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

August 10, 2021

– Reported positive interim results from ongoing Phase 1 trial in healthy adult volunteers with FTX-6058 for sickle cell disease demonstrating proof of mechanism and proof of biology –

– Company plans to initiate enrollment in a Phase 1b clinical trial in sickle cell patients in 4Q 2021 –

– Cash runway into 1Q 2023 –

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

CAMBRIDGE, Mass., Aug. 10, 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 second quarter of 2021.

"This quarter was marked by meaningful progress, particularly as we furthered our efforts with our lead candidates for FSHD and sickle cell disease," said Bryan Stuart, president and chief executive officer. "We made groundbreaking progress with losmapimod and reported clinical data from ReDUX4 demonstrating slowed disease progression and improved function in FSHD. We are also pleased with the dose proportional target engagement data, fetal hemoglobin (HBG) mRNA induction and F-reticulocyte increases that we observed in our ongoing Phase 1 trial in healthy adult volunteers with FTX-6058, demonstrating proof of mechanism and proof of biology. These results, along with the safety, tolerability and pharmacokinetics observed to date, reinforce our belief in FTX-6058's potential to be a best-in-class treatment for select hemoglobinopathies. 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, we are on track to submit two investigational new drug applications (INDs) by the end of the first quarter of 2023. With these important advances and cash runway that takes us into the first quarter of 2023, 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

- Reported positive interim results today from the ongoing single- and multiple-ascending dose (SAD and MAD) Phase 1 trial in healthy adult volunteers with FTX-6058. FTX-6058 is an investigational, potent and selective small molecule inhibitor of EED designed to induce expression of fetal hemoglobin (HbF) with the potential to treat hemoglobinopathies, such as sickle cell disease and beta-thalassemia.
    - Results from the MAD portion of the trial demonstrated proof of biology as evidenced by a dose proportional induction in HBG mRNA and accompanying increases in HbF-containing reticulocytes (F-reticulocytes). At 10mg, the highest dose studied to date, the mean changes were 4.5-fold and 4.2-fold, respectively. The increases in F-reticulocytes indicate that the HBG mRNA increases observed with FTX-6058 treatment are translating to HbF protein production.
    - All FTX-6058 doses from the MAD portion of the trial achieved maximal target engagement.
    - FTX-6058 was generally well-tolerated with no serious adverse events observed to date.
    - Fulcrum plans to initiate enrollment in a Phase 1b clinical trial in sickle cell patients with FTX-6058 in the fourth quarter of 2021.
    - Fulcrum plans to submit an IND in non-sickle cell disease hemoglobinopathies (e.g., beta thalassemia) by year-end 2021.
- Data reported in June from ReDUX4, a Phase 2b trial of losmapimod, a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor, demonstrated slowed disease progression and improved function in FSHD.
    - Results showed clinically relevant and nominally statistically significant benefits versus placebo on multiple measures of structural and functional FSHD disease progression and patient reported outcomes at 48 weeks. Consistent with the previously reported interim analyses, the primary endpoint was not met.
    - Losmapimod was generally well-tolerated, with no drug-related serious adverse events reported.
    - Fulcrum plans to meet with health authorities, including the U.S. Food and Drug Administration (FDA), in the second half of 2021 to determine the regulatory path for losmapimod in FSHD.
- 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 SAD 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.

- Mani Sundararajan, Ph.D., joined Fulcrum in July 2021 as Senior Vice President, Technical Operations.
- Christopher J. Morabito, M.D. joined Fulcrum in May 2021 as Chief Medical Officer.
- Judith A. Dunn, Ph.D. joined Fulcrum in April 2021 as President of Research and Development.

Second Quarter 2021 Financial Results

- **Cash Position:** As of June 30, 2021, cash, cash equivalents, and marketable securities were $125.6 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 first quarter of 2023.

- **Collaboration Revenue:** Collaboration revenue was $4.4 million for the second quarter of 2021, as compared to $2.0 million for the second 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 $17.4 million for the second quarter of 2021, as compared to $12.8 million for the second quarter of 2020. The increase of $4.6 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 $6.7 million for the second quarter of 2021, as compared to $5.1 million for the second quarter of 2020. The increase of $1.6 million was primarily due to increased employee-compensation costs to support the growth of the organization, including increased stock-based compensation expense, as well as increased professional services costs.

- **Net Loss:** Net loss was $19.6 million for the second quarter of 2021, as compared to a net loss of $15.7 million for the second 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 second 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: 3291056

Replay Dial-in Number: 855-859-2056
Replay International Dial-in Number: 404-537-3406
Conference ID: 3291056

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, FulcrumSeek, 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, the Company's planned meetings with regulatory agencies, the Company's ability to submit an IND by the end of 2021 and the Company's ability to submit two INDs by the end of the first quarter of 2023, 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)

	June 30, 2021	December 31, 2020
Cash, cash equivalents, and marketable securities	$ 125,550	$ 112,914
Working capital[(1)]	106,001	92,785
Total assets	137,879	129,577
Total stockholders' equity	110,890	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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Collaboration revenue	$ 4,381	$ 2,000	$ 9,170	$ 2,750
Operating expenses:				
Research and development	17,378	12,775	33,712	27,257
General and administrative	6,685	5,149	12,183	10,213
Total operating expenses	24,063	17,924	45,895	37,470
Loss from operations	(19,682)	(15,924)	(36,725)	(34,720)
Other income, net	34	239	78	583
Net loss	$ (19,648)	$ (15,685)	$ (36,647)	$ (34,137)
Net loss per share, basic and diluted	$ (0.60)	$ (0.66)	$ (1.14)	$ (1.47)
Weighted-average common shares outstanding, basic and diluted	32,636	23,854	32,076	23,287

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