Fulcrum Therapeutics Reports Recent Business Highlights and First Quarter 2021 Financial Results

May 6, 2021

– On track to present data from Phase 2b ReDUX4 trial with losmapimod in facioscapulohumeral muscular dystrophy (FSHD) at virtual FSHD International Research Congress in June 2021 –

– On track to report data from Phase 1 trial in healthy adult volunteers with FTX-6058 for sickle cell disease in mid-2021 –

– Conference call scheduled for 8:00 a.m. ET today –

CAMBRIDGE, Mass., May 06, 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 provided a business update and reported financial results for the first quarter of 2021.

"Fulcrum has continued to make great progress in advancing our business and progressing our pipeline in the first quarter," said Bryan E. Stuart, president and chief executive officer. "We are on track to report data from ReDUX4 in FSHD later this quarter. Our Phase 1 trial in healthy adult volunteers with FTX-6058 for sickle cell disease continues to move forward with the initiation of the multiple ascending dose cohort. Our team continues to optimize the potential of FulcrumSeek™, our proprietary product engine, driven by our focus on the patient and our ability to rapidly identify novel, high quality targets that modulate the root cause of genetically defined rare diseases. In addition, we have expanded our leadership team to include Dr. Judith Dunn, President of Research and Development, and today announced that Dr. Chris Morabito has been appointed Chief Medical Officer. With these important advances and cash runway that takes us into the fourth quarter of 2022, we believe we are well positioned to continue to build on our momentum to bring important therapies to patients with genetically defined rare diseases."

Recent Business Highlights

- On track to present data from ReDUX4, a Phase 2b trial of losmapimod, a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor, in FSHD at the virtual FSHD International Research Congress taking place June 24-25, 2021.
    - Data will include the primary endpoint, reduction from baseline of DUX4-driven gene expression, as well as a pre-specified sensitivity analysis assessing biopsies with the highest pre-treatment level of DUX4-driven gene expression. Additional data to be reported include secondary endpoints evaluating disease progression via skeletal muscle MRI, exploratory endpoints assessing muscle function measures and patient reported outcomes.
    - Continued evaluation of the Phase 2 Open Label Study.
- On track to report data from the Phase 1 trial in healthy adult volunteers with FTX-6058 in development for sickle cell disease (SCD) in mid-2021, and to begin dosing patients with SCD in a clinical trial by year end.
    - FTX-6058, a highly potent small molecule EED inhibitor, is designed to induce expression of fetal hemoglobin (HbF) in red blood cells following oral administration to compensate for the mutated adult hemoglobin associated with hemoglobinopathies, including SCD and beta-thalassemia.
    - Preclinical data generated in CD34+ cells from healthy and SCD donors with FTX-6058 showed an increase in HbF levels up to approximately 30% of total hemoglobin, indicating the potential to have a significant impact on patients with sickle cell disease.
    - US patent 10,973,805 issued, providing composition of matter coverage for FTX-6058 until 2040.
- Multiple scientific meeting presentations
    - Presented new data related to the use of imaging biomarkers and clinical outcome assessments for FSHD at the virtual Muscular Dystrophy Association Clinical and Scientific Conference. Presentations included development of the whole-body musculoskeletal MRI (WB-MSK-MRI) protocol. Data showed that WB-MSK-MRI can capture heterogeneity and provide important information about disease severity. Meaningful composite MRI measurements demonstrated correlation with relevant FSHD clinical endpoints.
    - Presented the medicinal chemistry strategy for FTX-6058 at the First Time Disclosure Session at the American Chemical Society (ACS) Spring 2021 National Meeting. The presentation included initial pharmacokinetic data from the single ascending dose cohort of the Phase 1 trial in healthy adult volunteers.
- Advanced FulcrumSeek discovery efforts and strategic collaborations with Acceleron and MyoKardia, a wholly owned subsidiary of Bristol-Myers Squibb Company.
- Senior management updates:
    - *CSO transition:* On January 19, 2021, Fulcrum announced that Christopher Moxham, Ph.D. was promoted to chief scientific officer and Owen Wallace, Ph.D. stepped down from his role as chief scientific officer, each effective February 5, 2021. Dr. Wallace was appointed to Fulcrum's Scientific Advisory Board.
    - *CEO transition:* On March 4, 2021, Fulcrum announced that Bryan E. Stuart was promoted to president and chief

executive officer and was appointed to Fulcrum's Board of Directors following the retirement of Robert J. Gould, Ph.D., each effective March 31, 2021. Dr. Gould continues to serve on Fulcrum's Board and was appointed to the Scientific & Technology committee.

- *President R&D:* On March 24, 2021, Fulcrum announced that Judith A. Dunn, Ph.D. was appointed President of Research and Development, effective April 1, 2021.
- *Chief Medical Officer:* On May 6, 2021, Fulcrum announced that Christopher J. Morabito, M.D. has been appointed Chief Medical Officer, effective May 10, 2021.

