Disc Reports Topline Results from Phase 2 AURORA Study of Bitopertin in Patients with Erythropoietic Protoporphyria (EPP)

April 1, 2024

- *Met primary endpoint, demonstrating dose-dependent, statistically significant reductions in protoporphyrin IX (PPIX) compared to placebo in both 20 mg and 60 mg dose groups*
- *Improved measures of light tolerance, including the key secondary endpoint, in both 20 mg and 60 mg dose groups, but did not meet statistical significance compared to placebo*
- *Dose-dependent reductions in the rate of phototoxic reactions with pain, with statistical significance at the 60 mg dose group compared to placebo*
- *Dose-dependent improvements in the Patient Global Impression of Change (PGIC), with statistical significance at the 60 mg dose group compared to placebo*
- *Investor webcast at 8:30 am ET to discuss top-line data*

WATERTOWN, Mass., April 01, 2024 (GLOBE NEWSWIRE) -- Disc Medicine, Inc. (NASDAQ:IRON), a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel treatments for patients suffering from serious hematologic diseases, today presented topline data from AURORA, a phase 2 study of bitopertin in patients with EPP. Treatment with bitopertin resulted in statistically significant reductions in PPIX, the primary endpoint, and significant improvements in the rate of phototoxic reactions with pain and the Patient Global Impression of Change (PGIC). On the key secondary endpoint of cumulative time in sunlight on days without pain, bitopertin patients had a positive response consistent with BEACON results, but the endpoint did not meet statistical significance due to strong placebo performance.

“This study has confirmed that bitopertin significantly reduces the toxic metabolite, PPIX, in patients with EPP, and we have shown that bitopertin-treated patients experience improvements in the clinically meaningful outcomes of Patient Global Impression of Change and the number and rate of phototoxic reactions with pain, with the 60 mg dose reaching statistical significance compared to placebo. Despite the strong performance of bitopertin on the key secondary endpoint of cumulative time in light, consistent with results seen in BEACON, statistical significance was not met due to an outsized placebo response,” said John Quisel, J.D., Ph.D., President and Chief Executive Officer. “Given that, we will need to conduct an analysis of our final data set and work with investigators, regulators, and patient advocacy groups to define the optimal registrational endpoints moving forward. While we do this additional work, we continue to be excited about the upcoming readouts from our other programs, including updated data from our DISC-0974 study in anemia of myelofibrosis in Q2.”

The AURORA study is a randomized, double-blind, placebo-controlled phase 2 study that enrolled 75 adult subjects with EPP. Subjects were randomized 1:1:1 to receive 20 mg of bitopertin, 60 mg of bitopertin, or placebo once daily for 17 weeks.

Summary of topline results

Primary endpoint

- Bitopertin resulted in significant, dose-dependent, and sustained reductions in whole blood PPIX levels: -21.6% for 20 mg ($p=0.003$ vs placebo) and -40.7% for 60 mg ($p<0.001$ vs placebo); the placebo group had mean increases of +8.0%

Secondary endpoints

- Cumulative total time in sunlight between 10 am and 6 pm on days without pain observed over the 4-month treatment period: bitopertin-treated patients recorded a mean of 175.1 hours at 20 mg and 153.1 hours at 60 mg, compared with 133.9 hours for placebo; results were not statistically significant compared to placebo
    - The magnitude of the improvement in the bitopertin-treated patients was comparable to that observed in the BEACON study, but the benefit in the placebo arm in the AURORA trial was greater than expected
- Large improvements in light tolerance from baseline in 20 mg and 60 mg bitopertin treatment groups as measured by time to prodrome; results were not statistically significant relative to placebo.
- Substantial and dose-dependent reductions in phototoxic reactions with pain during the 4-month study period:
    - 75% reduction in the incidence rate of new phototoxic reactions with pain at the 60 mg dose group compared to placebo ($p=0.011$); 60% reduction in the 20 mg dose group ($p=0.109$)
    - Fewer bitopertin-treated patients reported a phototoxic event compared to placebo: 19% for 20 mg and 12% for 60 mg compared to 46% for placebo
- Dose-dependent improvements in PGIC, which were statistically significant for the 60 mg dose: 77% of completers at 20 mg and 86% at 60 mg ($p=0.022$ vs placebo) reported that their EPP was “much better” compared with 50% for placebo

- Bitopertin was generally well tolerated in both dose groups with no serious adverse events and stable hemoglobin levels. Two patients discontinued treatment due to treatment-emergent AEs, both in the 60 mg dose group: one due to dizziness and one due to a skin rash. The most common AE reported with bitopertin treatment was dizziness: n=4 in the 20 mg dose group, n=11 in the 60 mg dose group compared with n=4 in the placebo group (median durations of 4.5, 5, and 2 days, respectively)

Webcast Conference Call Information
Management will host a call on Monday, April 1 at 8:30 am ET to review the data. Please register for management's webcast on the Events and Presentations page of Disc's website (https://ir.discmedicine.com/).

