Fulcrum Therapeutics to Present New Data from the Open Label Extension of Phase 2 ReDUX4 Study at the World Muscle Society (WMS) Congress in Halifax, Canada

October 12, 2022 at 7:30 AM EDT

- 96-week findings support losmapimod as a disease-modifying therapy for FSHD

- U.S. Food and Drug Administration (FDA) granted Fast Track Designation in 2021

- Industry Symposium on October 12, 2022, at 4:30pm EDT

CAMBRIDGE, Mass., Oct. 12, 2022 (GLOBE NEWSWIRE) -- Fulcrum Therapeutics, Inc® (Nasdaq: FULC), a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases, announced today that new data from the open label extension (OLE) portion of the Phase 2 ReDUX4 study of losmapimod for the treatment of FSHD will be featured in a poster presentation at the World Muscle Society (WMS) Hybrid Congress taking place October 11-15 in Halifax, Canada. Fulcrum will also host a symposium entitled "*Measuring Progression in FSHD: Implications for Clinical Trials,"* featuring an overview of the OLE data on October 12, 2022, at the Halifax Convention Center.

ReDUX4 was a 48-week, placebo-controlled study that enrolled 80 participants between the ages of 18-65 with genetically confirmed FSHD1 (Ricci score 2-4). Study participants were randomized 1:1 to receive 15 mg losmapimod twice daily or placebo. Following the initial 48-week study period, all participants were given the option to enroll in the OLE portion of the study during which all participants received losmapimod. Of the 77 participants who completed the initial 48-week study, 99% (n=76) enrolled in the OLE. At week 96, 74 (97%) participants remained on treatment.

Data from the OLE support findings that losmapimod modifies FSHD disease progression and preserves or improves muscle function. Patients who crossed over to losmapimod treatment from the placebo arm and remained on treatment through 96 weeks (n= 36) demonstrated trends of slowing or stopping disease progression as measured by reachable workspace (RWS). Participants who originally received losmapimod and remained on therapy (n=38), continued to show slowing or stopping of disease progression and demonstrated improvement in muscle function, as measured by RWS. Losmapimod maintained a favorable safety profile and was generally safe and well tolerated. No treatment-related serious adverse events (SAEs) or treatment-emergent adverse events (TEAEs) leading to study drug discontinuation were reported through 96 weeks of dosing.

"Every FSHD patient faces relentless and accumulating muscle and functional loss. These long-term data further demonstrate that losmapimod can provide meaningful benefits to patients living with this relentless, debilitating disease," said Bryan Stuart, chief executive officer at Fulcrum. "The sustained ability to slow or halt the progression of FSHD over two years underscores the significance of our Phase 3 REACH trial and the potential of losmapimod to be the first approved treatment for FSHD."

Fulcrum is currently investigating losmapimod in the ongoing Phase 3 REACH trial. For more information about the trial please visit https://clinicaltrials.gov/ct2/show/NCT05397470.

Additional Poster Presentation Information
All posters will be presented on October 14th at 1:30 EDT/14:30 ADT

- **Title:** Results from 96 Weeks of Dosing from the Open-Label Extension of a Phase 2 Trial of Losmapimod in Subjects with FSHD: ReDUX4
  Presenter: Leo H. Wang MD PhD, University of Washington *(virtual presentation)*
- **Title:** Design of REACH: Phase 3 Randomized, Double-Blind, Placebo-Controlled, 48-Week Study of the Efficacy and Safety of Losmapimod in FSHD
  Presenter: Rabi Tawil, MD, University of Rochester
- **Title:** Reachable Workspace to Evaluate Efficacy of Losmapimod in Subjects with FSHD in Two Phase 2 Studies
  Presenter: Rabi Tawil, MD, University of Rochester
- **Title:** Annualized Rates of Change from A Phase 2, Randomized, Double-Blind, Placebo-Controlled, 48-Week Study of Losmapimod in Subjects with FSHD: ReDUX4
  Presenter: Rabi Tawil, MD, University of Rochester
- **Title:** Muscle Ultrasound in an Open-Label Study of Losmapimod in Subjects with FSHD1
  Presenter: Jenny Shoskes, PharmD, Fulcrum Therapeutics; Joost Kools MD, Radboud University Medical Center
- **Title:** Feasibility of measuring functional performance of FSHD patients using wearable sensors to quantify physical activity
  Presenter: Jenny Shoskes, PharmD, Fulcrum Therapeutics; Joost Kools MD, Radboud University Medical Center
- **Title:** Safety and Tolerability of Losmapimod for the Treatment of FSHD
  Presenter: Jenny Shoskes, PharmD, Fulcrum Therapeutics

About FSHD
FSHD is a serious, rare, progressive, and debilitating disease that is caused by an abnormal expression of the DUX4 gene, which results in skeletal muscle being replaced with fat. Patients with FSHD experience progressive muscle weakness leading to significant impairment in functioning, including the inability to use their upper limbs, communicate via facial expression, and walk unassisted.

