Fulcrum Therapeutics Announces Publication of Results from Phase 2b Clinical Trial of Losmapimod in Facioscapulohumeral muscular dystrophy (ReDUX4) in The Lancet Neurology

May 8, 2024 at 8:00 AM EDT

— Phase 2b ReDUX4 clinical trial indicates improvements in functional, structural, and patient-reported outcomes; findings informed the design and choice of efficacy endpoints in the ongoing Phase 3 clinical trial—

— Topline data for the Phase 3 REACH clinical trial of losmapimod in FSHD expected during 4Q'24—

CAMBRIDGE, Mass., May 08, 2024 (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 the publication of results from its Phase 2b clinical trial of losmapimod for the treatment of facioscapulohumeral muscular dystrophy (FSHD). The data are published in the peer-reviewed journal The Lancet Neurology.

FSHD is a serious, rare, and progressively disabling disease characterized by fat infiltration of skeletal muscle leading to muscular atrophy involving primarily the face, shoulder girdle, upper arms, abdomen, and lower limbs. It is caused by the aberrant expression of the DUX4 protein. It is characterized by accumulating muscle weakness and functional impairment. There are no approved disease-modifying treatments for FSHD.

"The publication of these results, which informed the design and choice of efficacy endpoints in our Phase 3 clinical trial, also provide important validation for the therapeutic potential of losmapimod," said Patrick Horn M.D., Ph.D., Fulcrum's chief medical officer. "Looking ahead, we remain on track to report topline data for REACH in the fourth quarter of 2024, which will bring us one step closer to addressing the high unmet needs of the FSHD patient community. With an unwavering commitment to our patients, we continue to take important steps toward a potential NDA filing and commercial launch for losmapimod."

While the primary endpoint of change in DUX4-driven gene expression in muscle biopsies did not show significant differences between the treatment and placebo groups, losmapimod was associated with improvements in structural and functional outcomes, including muscle fat infiltration and reachable workspace – a measure of shoulder girdle function, and patient-reported global impression of change when compared to placebo.

Losmapimod was also found to be well tolerated by trial participants. No serious adverse events related to the drug were reported, and there were no discontinuations of treatment due to adverse events.

In September 2023, Fulcrum announced the enrollment completion for the Phase 3 clinical trial evaluating losmapimod in patients with FSHD at sites in the United States, Canada, and Europe. The clinical trial remains on track with topline data expected in Q4 2024.

About the ReDUX4 Phase 2b Clinical Trial
The Phase 2b clinical trial, ReDUX4, enrolled 80 participants from the United States, Canada, and Europe between the ages of 18 and 65 with FSHD type 1 who were randomized to receive losmapimod or placebo orally at the dosage of 15 mg twice daily for 48 weeks.

About Losmapimod
Losmapimod is a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor. Fulcrum exclusively in-licensed losmapimod from GSK following the identification of the role of p38α/β inhibitors in the reduction of DUX4 aberrant expression. Results from the Phase 2b ReDUX4 clinical trial show that losmapimod has the potential to slow disease progression, improve upper extremity function and be a transformative therapy for the treatment of FSHD. Although losmapimod had never previously been tested in muscular dystrophies, it had been evaluated in more than 3,600 subjects in studies across multiple other indications with no safety signals attributed to losmapimod. Losmapimod has been granted U.S. Food and Drug Administration (FDA) Fast Track designation and Orphan Drug Designation for the treatment of FSHD.

About FSHD
FSHD is a serious, rare, debilitating disease characterized by fat infiltration of skeletal muscle leading to muscular atrophy involving primarily the face, shoulder girdle, upper arms, abdomen, and lower limbs. Patients progressively lose their ability to perform activities of daily living due to the loss of upper limb function, mobility and independence, and chronic pain. FSHD is one of the most common forms of muscular dystrophy and has an estimated patient population of 30,000 in the United States alone.

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 pociredir, formerly FTX-6058, a small molecule designed to increase expression of fetal hemoglobin for the treatment of sickle cell disease (SCD) and other hemoglobinopathies. 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 express or implied statements regarding timing of REACH topline data; losmapimod's potential to slow progression of FSHD; the losmapimod clinical program and potential for FDA approval as a therapy for FSHD; among others. 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; initiating, enrolling and reporting data from clinical trials on the timeline expected or at all; obtaining and maintaining necessary approvals from the FDA and other regulatory authorities; replicating in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials; obtaining, maintaining or

protecting intellectual property rights related to its product candidates; managing expenses; managing executive and employee turnover, including integrating a new CEO and CFO; and raising the substantial additional capital needed to achieve its business objectives, among others. 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.

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