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): **January 2, 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** (Address of principal executive offices)	**02139** (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**	**The 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.

To the extent applicable to this Item, the disclosure set forth in Item 8.01 is incorporated by reference herein.

Item 5.02 Departure of Director or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On January 2, 2023, Bryan Stuart and Fulcrum Therapeutics, Inc., or Fulcrum, mutually agreed that he would transition from his role as president, chief executive officer and as Class II director, and in connection therewith, Fulcrum and Bryan Stuart entered into a severance agreement dated January 2, 2023. The severance agreement memorializes Mr. Stuart's transition effective as of January 2, 2023 and provides for payment of the severance benefits as contemplated by his previously filed employment agreement dated March 31, 2021, as well as for payment of his 2022 bonus in the amount of $220,000, and an extended exercise period (18-months) for his vested and unexercised options following the January 2, 2023 separation from service.

On January 3, 2023, the board of directors of Fulcrum, or the Board, appointed Robert J. Gould, former chief executive officer and president and current Class III director, as interim president and chief executive officer and as Fulcrum's principal executive officer, effective January 3, 2023.

Robert J. Gould, Ph.D., age 68, has served as a member of the Board since July 2016, served as Fulcrum's president and chief executive officer from July 2016 to March 2021, and was appointed interim president and chief executive officer in January 2023. Dr. Gould has served as an operating partner of Khosla Ventures since September 2021. Dr. Gould previously served as president and chief executive officer of Epizyme, Inc., or Epizyme, a biopharmaceutical company, from March 2010 to September 2015. Prior to joining Epizyme, he served as director of novel therapeutics at the Broad Institute of Massachusetts Institute of Technology, or MIT, and Harvard, a research institute, from December 2006 to March 2010. Dr. Gould spent 23 years at Merck, a healthcare company, where he held a variety of leadership positions, culminating in the role of vice president, licensing and external research. Dr. Gould currently is on the board of directors of Hemoshear Therapeutics, Inc., a biotechnology company, Turnstone Biologics Corp, a biotechnology company, and Faeth Therapeutics, Inc., a biotechnology company. Dr. Gould served as a member of the board of directors of Epizyme from March 2010 to March 2016. Dr. Gould received a B.A. from Spring Arbor University and a Ph.D. from the University of Iowa and completed postdoctoral studies at the Johns Hopkins University.

In connection with his appointment as interim chief executive officer and president, Fulcrum and Dr. Gould entered into a letter agreement effective January 3, 2023 providing for annual salary of $600,000, paid $50,000 monthly.

Fulcrum intends to file a copy of Mr. Stuart's severance agreement and a copy of Dr. Gould's letter agreement as exhibits to its Annual Report on Form 10-K for the year ended December 31, 2022.

Item 8.01 Other Events.

On January 4, 2023, Fulcrum Therapeutics, Inc., or Fulcrum, issued a press release providing a business update and 2023 outlook, which will be discussed as part of Fulcrum's presentation at the 41st Annual J.P. Morgan Healthcare Conference on January 11, 2023. A copy of the press release is filed as Exhibit 99.1 to this current report on Form 8-K and incorporated by reference herein.

On January 4, 2023, Fulcrum published an updated corporate presentation on its Website that includes an updated pipeline chart and updated clinical data from its ongoing Phase 1b clinical trial of FTX-6058 for the treatment of sickle cell disease. Fulcrum is filing as Exhibit 99.2 to this current report on Form 8-K a copy of the slides from such presentation, which updated information is incorporated by reference herein.

Forward-Looking Statements

This current report on Form 8-K and the materials filed herewith contain "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 current report on Form 8-K and the materials filed herewith 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 current report on Form 8-K and the materials filed herewith 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 dated January 4, 2023
99.2	Slide from Corporate Presentation dated January 4, 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: January 4, 2023

By: /s/ Curtis Oltmans
Name: Curtis Oltmans
Title: Chief Legal Officer

Fulcrum Therapeutics Provides Business Update and 2023 Outlook

— 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. – January 4, 2023 – 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. Fulcrum will present at the upcoming 41st Annual J.P. Morgan Healthcare Conference in San Francisco on Wednesday, January 11, 2023, at 4:30 p.m. PST. A live webcast will be available on the Investor Relations section of Fulcrum's website.

"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.

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/b mitogen activated protein kinase (MAPK) inhibitor. Fulcrum exclusively in-licensed losmapimod from GSK following Fulcrum's discovery of the role of p38α/b 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.

