FDA Lifts Clinical Hold on Fulcrum Therapeutics' FTX-6058 for Sickle Cell Disease

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CAMBRIDGE, Mass., Aug. 22, 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 announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold on the Investigational New Drug (IND) application for FTX-6058 for the potential treatment of sickle-cell disease (SCD).

"We are pleased with the FDA's decision to lift the clinical hold and are eager to advance FTX-6058 through clinical development to address the significant unmet need in the sickle cell disease community," said Alex C. Sapir, Fulcrum's president and chief executive officer. "Based on the initial data from the Phase 1b trial, which showed increasing levels of HbF with each dose escalation, we believe in the potential of FTX-6058 to not only shift the current standard of care but importantly, offer these patients a differentiated oral option. We look forward to building on these results with plans to resume enrollment for patients with SCD."

On February 23, 2023, the FDA placed the IND for FTX-6058 on clinical hold. In its communication, the Agency noted preclinical data previously submitted in April, October and December 2022, and non-clinical and clinical evidence of hematological malignancies observed with other inhibitors of polycomb repressive complex 2 (PRC2). In connection with the clinical hold, Fulcrum suspended dosing in the Phase 1b trial of FTX-6058 and worked diligently with the Agency to resolve the hold.

To learn more about the amended protocol and planned Phase 1b trial of FTX-6058, please see the program update presentation on the Investor Relations section of Fulcrum's website at www.fulcrumtx.com or by clicking **here**.

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. Initial data in SCD demonstrated proof-of-concept and achieved absolute levels of HbF increases associated with potential overall patient benefit. In clinical trials conducted prior to the clinical hold, FTX-6058 was generally well-tolerated in people with SCD with up to three months of exposure, with no serious treatment-related 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. To learn more about these studies please visit ClinicalTrials.gov.

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. People with SCD 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 (SCD) and other hemoglobinopathies. 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**.

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 advancing clinical development of FTX-6058; FTX-6058's ability to address unmet needs in the SCD community and shift the standard of care; and resuming enrollment in the FTX-6058 clinical trial; 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; initiating and enrolling clinical trials on the timeline expected or at all; obtaining and maintaining necessary approvals from the FDA and other regulatory authorities; replicating in clinical trials positive results found in preclinical studies and/or earlier-stage clinical trials; obtaining, maintaining or protecting intellectual property rights related to its product candidates; managing expenses; managing executive and employee turnover, including integrating a new CEO and CFO; and raising 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.

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