Fulcrum Therapeutics Reports Recent Business Highlights and First Quarter 2020 Financial Results

May 13, 2020

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

CAMBRIDGE, Mass., May 13, 2020 (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 2020.

"Despite these unprecedented times, the first quarter was a period of important progress for Fulcrum and the fundamentals of our business remain strong," said Robert J. Gould, Ph.D., president and chief executive officer. "I am proud of our continued commitment to patients and the dedication demonstrated by our employees in these challenging times. In the wake of COVID-19, a number of our clinical trial sites postponed their activities. Our team acted swiftly to minimize the health risks to patients, families and healthcare professionals involved in our studies of losmapimod in the treatment of facioscapulohumeral dystrophy (FSHD). We amended our Phase 2b trial, ReDUX4, to extend the trial from 24 to 48 weeks, added an interim analysis for subjects who underwent their 16-week biopsy as originally planned, and added a 36-week biopsy for patients who cannot undergo their 16-week biopsy. We believe these changes will enable patients and investigators to continue participation in the trial and will allow us to collect the essential data needed to evaluate the potential efficacy and safety of losmapimod for the treatment of FSHD."

Recent Business Highlights

- Amended ReDUX4, a Phase 2b trial of losmapimod, a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor, to accommodate COVID-19 impact; extended the trial from 24 to 48 weeks, adding a 36-week biopsy for those subjects unable to undergo their 16-week biopsy, and included an interim analysis on patients who completed their 16-week biopsy as planned in the original protocol.
    - ReDUX4 enrollment completed.
    - ReDUX4 open label extension initiated.
    - Data from interim analysis expected in the third quarter of 2020.
- Received U.S. and European Orphan Designation for losmapimod in FSHD.
- Completed investigational new drug application (IND)-enabling studies, including toxicology work with FTX-6058.
    - Remain on track to initiate Phase 1 trial in the second half of 2020.
    - FTX-6058 is an oral small molecule therapeutic discovered by Fulcrum and designed to induce expression of fetal hemoglobin (HbF) in red blood cells to compensate for the mutated adult hemoglobin in sickle cell disease.
- Presented evidence of dose-dependent target engagement observed in skeletal muscle with losmapimod 15 mg twice per day in a Phase 1 trial during the Muscular Dystrophy Association virtual clinical trials session.
    - Builds on previously announced dose-dependent pharmacokinetics and target engagement in blood.
- Continued evolution of Fulcrum's proprietary product engine, which is designed to identify drug targets, programs and clinical development candidates in a broad range of genetically defined diseases (FulcrumSeek), and initiated research activities under the Acceleron collaboration.

ReDUX4 Trial Amendment

ReDUX4 is a randomized, double-blind, placebo-controlled multicenter international Phase 2b clinical trial in 80 subjects with FSHD to investigate the efficacy and safety of oral administration of losmapimod 15 mg twice per day. The primary endpoint is to evaluate the reduction of DUX4-driven gene expression in affected skeletal muscle biopsies. The original design of ReDUX4 included a muscle biopsy at week 16 during the 24-week treatment period followed by an open label extension. Twelve of the 80 subjects have completed the 24-week treatment period and rolled over to the open label extension portion of the trial.

As a result of the COVID-19 pandemic, Fulcrum has extended the trial from 24 to 48 weeks through a protocol amendment to ensure the safety of the subjects and to allow for the opportunity for a biopsy at week 16 as originally intended or at week 36. Approximately 68 subjects who did not complete the original 24-week treatment period remain active in the randomized portion of the trial. An interim analysis of approximately 25 subjects who completed their 16-week biopsy will be conducted. The Company expects to report data from this interim analysis in the third quarter of 2020. The extension from 24 to 48 weeks also allows for a longer assessment in a placebo-controlled design of the skeletal muscle MRI secondary endpoint and the various exploratory clinical endpoints, such as reachable workspace, FSHD-Timed Up and GO, muscle function measures and patient reported outcomes. Topline data from approximately 80 patients is expected in the first quarter of 2021. Fulcrum believes the amendment to the trial provides flexibility to address the challenges presented by the COVID-19 pandemic and supports collection of efficacy and safety data to support continued discussions with health authorities regarding potential registration strategies.

First Quarter 2020 Financial Results

- **Cash Position:** As of March 31, 2020, cash, cash equivalents, and marketable securities were $81.2 million, as compared to $96.7 million as of December 31, 2019. Based on its 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 third quarter of 2021.
- **R&D Expenses:** Research and development expenses were $14.5 million for the first quarter of 2020, as compared to $34.6 million for the first quarter of 2019. Research and development expenses for the first quarter of 2019 include $25.6 million of one-time costs incurred associated with the issuance of Series B convertible preferred stock under the Company's license agreement with GSK for losmapimod. Excluding these one-time costs, the increase of $5.5 million was

primarily due to increased costs related to the advancement of losmapimod for the treatment of FSHD, as well as increased personnel-related costs to support the growth of Fulcrum's research and development organization.

- **G&A Expenses:** General and administrative expenses were $5.1 million for the first quarter of 2020, as compared to $2.6 million for the first quarter of 2019. The increase of $2.5 million was primarily due to increased personnel-related costs to support the growth of our organization, as well as increased consulting and professional fees associated with operating as a public company.
- **Net Loss:** Net loss was $18.5 million for the first quarter of 2020, as compared to a net loss of $36.8 million for the first quarter of 2019.

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 2020 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: 8297069

Replay Dial-in Number: 855-859-2056
Replay International Dial-in Number: 404-537-3406
Conference ID: 8297069

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 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 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) and has completed extensive preclinical research for FTX-6058 for the treatment of sickle cell disease and beta-thalassemia.

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 timing of availability of clinical trial data and initiation of clinical trials, 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; replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of losmapimod 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, 2020	December 31, 2019
Cash, cash equivalents, and marketable securities	$ 81,207	$ 96,713
Working capital[(1)]	70,141	87,943
Total assets	94,856	110,439
Total stockholders' equity	70,631	87,153

(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,	
	2020	2019
Collaboration revenue	$ 750	$ —
Operating expenses:		
Research and development	14,482	34,629
General and administrative	5,064	2,598
Total operating expenses	19,546	37,227
Loss from operations	(18,796)	(37,227)
Other income, net	344	384
Net loss	$ (18,452)	$ (36,843)
Cumulative convertible preferred stock dividends	—	(3,041)
Net loss attributable to common stockholders	$ (18,452)	$ (39,884)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.81)	$ (24.29)
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted	22,719	1,642

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