Cytokinetics Granted European Orphan Designation for Reldesemtiv for the Treatment of Spinal Muscular Atrophy

July 23, 2019 11:30 AM EDT

SOUTH SAN FRANCISCO, Calif., July 23, 2019 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced that the European Medicines Agency (EMA) has granted orphan medicinal product designation to *reldesemtiv* for the potential treatment of spinal muscular atrophy (SMA). The U.S. Food and Drug Administration previously granted orphan drug designation to *reldesemtiv* for the potential treatment of SMA in 2017. In collaboration with Astellas, Cytokinetics is developing *reldesemtiv*, a fast skeletal muscle troponin activator (FSTA), as a potential treatment for people with SMA and certain other debilitating diseases and conditions associated with skeletal muscle weakness and/or fatigue.

Orphan medicinal product designation is adopted by the European Commission based on an opinion by the EMA's Committee for Orphan Medicinal Products (COMP). Orphan medicinal product designation is granted by the EMA to medicines intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating disease affecting fewer than 5 in 10,000 persons in the European Union, or for which it is unlikely that the costs associated with the development and commercialization of the medicine would be recovered by expected sales under normal market conditions without the incentives provided by the designation. The designation offers potential incentives, which may include a ten-year period of EU marketing exclusivity from the date of marketing authorization, EU-funded research, protocol assistance and fee reductions.

"We're pleased that *reldesemtiv* received orphan designation from the European Commission," said Fady I. Malik, M.D., Ph.D., Cytokinetics' Executive Vice President of Research & Development. "Despite advances with SMN-directed treatments, residual muscle impairment and weakness are expected to present continuing challenges for patients with SMA. Treatment with *reldesemtiv* may represent an additive and complementary approach to increase muscle function."

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 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 skeletal muscle weakness and fatigue.

In non-clinical models of spinal muscular atrophy, a skeletal muscle activator increased submaximal skeletal muscle force and power in response to neuronal input, delayed the onset of skeletal muscle fatigue and reduced the degree of skeletal muscle fatigue. Data from preclinical studies of *reldesemtiv* showed that the addition of *reldesemtiv* to treatment with SMN upregulators significantly increased muscle force in a mouse model of spinal muscular atrophy. In these studies, the addition of *reldesemtiv* to SMN upregulators resulted in a leftward shift of the force-frequency curve, indicating an increase in calcium sensitivity of the muscle at submaximal stimulation frequencies and confirming the efficacy of fast skeletal muscle activation in muscle in conjunction with SMN upregulators. In a Phase 2 hypothesis-generating clinical study in patients with SMA, patients treated with *reldesemtiv* demonstrated increases in measures of endurance and stamina consistent with the mechanism of action.

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 unless treated with SMN-directed therapies; 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 SMN-directed 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.[i] 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.[ii]

About Cytokinetics and Astellas Collaboration

In 2013, Cytokinetics and Astellas formed a partnership focused on the research, development, and potential 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. Cytokinetics initially exclusively licensed to Astellas rights to co-develop and potentially co-commercialize *reldesemtiv* and other FSTAs in non-neuromuscular indications and to develop and commercialize other novel mechanism, skeletal muscle activators in all indications. Under the agreement as subsequently expanded and amended, Astellas also has exclusive rights to co-develop and commercialize *reldesemtiv* and other FSTAs in certain neuromuscular indications (including SMA and ALS). Cytokinetics has certain development and commercialization rights, including the right to co-promote FSTAs for neuromuscular indications in the U.S., Canada and Europe and to co-promote the other collaboration products in the U.S. and Canada.

About Cytokinetics

Cytokinetics is a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and best-in-class muscle inhibitors 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 impact 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 an international clinical trials program in patients with heart failure including GALACTIC-HF and METEORIC-HF. 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 fast skeletal muscle troponin activator (FSTA) for diseases of neuromuscular dysfunction, including SMA and ALS. Astellas holds an exclusive worldwide license to develop and commercialize *reldesemtiv*. Licenses held by Amgen and Astellas are subject to specified co-development and co-commercialization rights of Cytokinetics. Cytokinetics is also developing CK-274, a novel cardiac myosin inhibitor that company scientists discovered independent of its collaborations, for the potential treatment of hypertrophic cardiomyopathies. Cytokinetics continues its over 20-year history of pioneering innovation in muscle biology and related pharmacology focused to diseases of muscle dysfunction and conditions of muscle weakness.

For additional information about Cytokinetics, visit www.cytokinetics.com and follow us on Twitter, LinkedIn, Facebook and YouTube.

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 the potential benefits of *reldesemtiv*, including its ability to represent an additive and complementary approach to increase muscle function; Cytokinetics' and its partners' research and development activities; the timing of enrollment of patients in Cytokinetics' and its partners' clinical trials; the design, timing, results, significance and utility of preclinical and clinical results; 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; 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 FDA 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; Astellas' decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *reldesemtiv*; 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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[i] Zeres er al. *Journal of Neurological Sciences* 146 (1997) 67-72

[ii] Proprietary market research and company estimates

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Source: Cytokinetics, Incorporated