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Pipeline and Catalysts

Indication	MOA	Preclinical	Phase 1	Phase 2	Phase 3	2023 Catalysts
Wholly Owned Clinical Programs						
FSHD	Losmapimod (DUX4 Inhibitor)					Complete Phase 3 enrollment in 2H'23
SCD	FTX-6058 (Oral HbF Inducer)					Phase 1b data update in 4Q'23
Wholly Owned Discovery Programs						
Blood Disorder						
Neurologic Disorder						
Muscle Disorder						
Collaborations						
Cardiomyopathies	Bristol Myers Squibb					

HbF: Fetal hemoglobin


Fast Track Designation Granted
in December 2022

FTX-6058: Potential Best-in-Class Therapeutic Profile

HbF Induction

Hydroxyurea, Gene Editing, FTX-6058

Physiologic Disease Modification

HbS Polymerization Inhibition

Anemia Amelioration

P-selectin Inhibition

Improved Disease Symptoms

FTX-6058: Best-in-Class Profile

- Raises HbF level
- Potential to ameliorate disease pathology
- Convenient oral dosing
- Potential to differentiate on safety and tolerability

Fulcrum Therapeutics

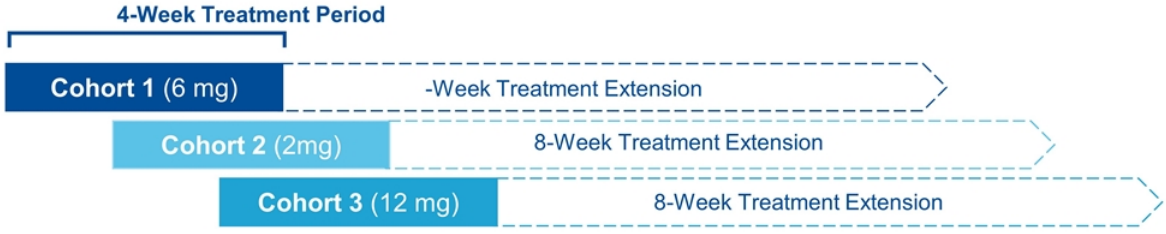
FTX-6058 Phase 1b Clinical Trial

Ongoing Phase 1b Clinical Trial in SCD Subjects

Study Population

Subjects with SCD, Age 18 – 65, on or off hydroxyurea
(if on HU, must have been on stable dose for 3 months, if not on HU, must have been off for 60 days)

Study Design



Study Endpoints

Primary
- Safety and tolerability
- Pharmacokinetic measurements

Secondary
- %HbF protein and %F-cells

Exploratory
- Target engagement
- Incidence of VOCs
- Biomarkers of hemolysis
- QOL measures

QOL: Quality of Life

SCD Phase 1b Demographics

	2 mg Cohort	6 mg Cohort	Total
Number of subjects enrolled, n	2	10	12
Average age, years (range)	37 (25, 48)	28 (21, 48)	30 (21, 48)
Gender, Male (%)	1 (50%)	2 (20%)	3 (25%)
Mean baseline HbF (range %)	4.0 (3.2, 4.8)	9.3 (3.7, 19.9)	8.4 (3.2, 19.9)
Genotype, n (%)			
HbSS	2 (100%)	10 (100%)	12 (100%)
HbSβ^0	0 (0%)	0 (0%)	0 (0%)
HbSβ$^+$	0 (0%)	0 (0%)	0 (0%)
Hydroxyurea Utilization, n (%)	0 (0%)	3 (30%)	3 (25%)

- Mean baseline HbF of 8.4% is consistent with recent SCD clinical studies and published data
- 3 subjects were on hydroxyurea
- All subjects enrolled to-date have the HbSS genotype

Data analysis cutoff : December 21, 2022;

Overall FTX 6058 Was Generally Well Tolerated

- 14 Treatment Emergent Adverse Events (TEAEs) in 7/12 (58%) subjects
  - 2/14 TEAEs reported as possibly related to study drug (headache, lip numbness)
  - Mild severity and non-serious
- 2/14 TEAEs characterized as VOCs (i.e., sickle cell anemia with crisis) per protocol definition
  - One VOC reported as an SAE with acute chest syndrome; deemed not related to study drug by investigator (non-adherent patient)
- No lab related adverse events
- No discontinuations reported due to TEAEs

Data analysis cutoff : December 21, 2022;

Instituted Observed Dosing and On-Treatment Analysis Following Initial Non-Adherence

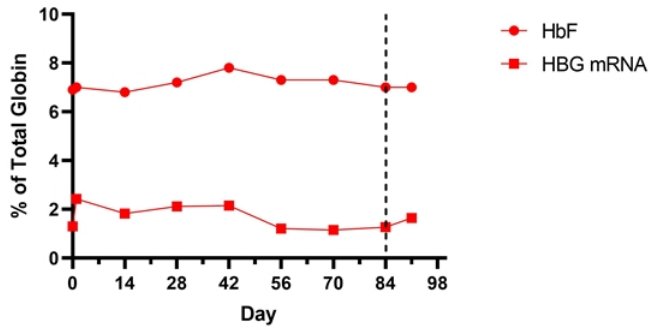
- Initial 6 subjects were either not fully adherent or not adherent to study drug
- Observed dosing was instituted in subjects 7-12
- An on-treatment analysis was established to allow interpretation of efficacy (HbF) data
- To be included in on-treatment analysis subjects must demonstrate :
  - Detectable Drug Levels (PK)
  - Drug Accountability and Subject Interview

