Fulcrum Therapeutics Reports Third Quarter 2019 Financial Results and Recent Business Highlights

November 14, 2019 at 7:00 AM EST

– Announced preliminary results of a Phase 1 clinical trial of losmapimod in FSHD patients –

– Initiated IND-enabling studies for FTX-6058 for the potential treatment of sickle cell disease and beta-thalassemia and announced pre-clinical data showing increase in HbF levels to ~30% of total hemoglobin –

CAMBRIDGE, Mass., Nov. 14, 2019 (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 provided a business update and reported financial results for the third quarter of 2019.

“This past quarter, we made significant progress in advancing our pipeline and executing on our goal of creating therapeutics targeted at genetically defined rare diseases. We presented encouraging Phase 1 clinical results from our lead program, losmapimod in patients with FSHD, which support the design and dose selection of our ongoing Phase 2 clinical trials. Additionally, we announced our plans to advance our second program, FTX-6058 for the potential treatment of sickle cell disease and beta-thalassemia,” said Robert J. Gould, Ph.D., Fulcrum’s president and chief executive officer. “We look forward to advancing these two programs through our ongoing Phase 2 trials with losmapimod and our IND-enabling studies with FTX-6058 and utilizing our product engine to identify and validate drug targets to address diseases caused by the mis-expression of certain genes.”

Third Quarter 2019 and Recent Business Highlights

- In October 2019, Fulcrum presented Phase 1 data from its clinical trial of losmapimod in facioscapulohumeral dystrophy (FSHD) patients and related plans for using molecular biomarkers indicative of the root cause of disease in the Company’s ongoing Phase 2 clinical trials of losmapimod at the International Annual Congress of the World Muscle Society in Copenhagen. The results showed that losmapimod was well tolerated with no serious adverse events (SAEs) reported, and that treatment with losmapimod demonstrated dose-dependent pharmacokinetics (PK) and target engagement (TE) in blood. These data support the selection of the 15 mg dose of losmapimod taken orally twice daily in the Company’s ongoing Phase 2b placebo-controlled 24-week clinical trial, referred to as ReDUX4, as well as its ongoing Phase 2 open label-study, of losmapimod for the treatment of patients with FSHD.
- In October 2019, Fulcrum announced progress in the Company’s plan to advance the development program for FTX-6058 for the potential treatment of sickle cell disease and beta-thalassemia. Fulcrum has initiated IND-enabling studies for FTX-6058 and anticipates filing an IND in mid-2020. In pre-clinical research, treatment with FTX-6058 was shown to increase HbF levels to ~30% of total hemoglobin as measured by HPLC and mass spectrometry methods in human erythroid progenitor cells from multiple donors.
- In September 2019, Fulcrum announced the appointment of Pamela Strode as senior vice president, regulatory affairs and quality assurance. She previously served as senior vice president, regulatory affairs and quality assurance at Epizyme, Inc.

Third Quarter 2019 Financial Results

- **Cash Position:** As of September 30, 2019, cash and cash equivalents were $101.6 million, as compared to $72.8 million as of December 31, 2018. Based on its current plans, the Company expects that its existing cash and cash equivalents, including the proceeds from its July 2019 initial public offering, will be sufficient to enable it to fund its operating expenses and capital expenditure requirements into the third quarter of 2021.
- **R&D Expenses:** Research and development expenses were $13.5 million for the third quarter of 2019, as compared to $7.0 million for the third quarter of 2018. The increase of $6.5 million was primarily due to a $2.5 million increase associated with the achievement of a milestone due under the right of reference and license agreement with GlaxoSmithKline plc during the third quarter of 2019, increased costs related to the advancement of losmapimod for the treatment of FSHD, including increased external costs to support Fulcrum’s ongoing and planned clinical trials, as well as increased personnel-related costs due to additional headcount to support the growth of Fulcrum’s research and development organization.
- **G&A Expenses:** General and administrative expenses were $3.5 million for the third quarter of 2019, as compared to $2.1 million for the third quarter of 2018. The increase of $1.4 million was primarily due to increased personnel-related costs due to additional headcount, as well as increased consulting and professional fees.
- **Net Loss:** Net loss was $16.5 million for the third quarter of 2019, as compared to a net loss of $8.9 million for the third quarter of 2018.