First Quarter 2021 Financial Results

- **Cash Position:** As of March 31, 2021, cash, cash equivalents, and marketable securities were $143.9 million, as compared to $112.9 million as of December 31, 2020. Based on current plans, the company expects that its existing cash, cash equivalents, and marketable securities will be sufficient to enable it to fund its operating expenses and capital expenditure requirements into the fourth quarter of 2022.
- **Collaboration Revenues:** Collaboration revenue was $4.8 million for the first quarter of 2021, as compared to $0.8 million for the first quarter of 2020. The increase in collaboration revenue was due to the execution of the company's collaboration and license agreement with MyoKardia in July 2020, as well as due to an increase in collaboration revenue associated with the company's collaboration and license agreement with Acceleron.
- **R&D Expenses:** Research and development expenses were $16.3 million for the first quarter of 2021, as compared to $14.5 million for the first quarter of 2020. The increase of $1.8 million was primarily due to increased costs to support the company's ongoing and planned clinical trials.
- **G&A Expenses:** General and administrative expenses were $5.5 million for the first quarter of 2021, as compared to $5.1 million for the first quarter of 2020. The increase of $0.4 million was primarily due to increased employee-compensation costs to support the growth of the organization, including increased stock-based compensation expense.
- **Net Loss:** Net loss was $17.0 million for the first quarter of 2021, as compared to a net loss of $18.5 million for the first quarter of 2020.

Conference Call and Webcast

Fulcrum Therapeutics, Inc. will host a conference call and webcast today at 8:00 a.m. ET to discuss the Company's first quarter 2021 recent business highlights and financial results. The webcast will be accessible through the Investor Relations section of Fulcrum's website at www.fulcrumtx.com. Following the live webcast, an archived replay will also be available.

Dial-in Number
U.S./Canada Dial-in Number: 800-527-6973
International Dial-in Number: 470-495-9162
Conference ID: 5767008

Replay Dial-in Number: 855-859-2056
Replay International Dial-in Number: 404-537-3406
Conference ID: 5767008

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. Losmapimod has been evaluated in more than 3,600 subjects in clinical research across multiple indications, including in several Phase 2 trials and a large Phase 3 trial in acute myocardial infarction. No safety signals were attributed to losmapimod in any of these trials. In 2020, the company received U.S. and European Orphan Drug Designation for losmapimod for the treatment of FSHD. Fulcrum is currently conducting Phase 2 trials investigating the safety, tolerability, and efficacy of losmapimod to treat the root cause of FSHD.

About Sickle Cell Disease

Sickle cell disease (SCD) is a genetic disorder of the red blood cells caused by a mutation in the HBB gene. This gene encodes a protein that is a key component of hemoglobin, a protein complex whose function is to transport oxygen in the body. The result of the mutation is less efficient oxygen transport and the formation of red blood cells that have a sickle shape. These sickle shaped cells are much less flexible than healthy cells and can block blood vessels or rupture cells. SCD patients typically suffer from serious clinical consequences, which may include anemia, pain, infections, stroke, heart disease, pulmonary hypertension, kidney failure, liver disease and reduced life expectancy.

About FTX-6058

FTX-6058 is a highly potent small molecule inhibitor of Embryonic Ectoderm Development (EED) capable of inducing robust HbF protein expression in cell and murine models. Fulcrum believes the pharmacokinetics and human dose simulations support that FTX-6058 may be given as a once daily oral compound. The validation of EED as a target for sickle cell disease and the discovery of FTX-6058 as a novel HbF-inducing small molecule were conducted using Fulcrum's proprietary product engine. Preclinical data with FTX-6058 showed an increase in HbF levels up to approximately 30% of total hemoglobin. Fulcrum is conducting a Phase 1 trial with FTX-6058 in healthy adult volunteers.

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, FTX-6058 and its other product candidates; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; 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.

Fulcrum Therapeutics, Inc.

Selected Consolidated Balance Sheet Data

(In thousands)

(Unaudited)

	March 31, 2021	December 31, 2020
Cash, cash equivalents, and marketable securities	$ 143,856	$ 112,914
Working capital(1)	124,356	92,785
Total assets	156,476	129,577
Total stockholders' equity	127,754	95,181

(1) We define working capital as current assets minus current liabilities.

Fulcrum Therapeutics, Inc.

Consolidated Statements of Operations

(In thousands, except per share data)

(Unaudited)

	Three Months Ended March 31,	
	2021	**2020**
Collaboration revenue	$ 4,789	$ 750
Operating expenses:		
Research and development	16,334	14,482
General and administrative	5,498	5,064
Total operating expenses	21,832	19,546
Loss from operations	(17,043)	(18,796)
Other income, net	44	344
Net loss	$ (16,999)	$ (18,452)
Net loss per share, basic and diluted	$ (0.54)	$ (0.81)
Weighted-average common shares outstanding, basic and diluted	31,510	22,719

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