Fulcrum Therapeutics® Announces Upcoming Milestones to Support Its Mission of Treating the Root Cause of Rare Genetic Diseases

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First patient dosed in Phase 1b trial of FTX-6058 in sickle cell disease; Initial data expected in 2Q 2022

Submitted IND for FTX-6058 to support initiation of Phase 1b trial in select hemoglobinopathies in 2Q 2022

On track to provide update on losmapimod in FSHD in 1Q 2022

Kate Haviland appointed Chair of board of directors

CAMBRIDGE, Mass., Jan. 10, 2022 (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 outlined its recent accomplishments and expected upcoming milestones. Fulcrum will present at the virtual 40th Annual J.P. Morgan Healthcare Conference on Thursday, January 13 at 12:00 p.m. ET. A live webcast will be available on the Investor Relations section of Fulcrum's website.

"Fulcrum made substantial progress in 2021, positioning us for a transformative 2022," said Bryan Stuart, president and chief executive officer. "Our clinical results with losmapimod highlight its potential to slow or stop the progression of FSHD, a relentless form of muscular dystrophy that leads to loss of upper body function and mobility and for which there are no treatments. We also reported results from our clinical program with FTX-6058, supporting its potential to be a functional cure for sickle cell disease. Based on these results, we are intently focused on advancing this oral HbF inducer for people with sickle cell disease as well as other hemoglobinopathies."

"As we enter 2022, we are building on this progress, with multiple milestones expected across our clinical and discovery-stage pipeline," Mr. Stuart continued. "We plan to provide an update on losmapimod in the first quarter. I'm also pleased to share that we enrolled the first patient with sickle cell disease in our Phase 1b trial, putting us on track to report initial data in the second quarter of 2022. We also submitted an IND for FTX-6058 in select hemoglobinopathies and expect to start a Phase 1b trial in the second quarter of 2022. In parallel, we continue to advance our FulcrumSeek™ product engine and plan to nominate our next development candidate this year to support an IND by the end of the first quarter of 2023."

Recent Accomplishments

- Dosed first sickle cell disease patient in the Phase 1b clinical trial of FTX-6058, an oral fetal hemoglobin (HbF) inducer.
- Completed three-month preclinical toxicology studies and initiated chronic toxicology studies to advance FTX-6058 in multiple indications.
- Submitted Investigational New Drug (IND) application to initiate clinical development of FTX-6058 in select hemoglobinopathies, including beta-thalassemia.
- Announced the appointment of Esther Rajavelu as Chief Financial Officer.

Expected Milestones

Losmapimod

- Provide an update in the first quarter of 2022 on plans for a Phase 3 clinical trial of losmapimod in facioscapulohumeral muscular dystrophy (FSHD).

FTX-6058

- Report initial data, including measures of HbF protein induction, from the Phase 1b trial in people with sickle cell disease in the second quarter of 2022.
- Initiate Phase 1b trial in select hemoglobinopathies, including beta-thalassemia, in the second quarter of 2022.
- Initiate registrational trial in sickle cell disease in early 2023.

Preclinical Pipeline

- Nominate next development candidate by end of 2022 to support the company's fourth IND by the end of the first quarter of 2023.

Company Update

Today, Fulcrum also announced that Kate Haviland, chief operating officer and incoming chief executive officer of Blueprint Medicines, has been named chair of Fulcrum's board of directors. Ms. Haviland has been a member of Fulcrum's board since 2018. As part of a planned transition, she is succeeding Mark Levin. Mr. Levin is a partner at Third Rock Ventures and has served on Fulcrum's board of directors since the company's founding in 2015 and as chair of the board since 2016. Mr. Levin will remain on the board through April 18, 2022.

"I'm delighted that Kate will continue on our board in this new capacity," Mr. Stuart said. "Kate has an outstanding record in the biotechnology industry and has been a tremendous asset to Fulcrum. We are extremely grateful to Mark for his leadership as chair and for his contributions to our growth and evolution from a start-up to a publicly traded company with three potentially disease-modifying programs in clinical development."

"It's an exciting time at Fulcrum as the losmapimod and FTX-6058 programs advance in the clinic and the research pipeline continues to accelerate,"

said Ms. Haviland. “I’m very pleased to be part of this team and honored to lead this board in my new role. As we head into 2022 and beyond, I believe we are well positioned to advance our mission to bring life-changing therapies to patients with genetically defined rare diseases.”

