UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 12, 2024

Fulcrum Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-38978**	**47-4839948**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Landsdowne Street Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 651-8851

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	FULC	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events

On September 12, 2024, Fulcrum Therapeutics, Inc., or Fulcrum, issued a press release announcing topline results from its Phase 3 REACH clinical trial of losmapimod in facioscapulohumeral muscular dystrophy, or FSHD. As announced, Fulcrum's Phase 3 REACH trial did not achieve its primary endpoint of change from baseline in relative surface area with losmapimod compared to placebo. In addition, secondary endpoints did not achieve nominal statistical significance. The safety and tolerability profile of losmapimod was consistent with previously reported studies.

A copy of the press release is filed as Exhibit 99.1 hereto and incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits

Exhibit No.	Description
99.1	Press release dated September 12, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

FULCRUM THERAPEUTICS, INC.

Date: September 12, 2024

By: /s/ Alex C. Sapir
Name: Alex C. Sapir
Title: President and Chief Executive Officer

Fulcrum Therapeutics Announces Topline Results from Phase 3 REACH Clinical Trial of Losmapimod in Facioscapulohumeral Muscular Dystrophy (FSHD)

— Losmapimod failed to show an improvement in relative surface area (RSA), a measure of reachable workspace (RWS), versus placebo at week 48 —

— Fulcrum to suspend future losmapimod development —

— Robust cash position enables Fulcrum to continue its mission to develop therapies addressing diseases of high unmet need including pociredir for the treatment of sickle cell disease (SCD) —

CAMBRIDGE, Mass., September 12, 2024 (GLOBE NEWSWIRE) – Fulcrum Therapeutics, Inc.® (the "Company") (Nasdaq: FULC), a clinical-stage biopharmaceutical company focused on developing small molecules to improve the lives of patients with genetically defined rare diseases, today announced that its Phase 3 REACH trial evaluating losmapimod in patients with FSHD, did not achieve its primary endpoint of change from baseline in RSA with losmapimod compared to placebo. In addition, secondary endpoints did not achieve nominal statistical significance. The safety and tolerability profile of losmapimod was consistent with previously reported studies. The Company will complete a full evaluation of the data it received this week and plans to share the results at an upcoming medical meeting.

"We are deeply disappointed that the REACH trial did not replicate the clinical results observed in the Phase 2 ReDUX4 trial," said Alex C. Sapir, Fulcrum's president and chief executive officer. "In light of these results, we plan to suspend the losmapimod program in FSHD. We would like to thank the FSHD patients who participated in losmapimod clinical trials, their families, the investigators, the FSHD Society, and the broader FSHD community for their unwavering support for this program."

Top-line REACH study results:

- **Reachable Workspace (RWS)**: Participants receiving losmapimod demonstrated a 0.013 (±0.007) improvement in RSA at week 48 compared to placebo patients who showed a 0.010 (±0.007) improvement in RWS (p-value = 0.75).
- **Muscle Fat Infiltration (MFI) as measured by Magnetic Resonance Imaging (MRI):** Participants receiving losmapimod demonstrated an increase of 0.42% in MFI at week 48 compared to participants receiving placebo who showed an increase of 0.576% in MFI (p-value = 0.16).
- **Shoulder Abductor Strength as measured by Hand-Held Dynamometry:** Participants receiving losmapimod demonstrated a 9.63% improvement in abductor strength at week 48 compared to a 2.24% improvement in abductor strength seen in the placebo arm of the study (p-value = 0.51).
- **Patient Reported Outcomes (PRO):** Across the two PRO secondary endpoints in the REACH study, Patient Global Impression of Change (PGIC) and the Neuro QoL Upper Extremity, there were no statistically significant differences observed.
- **Safety and Tolerability:** The rate of treatment-related adverse events was similar in the two treatment arms, and there were no treatment-related serious adverse events in participants receiving losmapimod.

"These results in patients receiving losmapimod when compared to baseline were similar to those observed in our Phase 2 study," said Dr. Pat Horn, Fulcrum's chief medical officer. "However, in contrast to what was seen in the ReDUX4 study as well as what has been reported in other FSHD studies, the patients receiving placebo in REACH did not show a decline in functional status as measured by RWS and shoulder dynamometry over the 48 weeks of the study. As the largest interventional study ever completed in FSHD, we intend to share the full trial results with patients, study investigators, and the broader FSHD community to ensure others developing treatments for FSHD can benefit from these data."

As previously disclosed, Fulcrum had approximately $273.8 million in cash, cash equivalents, and marketable securities as of June 30, 2024. Fulcrum intends to use these resources to advance pociredir for the treatment of SCD, novel therapeutic agents for the treatment of Diamond-Blackfan Anemia (DBA), and early discovery programs.

About the REACH Trial

REACH (NCT05397470) is a Phase 3 multi-center, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of losmapimod for the treatment of FSHD. The trial enrolled 260 patients who were randomized 1:1 to receive either losmapimod, administered orally as a 15 mg tablet twice a day, or placebo over a 48-week treatment period. The primary endpoint was the absolute change from baseline in Reachable Workspace (RWS). Secondary endpoint measurements included Muscle Fat Infiltration (MFI) as measured by MRI, shoulder abductor strength as measured by hand-held dynamometry, Patient Global Impression of Change (PGIC), and the Neuro QoL Upper Extremity.

About Losmapimod

Losmapimod is a selective p38α/ß mitogen activated protein kinase (MAPK) inhibitor. Fulcrum exclusively in-licensed losmapimod from GSK following Fulcrum's discovery of the role of p38α/ß inhibitors in the reduction of DUX4 expression and an extensive review of known compounds. 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.

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 relentless and accumulating muscle and functional loss impacting their 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 30,000 in the United States alone.

About Fulcrum Therapeutics

Fulcrum Therapeutics is a clinical-stage biopharmaceutical company focused on developing small molecules to improve 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 in development for the treatment of facioscapulohumeral muscular dystrophy (FSHD), and pociredir, a small molecule designed to increase expression of fetal hemoglobin and in development for the treatment of sickle cell disease (SCD). Fulcrum uses proprietary technology to identify 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/X (@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 fact, contained in this press release are forward-looking statements, including express or implied statements regarding suspending losmapimod development and the future of the program; completing a full evaluation of the REACH data and sharing the same; intended use of cash and cash equivalents and marketable securities; further advancement of pociredir and Fulcrum's earlier stage program for DBA and other discovery programs; 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 continued development of losmapimod; resuming development of losmapimod following an unsuccessful Phase 3 trial; sufficiency of Fulcrum's cash resources; Fulcrum's ability to advance any earlier stage product candidates in or into clinical trials; initiating and enrolling clinical trials on the timeline expected or at all; 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 any product candidates; obtaining and maintaining necessary approvals from the FDA and other regulatory authorities; managing expenses; managing executive and employee turnover; 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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