Fulcrum Therapeutics Announces Multiple Presentations of Losmapimod Data at World Muscle Society Meeting

October 1, 2019

- *Oral presentation to highlight Phase 1 data on safety, tolerability and target engagement of losmapimod in treatment of FSHD*
- *Company also announces updated preclinical data on FTX-6058 for potential treatment of sickle cell disease; FTX-6058 showed an increase in HbF levels to ~30% total hemoglobin*

CAMBRIDGE, Mass., Oct. 01, 2019 (GLOBE NEWSWIRE) -- **Fulcrum Therapeutics, Inc.** (Nasdaq: FULC), a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases, today announces that the company will present data from multiple studies of losmapimod in facioscapulohumeral dystrophy (FSHD) patients during the International Annual Congress of the World Muscle Society being held from October 1-5 in Copenhagen, Denmark.

Michelle Mellion, MD, medical director at Fulcrum Therapeutics, will present data from the Phase 1 trial to assess the pharmacokinetics, safety and tolerability, and target engagement of losmapimod in FSHD patients during an oral presentation on Friday, October 4, 2019 from 10:30-12:30 CET. The company will highlight findings from the Phase 1 trial as well as information related to plans for using biomarkers in the ongoing Phase 2 clinical trials of losmapimod. A link to the Phase 1 data abstract is available here.

“We are very pleased to have such a strong presence at the World Muscle Society meeting this year, a testament to our progress and the significance of our efforts thus far to develop a treatment targeting the root cause of FSHD,” said Dr. Mellion. “We look forward to sharing these important insights with the research community during the meeting.”

Update on data related to Hemoglobinopathy Program

Fulcrum also announces recent progress in the company’s plan to advance the development program for FTX-6058, formerly referred to as FTX-HbF, for the potential treatment of sickle cell disease and beta-thalassemia. FTX-6058 is a novel upregulator of fetal hemoglobin. In pre-clinical research, treatment with FTX-6058 was shown to increase HbF levels to ~30% of total hemoglobin as measured by HPLC and mass spectrometry methods in human erythroid progenitor cells from multiple donors. FTX-6058 also elevated HbF *in vivo* in animal models at plasma concentrations reasonably expected to be achieved in humans. Fulcrum believes these results indicate that FTX-6058 could play a role in reducing the risk of crises in people living with sickle cell disease and may also help to address transfusion requirements in patients with beta-thalassemia as an oral therapeutic. Fulcrum has initiated IND-enabling studies for FTX-6058 and anticipates filing an IND in mid-2020.

“Our progress with both losmapimod and FTX-6058 highlights the strength of our research platform with the potential to rapidly advance development programs from our research efforts,” said Robert J. Gould, PhD, president and CEO of Fulcrum Therapeutics. “We look forward to providing updates on these important programs as we proceed.”

About FSHD
FSHD is characterized by progressive skeletal muscle loss that initially causes weakness in muscles in the face, shoulders, arms and trunk, and progresses to weakness throughout the lower body. Skeletal muscle weakness results in significant physical limitations, including an inability to smile and difficulty using arms for activities, with many patients ultimately becoming dependent upon the use of a wheelchair for daily mobility.

FSHD is caused by mis-expression of DUX4 in skeletal muscle, resulting in the presence of DUX4 proteins that are toxic to muscle tissue. Normally, DUX4-driven gene expression is limited to early embryonic development, after which time the DUX4 gene is silenced. In people with FSHD, the DUX4 gene is turned “on” as a result of a genetic mutation. The result is death of muscle and its replacement by fat, leading to skeletal muscle weakness and progressive disability. There are no approved therapies for FSHD, one of the most common forms of muscular dystrophy, with an estimated patient population of 16,000 to 38,000 in the United States alone.

About sickle cell disease
Sickle cell disease (SCD) is a genetic disorder of the red blood cells caused by a mutation in the HBB gene. This gene encodes a protein that is a key component of hemoglobin, a protein complex whose function is to transport oxygen in the body. The result of the mutation is less efficient oxygen transport and the formation of red blood cells that have a sickle shape. These sickle shaped cells are much less flexible than healthy cells and can block blood vessels or rupture cells. SCD patients typically suffer from serious clinical consequences, which may include anemia, pain, infections, stroke, heart disease, pulmonary hypertension, kidney failure, liver disease and reduced life expectancy.

About beta-thalassemia
Beta-thalassemia is a rare blood disorder caused by genetic mutations in the HBB gene, which are associated with the absence or reduced production of beta-globin – one of the two proteins that comprise adult hemoglobin. This results in an abnormally low level of hemoglobin as well as an excess of alpha-globin chains, causing destruction of red blood cells.

Beta-thalassemia has been clinically characterized into three forms, depending on disease severity: major, intermedia and minor. The most severe form is generally diagnosed shortly after birth and is characterized by life-threatening anemia. Pediatric patients do not grow and gain weight at the typical rates, and often have liver, heart and bone problems. Many patients with beta-thalassemia major require chronic blood transfusions due to severe anemia that results from low hemoglobin levels. Beta-thalassemia intermedia is a less severe form of the disease that results in mild to moderate anemia. These patients sometimes require blood transfusions depending on the severity of their symptoms. Patients with beta-thalassemia minor suffer from very mild anemia and generally do not require treatment.

About Losmapimod
Losmapimod is a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor that was exclusively in-licensed by Fulcrum Therapeutics following Fulcrum’s discovery of the role of p38α/β inhibitors in the reduction of DUX4 expression and an extensive review of known compounds. Utilizing its internal product engine, Fulcrum discovered that inhibition of p38α/β reduced expression of the DUX4 gene in muscle cells derived from

patients with FSHD. Although losmapimod has never previously been explored in muscular dystrophies, it has been evaluated in more than 3,500 subjects in clinical trials across multiple other indications, including in several Phase 2 trials and a Phase 3 trial. No safety signals were attributed to losmapimod in any of these trials.

About Fulcrum Therapeutics
Fulcrum Therapeutics is a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined diseases in areas of high unmet medical need, with an initial focus on rare diseases. Fulcrum's proprietary product engine identifies drug targets which can modulate gene expression to treat the known root cause of gene mis-expression. Please visit **www.fulcrumtx.com**.

Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding the development status of the Company's product candidates and the timing of availability of clinical trial data. All statements, other than statements of historical facts, contained in this press release, including statements regarding the Company's strategy, future operations, future financial position, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with Fulcrum's ability to obtain and maintain necessary approvals from the FDA and other regulatory authorities; continue to advance its product candidates in clinical trials; replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of losmapimod and its other product candidates; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in the Company's most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

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