2022 Financial Outlook

As of December 31, 2021, Fulcrum’s cash, cash equivalents and marketable securities were $218.2 million (unaudited). Based on its current operating plans, the company believes this is sufficient to fund its anticipated operating expenses and capital expenditure requirements into 2024.

Fulcrum to Present at the virtual 40th Annual J.P. Morgan Healthcare Conference

Fulcrum will present at the virtual 40th annual J.P. Morgan Healthcare Conference on Thursday, January 13, 2022, at 12:00 p.m. ET followed by a Q&A session. A live webcast will be accessible in the “Investor Relations” section of the company’s website, www.fulcrumtx.com and will be archived for 30 days following the event.

About Losmapimod
Losmapimod is an investigational, selective p38α/β mitogen activated protein kinase (MAPK) inhibitor. Fulcrum exclusively in-licensed losmapimod from GSK following Fulcrum’s discovery of the role of p38α/β inhibitors in the reduction of DUX4 expression and an extensive review of known compounds. Results reported from the ReDUX4 trial demonstrated slowed disease progression and improved function, including positive impacts on upper extremity strength, supporting losmapimod’s potential to be a transformative therapy for the treatment of FSHD. Although losmapimod had never previously been explored in muscular dystrophies, it had been evaluated in more than 3,500 subjects in clinical trials across multiple other indications, with no safety signals attributed to losmapimod. Losmapimod has been granted U.S. Food and Drug Administration (FDA) Fast Track designation and Orphan Drug Designation for the treatment of FSHD.

About FSHD
FSHD is one of the most common forms of muscular dystrophy. It is a serious, rare, progressive and disabling disease for which there are no approved treatments and has an estimated patient population of 16,000 to 38,000 in the United States alone. FSHD is characterized by muscle degeneration and fat infiltration, initially affecting movement of the face and eventually the arms, trunk and legs. Disease progression results in accumulation of disability, with many patients ultimately becoming dependent upon the use of a wheelchair for daily mobility. Impact on patients includes decreased ability to perform activities of daily living, maintain independence, and lost ability to function or work.

About FTX-6058
FTX-6058, an EED inhibitor, is an investigational oral HbF inducer being developed for the treatment of sickle cell disease and other hemoglobinopathies, such as beta-thalassemia. The validation of EED as a target for sickle cell disease and the discovery of FTX-6058 was conducted using FulcrumSeek™. Results from a Phase 1 healthy volunteer trial demonstrated proof of biology and proof of mechanism, including robust induction of HBG mRNA after 14 days of dosing. To date, FTX-6058 has been generally well-tolerated with no serious adverse events reported.

About Sickle Cell Disease
Sickle cell disease 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. Sickle cell disease 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 two lead programs in clinical development are losmapimod, a small molecule for the treatment of facioscapulohumeral muscular dystrophy (FSHD) and FTX-6058, a small molecule designed to increase expression of fetal hemoglobin for the treatment of sickle cell disease and other hemoglobinopathies, including beta-thalassemia. The company’s proprietary product engine, FulcrumSeek™, identifies drug targets that can modulate gene expression to treat the known root cause of gene mis-expression.

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. All statements, other than statements of historical facts, contained in this press release are forward-looking statements, including statements regarding the timing of data readouts and other clinical updates regarding Fulcrum’s product candidates, the potential advantages and therapeutic potential of Fulcrum’s product candidates, the initiation and enrollment of clinical trials and the timing and design of planned clinical trials and submission of INDs, and its 2022 financial outlook among others. 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 continue to advance its product candidates in clinical trials; initiate and enroll clinical trials on the timeline expected or at all; obtain and maintain necessary approvals from the FDA and other regulatory authorities; 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; 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 Fulcrum’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 Fulcrum’s most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent Fulcrum’s views as of the date hereof and should not be relied upon as representing Fulcrum’s views as of any date subsequent to the date hereof. Fulcrum anticipates that subsequent events and developments will cause Fulcrum’s views to change. However, while Fulcrum may elect to update these forward-looking statements at some point in the future, Fulcrum specifically disclaims any obligation to do so.

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