About Losmapimod

Losmapimod is an investigational, selective p38α/β mitogen activated protein kinase (MAPK) inhibitor. Fulcrum exclusively in-licensed losmapimod from GSK following Fulcrum's discovery of the role of p38α/β inhibitors in the reduction of DUX4 expression and an extensive review of known compounds. Results reported from the ReDUX4 trial demonstrated slowed disease progression and improved function, including positive impacts on upper extremity strength, supporting losmapimod's potential to be a transformative therapy for the treatment of FSHD. Although losmapimod had never previously been explored in muscular dystrophies, it had been evaluated in more than 3,600 subjects in clinical trials across multiple other indications, with no safety signals attributed to losmapimod. Losmapimod has been granted FDA Fast Track designation and Orphan Drug Designation for the treatment of FSHD.

About REACH
REACH is a randomized, double- blind, placebo-controlled, multi-national trial to evaluate the efficacy and safety of losmapimod for the treatment of FSHD. Patients will be randomized 1:1 to receive either losmapimod, administered orally as a 15 mg tablet twice a day, or placebo, and evaluated over a 48-week treatment period. The primary endpoint of the study is the absolute change from baseline in Reachable Workspace (RWS). Secondary endpoints include muscle fat infiltration (MFI), Patient Global Impression of Change (PGIC), and Quality of Life in Neurological Disorders of the upper extremity (Neuro QoL UE). REACH will also include patient-centered assessments of healthcare utilization.

About ReDUX4
ReDUX4 was an equally randomized, double-blind, placebo-controlled multicenter international Phase 2b clinical trial in 80 participants with FSHD designed to investigate the efficacy and safety of oral administration of losmapimod 15 mg twice per day. As a result of the COVID-19 pandemic, Fulcrum announced in May 2020 that the trial had been extended from 24 to 48 weeks to ensure the safety of participation during the pandemic. This extension also enabled the collection of safety and efficacy data over a longer time period. Over the course of the trial, there were three discontinuations, none of which were assessed to be related to study drug. Following the completion of the trial, 99% of eligible participants elected to continue in the Open Label Extension trial.

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 two lead programs in clinical development are losmapimod, a small molecule for the treatment of facioscapulohumeral muscular dystrophy (FSHD), and FTX-6058, a small molecule designed to increase expression of fetal hemoglobin for the treatment of sickle cell disease and other hemoglobinopathies, including beta-thalassemia. Fulcrum's proprietary product engine, FulcrumSeek™, identifies drug targets that can modulate gene expression to treat the known root cause of gene mis-expression. For more information, visit www.fulcrumtx.com and follow us on Twitter @FulcrumTx and LinkedIn.

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. All statements, other than statements of historical facts, contained in this press release are forward-looking statements, including statements regarding the RReDUX4 trial, the REACH trial, losmapimod's potential as a therapy for FSHD, the ability of the selected endpoints to support regulatory approval and the sufficiency of Fulcrum's cash resources. 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 continue to advance its product candidates in clinical trials; initiate and enroll clinical trials on the timeline expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials of losmapimod, FTX-6058 and its other product candidates; 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 Fulcrum'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 Fulcrum's most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent Fulcrum's views as of the date hereof and should not be relied upon as representing Fulcrum's views as of any date subsequent to the date hereof. Fulcrum anticipates that subsequent events and developments will cause Fulcrum's views to change. However, while Fulcrum may elect to update these forward-looking statements at some point in the future, Fulcrum specifically disclaims any obligation to do so.

Contact:

REACH trial information
clinicaltrials@fulcrumtx.com

Investors:
Stephanie Ascher
Stern Investor Relations, Inc.
stephanie.ascher@sternir.com
212-362-1200

Media:
Dee Smith
Executive Director, Corporate Communications
dsmith@fulcrumtx.com
202-746-1324