



Cytokinetics Announces Publication of Preclinical Data Demonstrating Fast Skeletal Muscle Troponin Activator Improves Muscle Energetics

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SOUTH SAN FRANCISCO, Calif., July 24, 2019 (GLOBE NEWSWIRE) -- Cytokinetics, Incorporated (Nasdaq: CYTK) today announced the publication of data in *The Journal of Physiology* demonstrating that a fast skeletal muscle troponin activator (FSTA) can decrease skeletal muscle fatigue by increasing the metabolic efficiency of muscle contraction. The manuscript, titled "Fast Skeletal Muscle Troponin Activator CK-2066260 Increases Fatigue Resistance by Reducing the Energetic Cost of Muscle Contraction," was published this month. Cytokinetics conducted the research in collaboration with the laboratory of Professor Håkan Westerblad at the Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. CK-2066260 is a preclinical tool compound of the FSTA class.

"While we have previously generated preclinical and clinical data demonstrating that FSTAs improve muscle force, power and the time to muscle fatigue, this is the first time we have been able to show that the mechanism of action reduces the metabolic cost of muscle contraction. This class of potential therapies may offer promise for patients who experience premature muscle fatigue while performing routine activities," said Brad Morgan, Ph.D., Cytokinetics' Senior Vice President, Research and Non-Clinical Development.

CK-2066260 is a FSTA from the same chemical structural series as *tirasemtiv*, the first-generation FSTA discovered and developed by Cytokinetics. Similar to *tirasemtiv* and *reldesemtiv*, the next-generation FSTA from a distinct chemical series, being developed in collaboration with Astellas for the potential treatment of neuromuscular diseases of impaired muscle function, CK-2066260 binds directly to fast skeletal muscle troponin, increases myofibrillar calcium sensitivity and amplifies the force response to submaximal nerve stimulation. The regulation of calcium levels associated with muscle excitation and contraction account for a significant amount of muscle energy utilization. Because a FSTA lowers the amount of calcium required to produce a given muscle force, the authors hypothesized that CK-2066260 could reduce the energetic cost of muscle activation, allowing muscle to contract for longer.

Key results from a series of *in vitro*, *in situ* and *in vivo* rodent experiments demonstrated that treatment with CK-2066260:

- Amplified the muscle force response to subtetanic electrical stimulation by increasing muscle calcium sensitivity
- Improved the force response under fatiguing conditions
- Produced muscle force at lower cytosolic calcium concentrations and accompanied by reduced ATP demand and muscle glycogen usage
- Improved exercise capacity in healthy rats and a rat model of peripheral artery insufficiency

The authors concluded, "In healthy human subjects, the FSTAs *tirasemtiv* and *reldesemtiv* have been shown to amplify the skeletal muscle force response to nerve stimulation. Thus, the performance-enhancing effects of FSTA observed in the present study may translate to humans and provide a promising pharmacological treatment to patients suffering from severe muscle weakness and exercise intolerance."

About FSTAs

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. 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. *Reldesemtiv* 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.

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. *Omeclamtiv 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 *omeclamtivmecarbil* 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). 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 *tirasemtiv*, *reldesemtiv* and

CK-2066260, including the potential ability of CK-2066260 to reduce the metabolic cost of muscle contraction and benefit patients who experience premature muscle fatigue while performing routine activities; Cytokinetics' and its partners' research and development activities; 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; 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 *rel-desemtiv*; 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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