# Fulcrum Therapeutics® Reports Recent Business Highlights and Third Quarter 2021 Financial Results

November 4, 2021 at 7:00 AM EDT

*–On-track to initiate enrollment by year-end in Phase 1b clinical trial of FTX-6058 in people with sickle cell disease–*

*– Losmapimod update planned for Q1 2022 –*

*–Raised $144.2 million in gross proceeds from August 2021 public offering, extending cash runway into 2024 –*

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

CAMBRIDGE, Mass., Nov. 04, 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 third quarter of 2021.

“Fulcrum made great progress in the third quarter, as we continued to advance our lead programs for FSHD and sickle cell disease,” said Bryan Stuart, president and chief executive officer. “Most notably, we reported compelling data from our Phase 1 trial of FTX-6058 that strengthen our belief in its potential as a functional cure for people with sickle cell disease and other hemoglobinopathies. Based on these data demonstrating proof-of-biology in healthy adults, we are moving quickly into a Phase 1b trial in people with sickle cell disease and plan to submit an investigational new drug application for FTX-6058 in other hemoglobinopathies, including beta thalassemia, by the end of this year. We are equally excited about losmapimod, which we believe has the potential to slow or stop the progression of FSHD, and we look forward to sharing next steps following our regulatory interactions. Looking ahead, we are well-funded with cash into 2024 beyond multiple expected milestones that bring us closer to our goal of delivering life-changing therapies to people with rare genetic diseases.”

**Upcoming Milestones**

- Initiate enrollment in a Phase 1b clinical trial of FTX-6058 in people with sickle cell disease by year-end 2021.
- Submit an investigational new drug application (IND) for FTX-6058 in non-sickle cell disease hemoglobinopathies, including beta thalassemia, by year-end 2021.
- Report an update from the ongoing Phase 1 trial of FTX-6058, including data from the 20mg and 30mg multiple-ascending dose (MAD) cohorts in healthy volunteers, by year-end 2021. In conjunction with the update, report new data for FTX-6058 further elucidating the relationship between EED inhibition and HBG mRNA induction.
- Meet with health authorities, including the U.S. Food and Drug Administration (FDA), on losmapimod in facioscapulohumeral muscular dystrophy (FSHD) by year-end 2021 and provide an update on losmapimod in the first quarter of 2022.
- Report initial data from the Phase 1b trial of FTX-6058 in people with sickle cell disease in the second quarter of 2022.
- Submit an additional IND from our portfolio by the first quarter of 2023.

**Recent Business Highlights**

- In August 2021, reported positive interim results from the ongoing Phase 1 trial in healthy adult volunteers treated 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 sickle cell disease and other hemoglobinopathies, such as beta-thalassemia.
    - Data from the MAD portion of the trial demonstrated proof-of-mechanism and proof-of-biology as evidenced by dose-proportional induction of HBG mRNA and accompanying increases in HbF-containing reticulocytes (F-reticulocytes). At 10mg, the highest dose completed as of the data cut-off, the mean changes were 4.5-fold and 4.2-fold at day 14, respectively. The increases in F-reticulocytes indicate that the HBG mRNA increases observed with FTX-6058 treatment are translating to HbF protein production.
    - FTX-6058 was generally well-tolerated with no serious adverse events observed.
    - Added a cohort in people with sickle cell disease to the ongoing Phase 1 clinical trial to further inform pharmacokinetic and pharmacodynamic modeling and dose selection.
- Highlighted the potential of losmapimod, a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor, in multiple presentations during the virtual Congress of the World Muscle Society, including data demonstrating slowed disease progression and improved function in people with FSHD in ReDUX4, a Phase 2b clinical trial.
- 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.

- Mel Hayes joined Fulcrum in September 2021 as chief commercial officer.
- Naomi Aoki joined Fulcrum in September 2021 as senior vice president, corporate communications and investor relations.
- Christopher Moxham, Ph.D., chief scientific officer, will be leaving the company, effective Nov. 8, 2021. The discovery organization will continue to report into Judith Dunn, Ph.D., president, research and development.

**Third Quarter 2021 Financial Results**

- **Cash Position:** As of September 30, 2021, cash, cash equivalents, and marketable securities were $240.3 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 2024.
- **Collaboration Revenue:** Collaboration revenue was $4.9 million for the third quarter of 2021, as compared to $1.8 million for the third 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 $17.1 million for the third quarter of 2021, as compared to $15.6 million for the third quarter of 2020. The increase of $1.5 million was primarily due to increased employee-compensation costs to support the growth of our research and development organization.
- **G&A Expenses:** General and administrative expenses were $8.6 million for the third quarter of 2021, as compared to $5.3 million for the third quarter of 2020. The increase of $3.3 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 $20.7 million for the third quarter of 2021, as compared to a net loss of $19.0 million for the third 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 third 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: 7525705

Replay Dial-in Number: 855-859-2056
Replay International Dial-in Number: 404-537-3406
Conference ID: 7525705

**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 clinical 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 clinical trial of FTX-6058 in healthy adult volunteers and people with SCD.

**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 INDs, 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)**

| | September 30, 2021 | December 31, 2020 |
|---|---|---|
| Cash, cash equivalents, and marketable securities | $ 240,345 | $ 112,914 |
| Working capital[(1)] | 225,590 | 92,785 |
| Total assets | 255,547 | 129,577 |
| Total stockholders' equity | 230,609 | 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 September 30, | Nine Months Ended September 30, |
|---|---|---|

| | 2021 | 2020 | 2021 | 2020 |
|---|---|---|---|---|
| Collaboration revenue | $ 4,935 | $ 1,848 | $ 14,105 | $ 4,598 |
| Operating expenses: | | | | |
| Research and development | 17,077 | 15,640 | 50,789 | 42,897 |
| General and administrative | 8,628 | 5,312 | 20,811 | 15,525 |
| Total operating expenses | 25,705 | 20,952 | 71,600 | 58,422 |
| Loss from operations | (20,770) | (19,104) | (57,495) | (53,824) |
| Other income, net | 54 | 142 | 132 | 725 |
| Net loss | $ (20,716) | $ (18,962) | $ (57,363) | $ (53,099) |
| Net loss per share, basic and diluted | $ (0.57) | $ (0.70) | $ (1.71) | $ (2.16) |
| Weighted-average common shares outstanding, basic and diluted | 36,606 | 27,261 | 33,603 | 24,621 |

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