Subject	Dose	Confirmed treatment duration (days)	On-treatment analysis eligible
1	6 mg	56	☑
2	6 mg	42	☑
3	6 mg	42	☑
4*	6 mg	0	
5	6 mg	0	
6	6 mg	0	
7	6 mg	84	☑
8	6 mg	84	☑
9	6 mg	28	☑
10	6 mg	28	☑
11	2 mg	56 (ongoing)	☑
12	2 mg	56 (ongoing)	☑

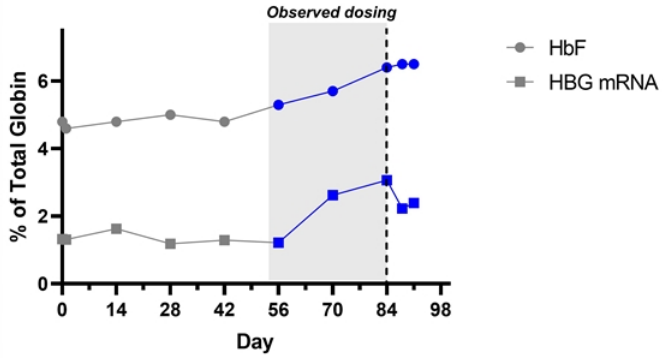
* Subject #4 initiated observed dosing on day 53
Confirmed treatment duration days are consecutive days of dosing starting on first day of dosing

Non-Adherent Subject Switched to Observed Dosing Demonstrated HbF Induction

Subject 5



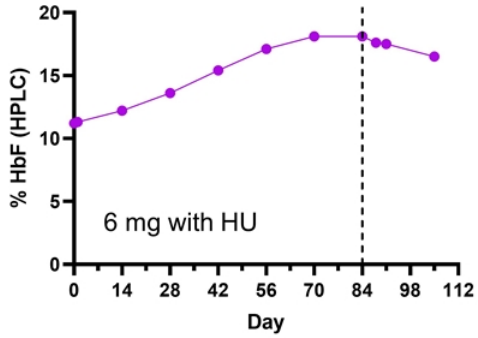
Subject 4
(Switched to Observed Dosing at ~Day 53)



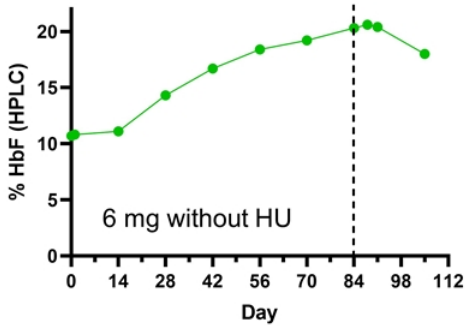
Subjects were not included in the on-treatment analysis
----- Represents last day of on drug measurements

Adherent Subjects, On and Off Hydroxyurea, Reach Robust HbF Increases

Subject 7



Subject 8



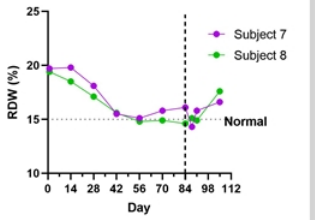
- **HbF increase was robust (6.8%-9.5%) at day 84**
- No apparent response differences in HU vs non-HU treated subjects
- Potential for further HbF induction beyond 3 months
- Observed dosing was used to ensure adherence

----- Represents last day of on drug measurements

FTX-6058 (6 mg) Improved Biomarkers of Hemolysis

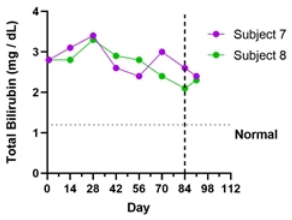
Hemolysis Impact

Red Cell Distribution Width



Reductions in RDW indicate RBCs are becoming more uniform in shape

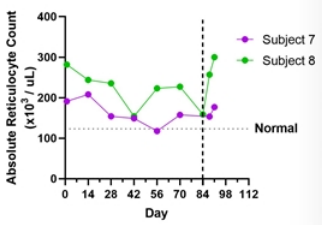
Total Bilirubin



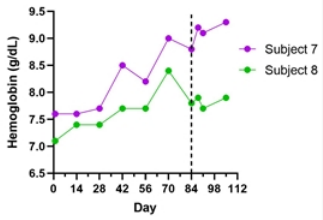
Bilirubin decreases indicate less hemolysis

