Fulcrum Therapeutics Announces Complete Data from Phase 1 Trial with Losmapimod in Facioscapulohumeral Muscular Dystrophy (FSHD)

March 24, 2020

– Losmapimod achieves target engagement in muscle –

– Oral presentation at Virtual Muscular Dystrophy Association (MDA) Clinical and Scientific Conference highlights safety, tolerability and pharmacokinetics of losmapimod –

CAMBRIDGE, Mass., March 24, 2020 (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 announced complete results from its Phase 1 clinical trial of losmapimod, which is being developed for the treatment of facioscapulohumeral muscular dystrophy (FSHD). Results were presented by Michelle Mellion, M.D., the Company's senior medical director, in a live Virtual Clinical Trial Session of the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference today. Presented material is available on Fulcrum's website at fulcrumtx.com.

The primary objective of the Phase 1 trial was to investigate the safety and tolerability of losmapimod in healthy volunteers and in FSHD patients. The secondary objective was to evaluate repeated dose pharmacokinetics (PK) and target engagement (TE), measured by phosphorylated and total HSP27, in FSHD patients in blood and muscle. In the first cohort, 10 healthy volunteers were randomized to a single oral dose of losmapimod (n=8) 7.5 mg followed by a single oral dose of 15 mg after a wash out period or to single oral dose placebo (n=2) in both dosing periods. In the second cohort, 15 FSHD patients were randomized and treated with placebo (n=3) or losmapimod 7.5 mg (n=6) or 15 mg (n=6) taken orally twice daily for 14 days. The third cohort was open label with five FSHD patients treated with losmapimod 15 mg twice daily for 14 days. Biopsies of normal appearing (second cohort) and actively involved (STIR+) muscle (third cohort) were performed at baseline and during treatment.

Dose-dependent and sustained target engagement was observed in blood with losmapimod. Evidence of target engagement was also observed in skeletal muscle biopsies. Consistent with previously reported safety data, losmapimod was well tolerated with no serious adverse events (SAEs). Similar tolerability, safety and PK were observed in healthy volunteers and patients with FSHD at the two doses examined. This safety data is consistent with previously reported data from more than 3,500 healthy volunteers and patients treated with losmapimod across multiple other indications.

These data support the selection of the 15 mg dose of losmapimod taken orally twice daily in the Company's ongoing Phase 2b randomized, double-blind, placebo-controlled 24-week clinical trial, ReDUX4, as well as its Phase 2 open-label study. Both Phase 2 trials completed enrollment in February 2020.

Fulcrum plans to hold a separate webcast event in the Spring to discuss the abstracts that were accepted for poster presentation at the Muscular Dystrophy Association meeting which was postponed due to the COVID-19 pandemic. Further details will be announced in the coming weeks.

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 Losmapimod
Losmapimod is a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor that was exclusively in-licensed from GSK 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. Fulcrum is currently conducting Phase 2 trials investigating the safety, tolerability, and efficacy of losmapimod to treat the root cause of FSHD.

About Fulcrum Therapeutics
Fulcrum Therapeutics is a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases in areas of high unmet medical need. Fulcrum's proprietary product engine identifies drug targets which can modulate gene expression to treat the known root cause of gene mis-expression. The company has advanced losmapimod to Phase 2 clinical development for the treatment of facioscapulohumeral muscular dystrophy (FSHD) and has completed extensive pre-clinical research for FTX-6058 for the treatment of sickle cell disease and beta-thalassemia.

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, the timing of availability of clinical trial data and the Company's planned presentations. 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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