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): March 09, 2023

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

Not applicable
(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 2.02 Results of Operations and Financial Condition.

On March 9, 2023, Fulcrum Therapeutics, Inc., or Fulcrum, announced its financial results for the quarter and year ended December 31, 2022. The full text of the press release issued in connection with the announcement is being furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in this Item 2.02, including Exhibit 99.1 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Forward Looking Statements

This current report on Form 8-K 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 report are forward-looking statements, including statements regarding the strategic operational realignment, estimated cost savings, estimated charges 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 realize the cost savings from the realignment; 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following exhibit is furnished herewith:

99.1	Press Release issued March 9, 2023
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 thereunto duly authorized.

FULCRUM THERAPEUTICS, INC.

Date: March 9, 2023

By: /s/ Robert J. Gould

Name: Robert J. Gould, Ph.D.
Title: Interim President and Chief Executive Officer

Fulcrum Therapeutics Announces Recent Business Highlights and Financial Results for the Fourth Quarter and Full Year 2022

— Company is working to address clinical hold on the Investigational New Drug application for FTX-6058 for the potential treatment of sickle cell disease —

— FTX-6058 data from 12 mg cohort of Phase 1b trial show clinically relevant fetal hemoglobin increases of up to 10.0%—

— On track to complete enrollment in Phase 3 REACH trial of losmapimod in facioscapulohumeral muscular dystrophy during 2H'23 —

— In 1Q'23 completed public offering generating approximately $117.3 million in net proceeds; Cash runway guidance into mid-2025 —

— Company announces departure of Chief Medical Officer Santiago Arroyo, MD, Ph.D.; Appoints Iain Fraser, MBChB, D.Phil, as Interim Chief Medical Officer —

— Conference call and webcast scheduled for 8:00 a.m. ET today —

CAMBRIDGE, Mass., – March 9, 2023 – Fulcrum Therapeutics, Inc.® (the "Company") (Nasdaq: FULC), a clinical-stage biopharmaceutical company focused on improving the lives of patients with genetically defined rare diseases, today reported financial results for the fourth quarter and full year 2022 and provided a business update, including on FTX-6058.

"We are confident that FTX-6058 has the potential to provide a differentiated therapeutic option for people living with sickle cell disease and that the clinical and preclinical data generated to date demonstrate a favorable benefit-risk profile. We are working diligently to address the clinical hold," said Robert J. Gould, Ph.D., Fulcrum's interim president and chief executive officer. "Additionally, we remain on track to complete enrollment in the losmapimod Phase 3 REACH trial in the second half of 2023, and are excited about potentially being first to market with a treatment for FSHD patients who have no approved therapies."

Key Business Updates

FTX-6058

- On February 23, 2023, the FDA placed the investigational new drug (IND) application for FTX-6058 for the potential treatment of sickle cell disease (SCD) on full 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).
- The Company received a formal Clinical Hold Letter from the Agency on February 24, 2023. Enrollment has been paused and dosing suspended in the Phase 1b trial of FTX-6058.
- The clinical hold noted that the profile of hematological malignancies observed in the non-clinical studies of FTX-6058 is similar to that observed with other inhibitors of PRC2, and that hematological malignancies have been reported clinically with other PRC2 inhibitors. The Agency requested that Fulcrum further define the population where the potential benefit of continued treatment with FTX-6058 outweighs potential risk.

Preceding the FDA hold:

- The Company made submissions to the FDA in April, October and December 2022 that included non-clinical data.
- In December, the FDA granted FTX-6058 Fast Track Designation for the treatment of SCD.
- The Company previously disclosed Phase 1b data from Cohort 1 subjects in the 6 mg cohort (n=10): Primary endpoint showed up to 9.5% absolute fetal hemoglobin (HbF) increases from baseline, data suggest no difference in response in subjects on (n=3) and off (n=7) background hydroxyurea.

- FTX-6058 treatment appears to result in dose dependent and clinically relevant increases in HbF; all subjects adherent to the dosing regimen showed a response.
- Improved biomarkers of hemolysis were observed in evaluable patients.
- FTX-6058 was generally well tolerated with no drug-related treatment emergent serious adverse events and no discontinuations due to treatment emergent adverse events to date.
- Data from subjects in the 2 mg cohort (n=2) demonstrated continued absolute HbF increases up to 4.6% through the end of treatment, suggesting 2 mg is a potentially minimally efficacious dose.

- Data from a subject in the 12 mg dose cohort (n=3), prior to the suspension of the trial, showed up to 10.0% absolute HbF increases from baseline after 42 days of treatment.
- On February 17, 2023, the Company responded to a request received on February 9, 2023, from the FDA about non-clinical data submitted in 2022.

The Company is confident in its ability to address the Agency's feedback and looks forward to providing further updates as the process unfolds.

Losmapimod

- Enrollment is ongoing in the REACH Phase 3 pivotal trial evaluating losmapimod in FSHD at sites in the United States, Canada and Europe.
- On track to complete enrollment in the second half of 2023.
- In October 2022, the Company presented new data from the open label extension portion of the Phase 2 ReDUX4 study of losmapimod for the treatment of FSHD.

