Fulcrum Therapeutics Acquires Global Rights to Losmapimod, a Potential Disease-Modifying Therapy for Facioscapulohumeral Muscular Dystrophy

April 23, 2019

Fulcrum plans to launch a Phase 2b clinical trial in FSHD in mid-2019

CAMBRIDGE, Mass., April 23, 2019 – Fulcrum Therapeutics, a biotechnology company focused on discovering and developing therapies to rebalance gene expression, today announced an exclusive worldwide license agreement with GlaxoSmithKline (GSK) for development and commercialization of the investigational drug losmapimod. Fulcrum intends to advance losmapimod into a Phase 2b trial in the rare and devastating genetic disease facioscapulohumeral muscular dystrophy (FSHD), for which there are currently no approved treatments.

Under the terms of the agreement, as payment for the license, GSK received shares of Fulcrum preferred stock representing a high single-digit ownership percentage of the company on a fully diluted basis, and will be eligible to receive future milestone payments and royalties. Fulcrum obtained all worldwide development and commercialization rights for losmapimod, as well as existing drug substance and drug product materials for use in its clinical trials. Fulcrum also received a right of reference to INDs filed with the FDA relating to losmapimod and an exclusive license to all related patents and data, which build on Fulcrum-generated intellectual property.

"Losmapimod is a foundational clinical asset for Fulcrum that has the potential to become the first approved therapy that targets the root cause of FSHD. Fulcrum believes losmapimod has the potential to slow or halt the progressive muscle weakness that characterizes the condition, which would significantly improve patients' quality of life," said Robert J. Gould, Ph.D., Fulcrum's president and chief executive officer. "The agreement shows confidence in our unique approach to rebalancing gene expression in severe genetically defined disorders. We will work urgently to advance the compound through the clinic."

Fulcrum's proprietary product engine identified inhibitors of p38a/b mitogen activated protein kinase (MAPK) as powerful inhibitors of DUX4 expression. DUX4 is the gene that is the root cause of FSHD, a progressive muscle wasting disorder. Losmapimod is a selective p38a/b MAPK inhibitor that GSK has tested extensively in clinical trials, but never in muscular dystrophies. Fulcrum's novel insight into the DUX4 regulatory pathway led the team to review existing p38a/b MAPK inhibitors, and Fulcrum identified losmapimod as a compound with the potential to address the root cause of FSHD by decreasing DUX4 expression.

GSK evaluated losmapimod in more than 3,500 healthy volunteers and patients in 24 clinical trials across multiple indications, including several Phase 2 trials and a Phase 3 trial in acute coronary syndrome. The data provide evidence that losmapimod is a well-tolerated agent. Fulcrum has conducted preclinical testing of losmapimod in patient-derived cell models and observed precise and potent downregulation of DUX4 expression and restoration of a healthy muscle phenotype without an effect on myogenesis. Fulcrum has developed an extensive clinical trial network of physicians working on FSHD. An ongoing

natural history study of the disease is informing the clinical development plan. Fulcrum expects to initiate a Phase 2b clinical trial of losmapimod in patients with FSHD at multiple clinical sites in the U.S. and Europe in mid-2019.

About FSHD

FSHD, one of the most common muscular dystrophies, is a progressive, degenerative and profoundly disabling disorder estimated to affect about 1 in 8,333 to 1 in 20,000 people globally. There are no approved treatments. Symptoms typically arise in adulthood, often beginning with muscle weakness in the face, leading to an inability to smile. The weakness progresses to the upper body and advances to the lower limbs, leaving many patients unable to lift their arms above shoulder level or to rise from a sitting position. People with FSHD often have difficulty performing daily tasks on their own and may experience severe fatigue and pain. FSHD is caused by a single gene, DUX4, which is normally switched off at the earliest stages of embryonic development. Patients with FSHD have a mutation that causes the gene to remain "on" and to continue producing a protein toxic to muscle tissue.

About Losmapimod

Losmapimod is a selective p38a/b mitogen activated protein kinase (MAPK) inhibitor initially developed by GlaxoSmithKline and in-licensed by Fulcrum Therapeutics. Fulcrum identified the compound as a potent regulator of the expression of the DUX4 gene, which causes FSHD. Losmapimod has been evaluated in more than 3,500 healthy volunteers and patients in 24 clinical trials across multiple indications, including in several Phase 2 trials and a Phase 3 trial. It has been shown to be generally well-tolerated.

About Fulcrum Therapeutics

Fulcrum Therapeutics is discovering and developing small molecule therapies to treat genetically defined diseases at their root cause by modulating the expression of the genes known to drive or ameliorate disease. Fulcrum's proprietary approach to studying disease biology in patient-derived and other relevant human cell lines, coupled with a computational biology engine, generates valuable insights into a wide array of genetically defined diseases. Please visit www.fulcrumtx.com.

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