Amelioration of Anemia

Absolute Reticulocyte Count



Total Hemoglobin

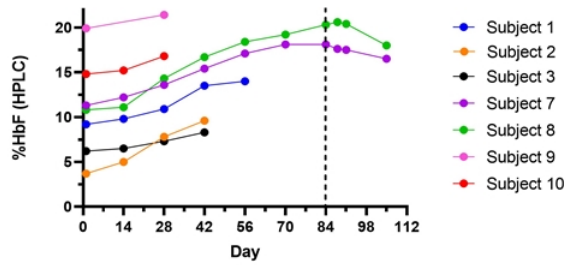


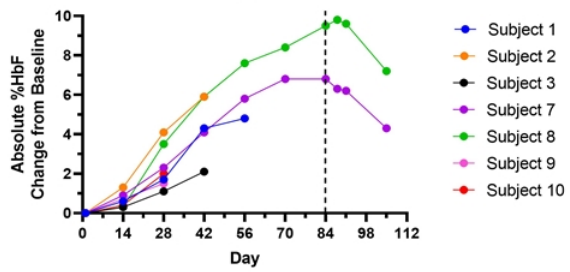
Reductions in reticulocytes and increases in total hemoglobin indicate less anemia and healthier bone marrow function

----- Represents last day of on drug measurements; RDW: red cell distribution width

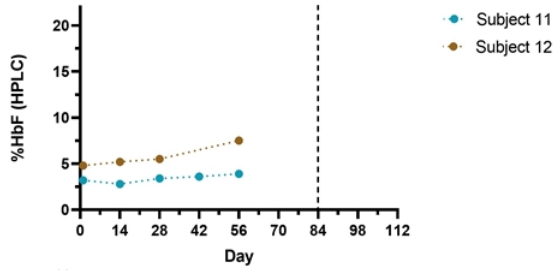
FTX-6058 Appears to Have a Dose Dependent, Clinically Relevant and Consistent Increase in HbF

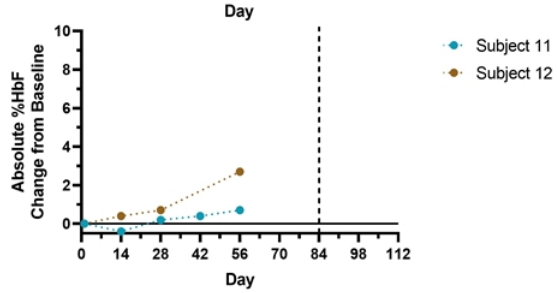
6mg





2mg (ongoing)





----- Represents last day of on drug measurements

FTX 6058 Demonstrates Best-in-Class Potential

- All patients on treatment have responded
- Levels of HbF increase are clinically relevant among patients both on HU and off HU
- Consistency of response demonstrated across patients, independent of baseline HbF
- Dose response at 2 mg and 6 mg
- Overall FTX 6058 Was Generally Well Tolerated

Healthy volunteer mRNA data indicate higher levels of HbF induction are possible

Data analysis cutoff : December 21, 2022;

Next Steps:
Complete Phase 1b to Enable Registration Dose Selection

Amend Protocol and Increase Number of Sites:
Streamline PK Collection and Reduce Patient Burden

→ **Accelerate Enrollment**

Optimize Treatment Effect:
Continue Dose Escalation to 12 mg

→ **Completion of Phase 1b**

Refine PK / PD Model:
Select Optimal Therapeutic Dose

→ **Final Dose for Pivotal Trial**

FTX-6058: Differentiated HbF Inducer with Best-in-Class Potential

Persistent unmet need

- SCD is a severe disorder (estimated US SCD population is ~100,000[1])
- Approximately 200,00 annual emergency department visits related to SCD[2]

Best-in-Class Potential

- Oral small molecule hemoglobin F (HbF) inducer
- Potential to be broadly protective of SCD symptomology

Demonstrated proof-of-concept

- Dose responsive target engagement and HbF increase*
- Robust HbF increases in adherent patients, on and off hydroxyurea*

Development path forward

- Completion of Phase 1b to Enable Registrational Dose Selection
- FDA Fast Track designation
- Composition of matter patent into 2040

Data analysis cutoff : December 21, 2022;
1. Sedrak and Kondamudi, StatPearls, last update August 29, 2022; 2. Hussain et al, Am J Prev Med, 2010

Diversified, Differentiated Pipeline of Clinical Assets

Losmapimod well-positioned to be first-to-market for patients living with FSHD

Enrollment for REACH Phase 3 trial to be completed in 2H 2023

FTX-6058 has best-in-class potential for SCD

Completion of Phase 1b to enable registrational dose selection in late 2023

Next data update in 4Q 2023

Well positioned to delivery on goals

Cash runway to late 2024