Fulcrum Therapeutics® Presents Data Highlighting Reachable Workspace (RWS) as Relevant Functional Endpoint in Facioscapulohumeral Muscular Dystrophy (FSHD) at MDA Clinical and Scientific Conference

March 14, 2022 at 8:00 AM EDT

RWS has been correlated with ability to perform activities of daily living and maintain independence

Losmapimod shown to improve or preserve function as measured by RWS in two Phase 2 studies, supporting RWS as the primary endpoint in Phase 3 REACH trial

Company on track to initiate REACH in 2Q 2022

CAMBRIDGE, Mass., March 14, 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, today announced data demonstrating that Reachable Workspace (RWS) is a quantitative and relevant measurement of function that can be used to assess disease progression as well as response to treatment in people with facioscapulohumeral muscular dystrophy (FSHD). Data from two Phase 2 clinical trials also showed that losmapimod preserved or improved function in people with FSHD, as measured by RWS. These data are being presented this week at the 2022 Muscular Dystrophy Association (MDA) Clinical and Scientific Conference.

“FSHD typically moves from the upper body down, with almost universal involvement of the shoulder girdle, leading to profound decreases in the ability to perform activities of daily living,” said Judith Dunn, Ph.D., Fulcrum’s president of research and development. “RWS is a quantitative measurement of function that assesses shoulder and arm mobility that has been used in clinical research in other muscular dystrophies and diseases affecting the upper extremities. Growing evidence now supports its use in FSHD as a relevant and reliable endpoint that has been shown to correlate with how people function and feel, making it an ideal primary endpoint for our Phase 3 REACH trial.”

“There is a need for objective, sensitive, and clinically meaningful outcome measures in neuromuscular diseases, including FSHD, to support clinical development of new therapies and to monitor disease severity and progression,” said Jay J. Han, MD, professor and vice chair of Physical Medicine & Rehabilitation at University of California, Irvine, and one of the developers of RWS. “RWS uses 3D motion sensor technology to reliably and reproducibly measure upper extremity range of motion and has been shown across numerous studies to quantify and track when people are having difficulties performing activities of daily living and maintaining independence.”

People with FSHD consistently rank difficulty with use of their shoulders and proximal arms as the most prevalent and severe impairment impacting their quality of life. RWS evaluates shoulder and proximal arm mobility by utilizing 3D motion sensor technology to track upper limb trajectory across five regions. Fulcrum compared the effect of losmapimod to placebo using RWS in its ReDUX4 Phase 2b study and in an open-label Phase 2 study. In both studies, losmapimod was shown to preserve function and, in some instances, improve function, as measured by RWS.

“The progressive loss of range of motion in my shoulders and arms has had a tremendous impact on my life,” said Carden Wyckoff, a member of Fulcrum’s FSHD patient advisory board and the FSHD Society board of directors. “Reaching out to open a door, putting a pot of water on the stove, dressing myself, or picking up my cat has all become harder. As I continue to decline, I am looking ahead to needing caretaking, and that is scary. Reachable Workspace is a clinical endpoint that recognizes the impact that this loss of range of motion in our shoulders and arms has on the lives of people with FSHD, and critical for developing a drug that slows the progression of disease and allows me to keep my independence longer.”

Fulcrum plans to begin enrolling patients in its Phase 3 REACH clinical trial in the second quarter of 2022. REACH will be a randomized, double-blind, placebo-controlled, multi-national trial to evaluate the efficacy and safety of losmapimod for the treatment of FSHD. The trial is expected to enroll approximately 230 adults with 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. RWS is the primary endpoint of the trial. Secondary endpoints include muscle fat infiltration (MFI) measured by MRI, 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.

In addition to the presentation on RWS, Fulcrum has multiple presentations at the MDA conference demonstrating its scientific and clinical leadership in FSHD drug discovery and development. Fulcrum’s posters can be found on the company website at https://www.fulcrumtx.com/pipeline/#publications.

About FSHD
FSHD is a serious, rare, progressive and debilitating disease for which there are no approved treatments. It is characterized by fat infiltration of skeletal muscle leading to muscular atrophy involving primarily the face, scapula and shoulders, upper arms, and abdomen. Impact on patients includes profound decreases in the ability to perform activities of daily living, loss of upper limb function, loss of mobility and independence and chronic pain. FSHD is one of the most common forms of muscular dystrophy and has an estimated patient population of 16,000 to 38,000 in the United States alone.

About Reachable Workspace (RWS)
RWS is a quantitative measure of upper extremity range of motion and function. Specifically, it evaluates total shoulder and proximal arm mobility by utilizing 3D motion sensor technology. Preserving function, as assessed by RWS, is critical for maintaining abilities for self-care and other activities of daily living that directly influence quality of life. Based on published results, reachable workspace is an important measure of independence.

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 3,500 subjects in clinical trials 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 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. The company's proprietary product engine, FulcrumSeek™, identifies drug targets that 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. All statements, other than statements of historical facts, contained in this press release are forward-looking statements, including statements regarding the planned REACH trial including its expected start date and enrollment target, 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.

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