Fulcrum Therapeutics Presents Data for Potential FSHD Biomarker and Clinical Outcome Assessments at 2021 Muscular Dystrophy Association (MDA) Virtual Clinical & Scientific Conference

March 18, 2021 at 11:30 AM EDT

– Demonstrated Whole-Body MRI captures heterogeneity and provides key disease severity and progression information correlated with FSHD clinical endpoints –

– Demonstrated potential of FSHD-TUG and Emerald in-home assessments as accurate, low-burden clinical assessments of mobility for FSHD patients –

– Company on track to report data from Phase 2b ReDUX4 trial with losmapimod in FSHD in late-2Q 2021 –

CAMBRIDGE, Mass., March 18, 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 the presentation of new data related to the use of imaging biomarkers and clinical outcome assessments for facioscapulohumeral muscular dystrophy (FSHD) at the 2021 Muscular Dystrophy Association (MDA) virtual Clinical and Scientific Conference. Presentations included evaluation of disease severity and progression with whole body musculoskeletal magnetic resonance imaging (WB-MSK-MRI), FSHD-TUG, a modified Timed Up and Go (TUG) assessment for FSHD patients, and in-home passive measurements of mobility and sleep. The presentation and posters can be found on Fulcrum's website at https://www.fulcrumtx.com/pipeline/#publications.

"There is a critical need for accurate, low patient burden assessments that can effectively track disease severity and progression, and correlate with clinical outcomes in FSHD," said Michelle Mellion, M.D., Fulcrum's senior medical director. "The Whole Body-MSK MRI can capture the heterogeneity and provide important information about disease severity as it correlates with FSHD relevant clinical endpoints. This protocol is currently being used in our Phase 2 clinical trials of losmapimod. WB-MSK-MRI also may enable an individualized assessment of disease progression, offering a more efficient screening of potential therapies and better facilitate decisions in the development of new treatments. Additionally, Emerald and FSHD-TUG help capture key metrics in FSHD patients."

Fulcrum and AMRA Medical have developed a quantitative WB-MSK-MRI protocol and analysis algorithms to volumetrically measure fat replacement of skeletal muscle in FSHD to use in multi-site clinical trials. WB-MSK-MRI is non-invasive and captures a holistic evaluation of the skeletal musculature, identifying small quantitative changes in muscle health that correlate with functional measures in FSHD patients and enable an assessment of disease heterogeneity. In the study being presented, the protocol was performed and standardized at six sites where patients were screened, biopsies were taken between 1-4 weeks and 5-12 weeks, and a final MRI scan was conducted between weeks 5-12.

WB-MSK-MRI was shown to capture heterogeneity and provide important information about disease severity and progression in 17 patients. Of 618 muscles, 478 were analyzed. Good reproducibility was found across all muscles, with higher reproducibility in larger muscles. Results also showed strong cross-sectional correlation between Regional Composite Measurement, TUG, FSHD-TUG and Reachable Work Space (RWS) assessments.

Fulcrum has also identified FSHD-TUG as a potential clinical outcome assessment of mobility in FSHD patients. In a separate study presented at the MDA meeting, FSHD-TUG demonstrated a correlation with clinical severity and patient reported physical function and lower extremity function. Existing assessments largely focus on walking parameters as a test of function, but most FSHD patients report difficulty getting up from lying down position. The FSHD-TUG was optimized to also include evaluation of sit to supine (laying on back) and the reverse.

The study was conducted to determine the reliability and validity of TUG, a traditional measure of mobility, and FSHD-TUG, over a one-year period. Twenty-two FSHD patients and twenty healthy volunteers were enrolled. Patients were screened and stratified into groups, and each group performed two trials of the classic TUG and FSHD TUG on two separate visits one week apart. A total of four trials over two separate visits were recorded for each participant. On average, FSHD subjects took approximately twice the time to complete TUG, FSHD-TUG, and components of the FSHD-TUG compared to healthy volunteers. These results support the reliability and validity of FSHD-TUG as a potential clinical assessment of mobility for ongoing and future clinical trials.

Study results also highlight the use of in-home monitoring from Emerald, a contactless radio-wave-based home monitoring system, to enable a large number of passively derived measurements of clinical progression including gait speed, time in bed, sleep and vital signs. Ten FSHD patients were observed in their homes for three months. In addition to in-home gait speed, novel metrics including assessments of sleep schedule variability and eTUG (the time from motion initiation within the bed to moving two meters away from the bed edge) were derived. Emerald's in-home measurements were strongly correlated with clinical metrics. As the number of measurements increased, Emerald's metrics became increasingly sensitive and were shown to detect smaller fluctuations in disease progression.

"As we advance our clinical development program for losmapimod for the treatment of FSHD, we are also continually working to improve our ability to assess disease progression based on the most clear and effective outcome measures," said Chris Moxham, Ph.D., Fulcrum's chief scientific officer. "Assessments based on musculoskeletal MRI and clinical outcomes may be key to demonstrating patient benefit in this population. We expect full data from our Phase 2b ReDux4 trial late in the second quarter of this year, which will provide additional insights to inform the path forward for losmapimod in the treatment of FSHD."

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). 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 Fulcrum's product candidates, initiation and enrollment of clinical trials and availability of clinical trial data, and the Company's ability to fund its operations with cash on hand. 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; 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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