Fulcrum Therapeutics Presents Published Structure of Investigational Small Molecule FTX-6058 at the American Chemical Society (ACS) Spring 2021 Virtual Conference

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Company initiates dosing in Phase 1 healthy volunteer multiple ascending dose (MAD) cohort

CAMBRIDGE, Mass., April 09, 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 presented the medicinal chemistry strategy for FTX-6058 at the First Time Disclosure Session at the American Chemical Society (ACS) Spring 2021 National Meeting. FTX-6058 is a highly potent orally bioavailable small molecule EED inhibitor for the potential treatment of select hemoglobinopathies, including sickle cell disease and β-thalassemia. The validation of EED as a fetal hemoglobin (HbF) inducer target for sickle cell disease was conducted using FulcrumSeek, Fulcrum's proprietary product engine.

"We are pleased to report progress on our development of FTX-6058 including the first publication of the structure of this compelling EED inhibitor," said Chris Moxham, Ph.D., Fulcrum's chief scientific officer. "We believe that this oral, once-a-day therapy with an impressive preclinical pharmacological profile has the potential to provide a meaningful therapeutic benefit to patients with sickle cell disease and β-thalassemia. We are also excited to report initial PK results from the SAD cohort and that our Phase 1 trial in healthy volunteers continues to progress with initiation of the multiple ascending dose cohorts. We expect to report the full data from this Phase 1 trial mid-year."

FTX-6058 inhibits PRC2 via binding to EED, which induces robust HbF protein expression in both cell and murine models. Increasing HbF has the potential to prevent or reduce disease-related pathophysiology and reduce the risk of recurring events such as vaso-occlusive crises and hemolysis. Preclinical data with FTX-6058 showed an increase in HbF levels up to approximately 30% of total hemoglobin, demonstrating the potential to have a significant impact in patients with sickle cell disease. Human genetic data further indicate that individuals with the sickle cell mutation and high HbF levels may have asymptomatic disease, underscoring the protective effect of increased HbF.

Fulcrum's Phase 1 trial in healthy volunteers is evaluating the safety, tolerability and pharmacokinetics of FTX-6058. Dosing has been initiated in the randomized, double-blind, placebo-controlled, multiple ascending dose (MAD) cohorts of the trial. Dosing continues in the single ascending dose (SAD) portion. The company anticipates sharing data from this Phase 1 trial in mid-2021 and initiating a clinical trial in sickle cell patients by the end of 2021.

Today's presentation, titled "Discovery of clinical candidate FTX-6058: a potent, orally bioavailable upregulator of fetal hemoglobin for treatment of sickle cell disease", will be available in the "Publications" section of fulcrumtx.com.

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 has initiated 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 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, 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; 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.

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