Corporate Updates

- Completed underwritten public offering of common stock in January 2023, raising approximately $117.3 million in net proceeds.
- Santiago Arroyo, MD, Ph.D., recently resigned from the Company, effective March 7, 2022, to pursue another opportunity.
- Iain Fraser, MBChB, D.Phil was appointed Interim Chief Medical Officer (CMO), effective March 9, 2023. Dr. Fraser brings over two decades of experience advancing therapies through early- and late-stage development, and possesses deep expertise in regulatory affairs. He most recently served as Vice President and Clinical Fellow at AlloVir, an Elevate Bio Company. He previously held clinical development roles of increasing responsibility at Abide Therapeutics (acquired by Lundbeck in 2019) and Merck where he led the first in-human clinical trials of a range of compounds across therapeutic areas, and contributed to the development of Zepatier®, Zinplava™ and Recarbrio™, as well as the pediatric development of Januvia® and Maxalt®. He received a Master of Science in Clinical Investigation from Harvard University and a Doctor of Philosophy in Experimental Pathology from the University of Oxford. Dr. Fraser received his Bachelor of Science in Biochemistry as well as his Bachelor of Medicine, Bachelor of Surgery – MBChB from the University of Cape Town.
- Alan Ezekowitz, MBChB, D.Phil, member of the Fulcrum Board of Directors since February 2017, will serve as a senior clinical advisor to provide program continuity.

Fourth Quarter and Full Year 2022 Financial Results

- **Cash Position:** As of December 31, 2022, cash, cash equivalents, and marketable securities were $202.9 million as compared to $218.2 million as of December 31, 2021. The decrease in cash is primarily due to our net cash used in operating activities during 2022, partially offset by proceeds from our equity offering in August 2022.
- **Collaboration Revenue:** Collaboration revenue was $0.7 million for the fourth quarter of 2022 as compared to $5.1 million for the fourth quarter of 2021. The decrease of $4.4 million was primarily due to the winding down of Fulcrum's collaboration agreement with Acceleron Pharma Inc., a wholly owned subsidiary of Merck & Co., Inc.

  Collaboration revenue was $6.3 million for the year ended December 31, 2022, as compared to $19.2 million for the year ended December 31, 2021. The decrease of $12.9 million was primarily due to the winding down of Fulcrum's collaboration agreement with Acceleron Pharma Inc., a wholly owned subsidiary of Merck & Co., Inc.
- **Operating Expenses:** Total operating expenses were $28.7 million for the fourth quarter of 2022 as compared to $28.6 million for the fourth quarter of 2021. An increase of $0.4 million in G&A expenses was primarily due to increased employee-related costs, including increased stock-based compensation expense. A decrease of $0.3 million in R&D expenses was primarily due to a decrease in employee-related costs, including increased stock-based compensation expense, partially offset by increased external research and development costs to support our lead programs.

  Total operating expenses were $118.9 million for the year ended December 31, 2022, as compared to $100.2 million for the year ended December 31, 2021. An increase of $7.1 million in R&D expenses was primarily due to increased external research and development costs to support our lead programs, including a $5.0 million milestone paid to GlaxoSmithKline plc, upon the initiation of the Phase 3 REACH trial under our right of reference and license agreement. An increase of $11.2 million in G&A expenses was primarily due to increased employee-related costs, including increased stock-based compensation expense, increased professional services costs, and increased facility-related costs.
- **Net Loss:** Net loss was $26.1 million for the fourth quarter of 2022, as compared to a net loss of $23.5 million for the fourth quarter of 2021.

  Net loss was $109.9 million for the year ended December 31, 2022, as compared to a net loss of $80.8 million for the year ended December 31, 2021.

Financial Guidance

Fulcrum expects that its existing cash, cash equivalents, and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements into mid-2025.

Conference Call and Webcast

Fulcrum Therapeutics, Inc. will host a conference call and webcast today at 8:00 a.m. ET to review the fourth quarter and full year 2022 recent business highlights and financial results. Individuals may participate in the live call via telephone by dialing (877) 407-0792 (domestic) or (201) 689-8263 (international) and using the conference ID: 13735955. Participants are asked to dial in 15 minutes before the start of the call to register. The webcast will be accessible through the Investor Relations section of Fulcrum’s website at www.fulcrumtx.com or by clicking here. Following the live webcast, an archived replay will also be available for 90 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. Initial data in SCD 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 (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 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 the clinical hold on FTX-6058, including Fulcrum’s ability to resolve such hold; enrollment in Fulcrum’s ongoing clinical trial of losmapimod and timing of completion; potential therapeutic benefit of FTX-6058 and losmapimod; Fulcrum’s ability to market a treatment for FSHD patients; 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 resolving the clinical hold on FTX-6058 and responding to FDA’s requests; 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 (if resumed) 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.

Fulcrum Therapeutics, Inc.

Selected Consolidated Balance Sheet Data

(In thousands)

(Unaudited)

	December 31, 2022	December 31, 2021
Cash, cash equivalents, and marketable securities	$ 202,921	$ 218,162
Working capital[(1)]	190,794	206,799
Total assets	226,685	235,000
Total stockholders' equity	198,942	211,539

(1) Fulcrum defines working capital as current assets minus current liabilities.

Fulcrum Therapeutics, Inc.

Consolidated Statements of Operations

(In thousands, except per share data)

(Unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Collaboration revenue	$ 685	$ 5,058	$ 6,342	$ 19,163
Operating expenses:				
Research and development	18,566	18,912	76,782	69,701
General and administrative	10,130	9,705	41,694	30,516
Restructuring expenses	(38)	—	427	—
Total operating expenses	28,658	28,617	118,903	100,217
Loss from operations	(27,973)	(23,559)	(112,561)	(81,054)
Other income, net	1,838	75	2,690	207
Net loss	$ (26,135)	$ (23,484)	$ (109,871)	$ (80,847)
Net loss per share, basic and diluted	$ (0.50)	$ (0.58)	$ (2.44)	$ (2.29)
Weighted-average common shares outstanding, basic and diluted	52,077	40,579	44,991	35,361

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