About Bitopertin
Bitopertin is an investigational, clinical-stage, orally-administered inhibitor of glycine transporter 1 (GlyT1) that is designed to modulate heme biosynthesis. GlyT1 is a membrane transporter expressed on developing red blood cells and is required to supply sufficient glycine for heme biosynthesis and support erythropoiesis. Disc is planning to develop bitopertin as a potential treatment for a range of hematologic diseases including erythropoietic porphyrias, where it has potential to be the first disease-modifying therapy. There are currently two ongoing phase 2 clinical trials of bitopertin in patients with EPP that have fully enrolled and have had key data readouts: the open-label trial called BEACON and a randomized, double-blind placebo-controlled trial called AURORA.

Bitopertin is an investigational agent and is not approved for use as a therapy in any jurisdiction worldwide. Disc obtained global rights to bitopertin under a license agreement from Roche in May 2021.

About Erythropoietic Protoporphyria (EPP) and X-linked Protoporphyria (XLP)
Erythropoietic protoporphyria (EPP) and X-linked Protoporphyria (XLP) are rare, debilitating and potentially life-threatening diseases caused by mutations that affect heme biosynthesis, resulting in the accumulation of a toxic, photoactive intermediate called protoporphyrin IX (PPIX). This causes severe reactions when patients are exposed to sunlight, characterized by excruciating pain, edema, burning sensations and potential blistering and disfigurement. PPIX also accumulates in the hepatobiliary system and can result in complications including gallstones, cholestasis, and liver damage in 20-30% of patients and in extreme cases liver failure. Current standard of care involves extreme measures to avoid sunlight, including restricting outdoor activities to nighttime, use of protective clothing and opaque shields, and pain management. This has a significant impact on the psychosocial development, quality of life, and daily activities of patients, particularly in young children and families. There is currently no cure for EPP and only one FDA-approved therapy, a surgically implanted synthetic hormone designed to stimulate melanin production called Scenesse® (afamelanotide).

About Disc Medicine
Disc Medicine is a clinical-stage biopharmaceutical company committed to discovering, developing, and commercializing novel treatments for patients who suffer from serious hematologic diseases. We are building a portfolio of innovative, potentially first-in-class therapeutic candidates that aim to address a wide spectrum of hematologic diseases by targeting fundamental biological pathways of red blood cell biology, specifically heme biosynthesis and iron homeostasis. For more information, please visit www.discmedicine.com.

Disc Medicine Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding Disc's expectations with respect to its BEACON Phase 2 clinical studies of bitopertin and projected timelines for the initiation and completion of its clinical trials and other activities. The use of words such as, but not limited to, "believe," "expect," "estimate," "project," "intend," "future," "potential," "continue," "may," "might," "plan," "will," "should," "seek," "anticipate," or "could" or the negative of these terms and other similar words or expressions that are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Disc's current beliefs, expectations and assumptions regarding the future of Disc's business, future plans and strategies, clinical results and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Disc may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and investors should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements as a result of a number of material risks and uncertainties including but not limited to: the adequacy of Disc's capital to support its future operations and its ability to successfully initiate and complete clinical trials; the nature, strategy and focus of Disc; the difficulty in predicting the time and cost of development of Disc's product candidates; Disc's plans to research, develop and commercialize its current and future product candidates; the timing of initiation of Disc's planned preclinical studies and clinical trials; the timing of the availability of data from Disc's clinical trials; Disc's ability to identify additional product candidates with significant commercial potential and to expand its pipeline in hematological diseases; the timing and anticipated results of Disc's preclinical studies and clinical trials and the risk that the results of Disc's preclinical studies and clinical trials may not be predictive of future results in connection with future studies or clinical trials and may not support further development and marketing approval; the other risks and uncertainties described in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2023 and other documents filed by Disc from time to time with the Securities and Exchange Commission (SEC), as well as discussions of potential risks, uncertainties, and other important factors in Disc's subsequent filings with the SEC. Any forward-looking statement speaks only as

of the date on which it was made. None of Disc, nor its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law.

Media Contact

Peg Rusconi
Verge Scientific Communications
prusconi@vergescientific.com

Investor Relations Contact

Christina Tartaglia
Stern Investor Relations
christina.tartaglia@sternir.com