Fulcrum Therapeutics Provides Business Update and 2023 Outlook

January 4, 2023 at 7:02 AM EST

— FTX-6058 granted Fast Track Designation for sickle cell disease (SCD) from FDA in December 2022 —
— Completed enrollment in 6 mg and 2 mg dose cohorts of the Phase 1b trial of FTX-6058 in SCD; enrollment ongoing in 12 mg dose cohort —
— Additional FTX-6058 data from 6 mg cohort of ongoing Phase 1b trial show clinically relevant HbF increases of up to 9.5% —
— Plan to complete enrollment in Phase 3 REACH trial of losmapimod in FSHD during 2H'23
— Fulcrum announces CEO transition; Robert J. Gould, Ph.D., former president and founding chief executive officer of Fulcrum has been appointed as interim CEO as Bryan Stuart departs to pursue other opportunities —
— Presentation at J.P. Morgan Healthcare Conference on Wednesday, January 11, 2023, at 4:30 p.m. PST/7:30 p.m. EST —

CAMBRIDGE, Mass., Jan. 04, 2023 (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 2023 milestones.

"We are entering 2023 with a tremendous amount of momentum and expect it to be a productive year for our two clinical programs: FTX-6058 for SCD, and losmapimod for FSHD," said Robert J. Gould, Ph.D., Fulcrum's interim president and chief executive officer. "FTX-6058 is a potential best-in-class oral HbF inducer candidate that could address critical gaps in the SCD treatment landscape. We are excited by the levels of HbF induction in our initial doses and look forward to further broadening our understanding of its effect at a higher dose. Meanwhile, the Phase 3 REACH trial with losmapimod, a potential first-to-market therapy in FSHD, is expected to complete enrollment in the second half of the year."

"We are encouraged by the new FTX-6058 data at 6 mg that show clinically relevant HbF increases, up to 9.5% from baseline with hemolysis and anemia improvement, suggesting its potential for best-in-class therapy for people living with sickle cell disease," said Santiago Arroyo, M.D., Ph.D., Fulcrum's chief medical officer.

Key Business Updates and Upcoming Milestones

FTX-6058

- Received Fast Track Designation from the U.S. Food and Drug Administration (FDA) for the treatment of SCD in December 2022
- Phase 1b data from Cohort 1 subjects in the 6 mg cohort (n=10) showed up to 9.5% absolute HbF increases from baseline; data suggest no difference in response in subjects on (n=3) and off (n=7) background hydroxyurea
- Improved biomarkers of hemolysis in evaluable patients dosed at 6 mg
- In the Phase 1b trial, FTX-6058 appears to have dose dependent and clinically relevant increases in HbF; all subjects adherent to dosing regimen showed a response
- Generally well tolerated with no drug-related treatment emergent serious adverse events and no discontinuations due to treatment emergent adverse events to date
- Enrolling 12 mg dose cohort of the Phase 1b trial
- Next data update planned during the fourth quarter of 2023

Losmapimod

- Enrollment ongoing in the REACH Phase 3 pivotal trial at sites in the U.S., Canada, and Europe
- Plan to complete enrollment in the second half of 2023

Financial Guidance

- Fulcrum maintains its cash runway guidance and expects its existing cash, cash equivalents, and marketable securities will be sufficient to fund its currently planned operating expenses and capital expenditure requirements into late 2024

Corporate

- Fulcrum announced CEO transition today; Robert J. Gould, Ph.D., former president and founding chief executive officer of Fulcrum has been appointed as interim CEO as Bryan Stuart departs to pursue other opportunities

J.P. Morgan Conference Webcast

- A live audio webcast of Fulcrum's presentation at the 41st Annual J.P. Morgan Healthcare Conference will be available through the Investor Relations section of the Fulcrum website at https://ir.fulcrumtx.com/events-and-presentations. An archived replay will be available on Fulcrum's website for 30 days.

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 (SCD) and other hemoglobinopathies, including beta-thalassemia. Fulcrum's proprietary product engine, FulcrumSeek™, identifies drug targets that can modulate gene expression to treat the known root cause of gene mis-expression. For more

information, visit www.fulcrumtx.com and follow us on Twitter @FulcrumTx and LinkedIn.

About FTX-6058
FTX-6058 is an investigational oral small-molecule inhibitor of Embryonic Ectoderm Development (EED) that was discovered using FulcrumSeek™, Fulcrum's proprietary discovery engine. Inhibition of EED leads to potent downregulation of key fetal globin repressors, including BCL11A, thereby causing an increase in fetal hemoglobin (HbF). FTX-6058 is being developed for the treatment of sickle cell disease (SCD) and other hemoglobinopathies. FTX-6058 is currently being evaluated in a Phase 1b multi-center open-label trial in people with SCD (NCT05169580). Initial data demonstrated proof-of-concept and achieved absolute levels of HbF increases associated with potential overall patient benefit. To date, FTX-6058 has been generally well-tolerated in people with SCD with up to three months of exposure, with no serious treatment-emergent adverse events reported. FTX-6058 has been granted U.S. Food and Drug Administration (FDA) Fast Track designation and Orphan Drug Designation for the treatment of SCD.

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. People with sickle cell disease 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 Losmapimod
Losmapimod is a 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 Phase 2b ReDUX4 trial demonstrated slowed disease progression and improved function, including positive impacts on upper extremity strength and functional measures 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 3,600 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. Losmapimod is currently being evaluated in a Phase 3 multi-center randomized, double-blind, placebo-controlled, 48-week parallel-group study in people with FSHD (NCT05397470).

About FSHD
FSHD is a serious, rare, progressive and debilitating disease for which there are no approved treatments. It is characterized by fat infiltration of skeletal muscle leading to muscular atrophy involving primarily the face, scapula and shoulders, upper arms, and abdomen. Impact on patients includes profound decreases in the ability to perform activities of daily living, loss of upper limb function, loss of mobility and independence and chronic pain. FSHD is one of the most common forms of muscular dystrophy and has an estimated patient population of 16,000 to 38,000 in the United States alone.

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 express or implied statements regarding enrollment in Fulcrum's ongoing clinical trials and timing of completion; potential therapeutic benefit of FTX-6058 and losmapimod; planned data announcements; and Fulcrum's cash runway, 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 any other product candidates; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; realize the anticipated benefits of the strategic realignment; manage executive and employee turnover; and raise the substantial additional capital needed to achieve its business objectives, among others. 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.

Contact:

Investors:
Stephanie Ascher
Stern IR, Inc.
stephanie.ascher@sternir.com
212-362-1200

Media:
Dee Smith
Executive Director, Corporate Communications
Fulcrum Therapeutics, Inc.
dsmith@fulcrumtx.com
202-746-1324