of Phase 2 clinical trials in patients with amyotrophic lateral sclerosis (ALS) and chronic obstructive pulmonary disease (COPD) as well as a Phase 1b clinical trial of *rel-desemtiv* in elderly adults with limited mobility.

### **About SMA**

SMA is a severe, genetic neuromuscular disease that leads to debilitating muscle function and progressive, often fatal, muscle weakness. It occurs in 1 in 6,000 to 10,000 live births each year and is one of the most common potentially fatal genetic disorders. Spinal muscular atrophy manifests in various degrees of severity as progressive muscle weakness resulting in respiratory and mobility impairment. There are four types of SMA, named for age of initial onset of muscle weakness and related symptoms: Type 1 (Infantile), Type 2 (Intermediate), Type 3 (Juvenile) and Type 4 (Adult onset). Of the prevalent population, approximately 80% of the patients are characterized as Type 2 and Type 3. Life expectancy and disease severity vary by type of SMA. Type 1 patients have the worst prognosis, with a life expectancy of no more than two years; Type 2 patients have delayed motor milestones with the most advanced milestone normally achieved being sitting unsupported; Type 3 patients can usually stand and walk but have increasingly limited mobility as their abilities regress as they age; Type 4 patients may have a normal life span but eventually suffer gradual weakness in the proximal muscles of the extremities, eventually resulting in mobility issues. With the recent introduction of gene

modifying therapies, it is expected that patients may live longer but will still have a significant need to address ongoing disabilities related to respiration and mobility. Approximately 50% of Type 3 patients with SMA are believed to maintain ambulatory function today and an increasing number of Type 2 patients with SMA are expected to remain ambulatory with the advent of complementary new therapies that can enable motor milestones. Over the next 5 years, the prevalence of ambulatory adolescents and adults with SMA may exceed 5-10,000 patients in the United States alone.

### **Cytokinetics Conference Call / Webcast**

Cytokinetics will host a conference call on June 18, 2018 at 8:30 a.m. Eastern Time including members of management and Dr. Day. The conference call will be simultaneously webcast and will be accessible in the Investors & Media section of Cytokinetics' website. The live audio of the conference call is also accessible via telephone to investors, members of the news media and the general public by dialing either (866) 999-2985 (CYTK) (United States and Canada) or (706) 679-3078 (International) and typing in the passcode 2491748. An archived replay of the webcast will be available via Cytokinetics' website until June 25, 2018. The replay will also be available via telephone from June 18, 2018 at 11:30 a.m. Eastern Time until June 25, 2018 by dialing (855) 859-2056 (United States and Canada) or (404) 537-3406 (International) and typing in the passcode 2491748.

### **About Cytokinetics and Astellas Collaboration**

In 2013, Astellas and Cytokinetics formed a partnership focused on the research, development, and commercialization of skeletal muscle activators. The primary objective of the collaboration is to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness. Under the collaboration, Cytokinetics exclusively licensed to Astellas rights to co-develop and potentially co-commercialize *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA), in non-neuromuscular indications. In 2014, Astellas and Cytokinetics agreed to expand the collaboration to include certain neuromuscular indications, including SMA, and to advance *reldesemtiv* into Phase 2 clinical development, initially in SMA. Under the agreement as further amended in 2016, Astellas has exclusive rights to co-develop and commercialize *reldesemtiv* and other FSTAs in non-neuromuscular indications and certain neuromuscular indications (including SMA and ALS) and other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics' development and commercialization rights; Cytokinetics may co-promote and conduct certain commercial activities in North America and Europe under agreed scenarios.

### **About Cytokinetics**

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, the company is developing small molecule drug candidates specifically engineered to increase muscle function and contractility. Cytokinetics is collaborating with Amgen Inc. ("Amgen") to develop *omecamtiv mecarbil*, a novel cardiac

muscle activator. *Omecamtiv mecarbil* is the subject of GALACTIC-HF, an international Phase 3 clinical trial in patients with heart failure. Amgen holds an exclusive worldwide license to develop and commercialize *omecamtiv mecarbil* with a sublicense held by Servier for commercialization in Europe and certain other countries. Cytokinetics is collaborating with Astellas Pharma Inc. (“Astellas”) to develop *reldesemtiv*, a next-generation FSTA. *Reldesemtiv* has been granted orphan drug designation by the FDA for the potential treatment of spinal muscular atrophy. *Reldesemtiv* is the subject of three Phase 2 clinical trials in patients with spinal muscular atrophy, chronic obstructive pulmonary disease and amyotrophic lateral sclerosis. Astellas is also conducting a Phase 1b clinical trial of *reldesemtiv* in elderly adults with limited mobility. Astellas holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. Licenses held by Amgen and Astellas are subject to Cytokinetics' specified co-development and co-commercialization rights. Cytokinetics continues its 20-year history of innovation with three new muscle biology directed compounds advancing from research to development in 2018. For additional information about Cytokinetics, visit [www.cytokinetics.com](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’ and its partners’ research and development activities, including the Phase 2 clinical study of *reldesemtiv* in patients with SMA and its potentially beneficial effects; and the properties and potential benefits of Cytokinetics’ 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, 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; Astellas’ decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; 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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