About FSHD

FSHD is characterized by progressive skeletal muscle loss that initially causes weakness in muscles in the face, shoulders, arms and trunk, and progresses to weakness throughout the lower body. Skeletal muscle weakness results in significant physical limitations, including an inability to smile and difficulty using arms for activities, with many patients ultimately becoming dependent upon the use of a wheelchair for daily mobility.

FSHD is caused by mis-expression of DUX4 in skeletal muscle, resulting in the presence of DUX4 proteins that are toxic to muscle tissue. Normally, DUX4-driven gene expression is limited to early embryonic development, after which time the DUX4 gene is silenced. In people with FSHD, the DUX4 gene is turned “on” as a result of a genetic mutation. The result is death of muscle and its replacement by fat, leading to skeletal muscle weakness and

progressive disability. There are no approved therapies for FSHD, one of the most common forms of muscular dystrophy, with an estimated patient population of 16,000 to 38,000 in the United States alone.

About Losmapimod

Losmapimod is a selective p38α/β mitogen activated protein kinase (MAPK) inhibitor that was exclusively in-licensed by Fulcrum Therapeutics following Fulcrum's discovery of the role of p38α/β inhibitors in the reduction of DUX4 expression and an extensive review of known compounds. Utilizing its internal product engine, Fulcrum discovered that inhibition of p38α/β reduced expression of the DUX4 gene in muscle cells derived from patients with FSHD. Although losmapimod has never previously been explored in muscular dystrophies, it has been evaluated in more than 3,500 subjects in clinical trials across multiple other indications, including in several Phase 2 trials and a Phase 3 trial. No safety signals were attributed to losmapimod in any of these trials. Fulcrum is currently conducting Phase 2 trials investigating the safety, tolerability, and efficacy of losmapimod to treat the root cause of FSHD.

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 Beta-thalassemia

Beta-thalassemia is a rare blood disorder caused by genetic mutations in the HBB gene, which are associated with the absence or reduced production of beta-globin – one of the two proteins that comprise adult hemoglobin. This results in an abnormally low level of hemoglobin as well as an excess of alpha-globin chains, causing destruction of red blood cells.

Beta-thalassemia has been clinically characterized into three forms, depending on disease severity: major, intermedia and minor. The most severe form is generally diagnosed shortly after birth and is characterized by life-threatening anemia. Pediatric patients do not grow and gain weight at the typical rates, and often have liver, heart and bone problems. Many patients with beta-thalassemia major require chronic blood transfusions due to severe anemia that results from low hemoglobin levels. Beta-thalassemia intermedia is a less severe form of the disease that results in mild to moderate anemia. These patients sometimes require blood transfusions depending on the severity of their symptoms. Patients with beta-thalassemia minor suffer from very mild anemia and generally do not require treatment.

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. 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 timing of 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; replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of losmapimod and its other product candidates; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; 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.

Fulcrum Therapeutics, Inc.
Selected Consolidated Balance Sheet Data
(In thousands)
(Unaudited)

	September 30, 2019	December 31, 2018
Cash and cash equivalents	$ 101,597	$ 72,797
Working capital[(1)]	96,637	69,866
Total assets	115,956	85,771
Convertible preferred stock	—	139,670

Total stockholders' equity (deficit)	102,128	(63,670)

(1) We define working capital as current assets minus current liabilities.

Fulcrum Therapeutics, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	**2018**	**2019**	**2018**
Operating expenses:				
Research and development	$ 13,496	$ 6,963	$ 58,985	$ 18,324
General and administrative	3,510	2,125	8,742	5,923
Total operating expenses	$ 17,006	$ 9,088	$ 67,727	$ 24,247
Loss from operations	(17,006)	(9,088)	(67,727)	(24,247)
Other income, net:				
Interest income, net	457	138	1,151	133
Other income	7	7	22	385
Net loss and comprehensive loss	$ (16,542)	$ (8,943)	$ (66,554)	$ (23,729)
Cumulative convertible preferred stock dividends	(796)	(1,858)	(7,128)	(3,736)
Net loss attributable to common stockholders	$ (17,338)	$ (10,801)	$ (73,682)	$ (27,465)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.97)	$ (8.08)	$ (10.33)	$ (23.28)
Weighted average number of common shares used in net loss per share attributable to common stockholders, basic and diluted	17,785	1,337	7,133	1,180

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