Fulcrum Therapeutics™ Announces Multiple Presentations During the Virtual Congress of the World Muscle Society

September 20, 2021

– Presentations highlight progress in the development of losmapimod for FSHD –

CAMBRIDGE, Mass., Sept. 20, 2021 (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 it will present multiple posters and presentations on losmapimod for facioscapulohumeral muscular dystrophy (FSHD) during the Virtual Congress of the World Muscle Society. These results highlight progress made in the development of losmapimod for the treatment of FSHD as well as imaging modalities for the management of FSHD.

"FSHD is a serious, relentless and debilitating disease for which there are currently no approved therapies," said Chris Morabito, MD, Fulcrum's chief medical officer. "The results from the Phase 2b ReDUX4 trial show clinically relevant benefit across multiple structural, functional and patient reported endpoints with losmapimod and represent a major advance for the potential treatment of FSHD. These data being presented support the benefit/risk of losmapimod as a disease-modifying therapy and its continued development. We remain on track to meet with regulators in the fourth quarter of this year and to provide an update on the clinical path forward in the first quarter of 2022."

Fulcrum-Sponsored Symposium:
Advances in Assessment of FSHD and Clinical Trial Results with Losmapimod
Date/Time: Monday, September 20, 12:00pm – 1:30pm EDT
Presenters:

- Jeffrey Statland, MD, PhD – University of Kansas Medical Center
- Michelle Mellion, MD – Fulcrum Therapeutics
- Rabi Tawil, MD – University of Rochester Medical Center
- Baziel van Engelen & Joost Kools – Radboud University Medical Center
- Chris Morabito, MD – Fulcrum Therapeutics

Oral Presentation:
A Phase 2, Randomized, Double-blind, Placebo-controlled, 48-Week Study of the Efficacy and Safety of Losmapimod in Subjects with FSHD: ReDUX4
Date/Time: Thursday, September 23rd, 10:30am – 10:40am EDT
Presenter:

- Rabi Tawil, MD – University of Rochester Medical Center

Poster Presentations:
Date/Time: Thursday, September 23rd, Available for viewing starting at 11:30am EDT
Posters will be available to registered conference attendees and will also be available in the "Publications" section of fulcrumtx.com.

Title: An Open-Label Study of Losmapimod to Evaluate the Safety, Tolerability, and Biomarker and Clinical Outcome Assessment Changes in Subjects with FSHD1
Author: Joost Kools – Radboud University Medical Center
Poster ID: EP 168

Title: Use of snRNA-seq to Characterize the Pathogenic Skeletal Muscle Microenvironment
Author: Anu Raman, Ph.D. – Fulcrum Therapeutics
Poster ID: EP 170

Title: Whole body MRI Quantitative Muscle Analysis to Evaluate Efficacy of Losmapimod in a Phase 2 Placebo-controlled Study in Subjects with FSHD (ReDUX4)
Author: Michelle Mellion, MD – Fulcrum Therapeutics
Poster ID: EP 330

Title: Quantitative Muscle Analysis in FSHD Using Whole-Body MRI: Composite Muscle Measurements for Cross-Sectional Analysis
Author: Michelle Mellion, MD – Fulcrum Therapeutics
Poster ID: EP 331

Title: Revolutionizing Drug Discovery in Genetically Defined Muscle Disease Using Single-Cell and High Dimensional Datasets
Author: Alejandro Rojas, Ph.D. – Fulcrum Therapeutics
Poster ID: EP 321

About FSHD
FSHD is a serious, rare, progressive and disabling disease for which there are no approved treatments. FSHD is characterized by muscle degeneration and fat infiltration, initially affecting movement of the face and eventually the arms, trunk and legs. Disease progression results in accumulation of disability, with many patients ultimately becoming dependent upon the use of a wheelchair for daily mobility. Impact on patients includes decreased ability to perform activities of daily living, maintain independence, and lost ability to function or work.

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 proprietary product engine, FulcrumSeek™, 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 3,600 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. Losmapimod has been granted U.S. Food and Drug Administration (FDA) Fast Track designation and Orphan Drug Designation for the treatment 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, FulcrumSeek™, 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). Fulcrum has also advanced FTX-6058, a small molecule designed to increase expression of fetal hemoglobin for the treatment of sickle cell disease and beta-thalassemia into Phase 1 clinical development.

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 potential advantages and therapeutic potential of the Company’s product candidates and planned meetings with regulatory agencies. 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; initiate and enroll clinical trials on the timeline expected or at all; correctly estimate the potential patient population and/or market for the Company’s product candidates; replicate in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials of losmapimod 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 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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