Fractyl Health Receives FDA IDE Approval for the Revita® Remain-1 Pivotal Study of Weight Maintenance in Obesity after Discontinuation of GLP-1 Based Drugs

Apr 1, 2024

Revita aims to be the first approved therapeutic option for durable weight maintenance after discontinuation of GLP-1 based drugs, as an adjunct to diet and exercise

With this FDA IDE approval, Fractyl Health will initiate the Remain-1 randomized, double blind pivotal study and begin providing updates on the open label cohort, which we refer to as the Reveal-1 cohort, in the second half of 2024

BURLINGTON, Mass., April 01, 2024 (GLOBE NEWSWIRE) -- Fractyl Health, Inc. (Nasdaq: GUTS) (the “Company”), a metabolic therapeutics company focused on pioneering new approaches for the treatment of obesity and type 2 diabetes (T2D), today announced U.S. Food and Drug Administration (FDA) approval of a pivotal Investigational Device Exemption (IDE) to study Revita’s efficacy in maintaining weight loss following the discontinuation of GLP-1 receptor agonist (GLP-1RA) drug therapy, addressing a key unmet need in the treatment of obesity. Obesity affects over 40% of the US population and is a critical precursor to various highly morbid and expensive chronic conditions such as type 2 diabetes, metabolic dysfunction-associated fatty liver disease, and cardiovascular disease.

The IDE approval launches the groundbreaking Remain-1 study, set to begin in the second half of 2024. Remain-1 is a randomized, double-blind trial of Revita versus sham in patients who have lost at least 15% total body weight on tirzepatide therapy. It is designed to be a pivotal study to potentially enable registrational filing for Revita for weight maintenance after GLP-1RA discontinuation. In parallel with the randomized portion of the Remain-1 study, Fractyl Health also announces Reveal-1, an open-label cohort that will follow a similar patient population and management protocol with anticipated open-label data updates as the study progresses.

The rationale for the Remain-1 pivotal study is based on a new need for therapeutic solutions that can offer durable weight maintenance without ongoing medical therapy. Highly potent drugs in the GLP-1RA class, including semaglutide (Wegovy®) and tirzepatide (Zepbound®), are now approved for the management of obesity and have dramatically altered the treatment landscape. However, real world studies report high discontinuation rates and clinical trials have indicated the risk of substantial weight rebound after discontinuation in many participants. Strategies to maintain weight loss independent of ongoing medical therapy could provide substantial clinical and economic benefits by extending the value of GLP-1RA drugs even after these medicines are discontinued.

“The unmet need in obesity is shifting from ‘How do we help people lose weight?’ to ‘How do we help people keep the weight off?’” said Christopher Thompson, MD MSc, Director of Endoscopy at Brigham and Women’s Hospital, Co-Director, Center for Weight Management and Wellness at Brigham Health, and Professor of Medicine at Harvard Medical School. “We now need new therapeutic strategies that can offer durable weight maintenance, and I am excited for the prospect of the Remain-1 pivotal study to hopefully address this massive challenge in obesity today.”

Revita is an outpatient endoscopic procedure that targets the duodenum and is designed to reverse pathology in the duodenal lining that is a root cause of obesity and T2D. In prior clinical studies of Revita conducted in people with T2D in the US and EU, pooled analyses of weight data provided evidence to support the potential for durable weight maintenance after a single Revita procedure.

The patient population for Remain-1 will consist of obese individuals with a BMI ≥ 30 kg/m^2. These GLP-1RA-naïve individuals will initiate tirzepatide therapy, titrated to achieve at least a 15% total body weight loss, followed by discontinuation of tirzepatide and randomization to either Revita treatment or a sham procedure. At least 315 subjects will be randomized 2:1 to Revita or sham.

The primary objectives of the study are

- to demonstrate that Revita is superior to sham in percent change in body weight from baseline to week 24, and
- to demonstrate that a majority of Revita participants maintain clinically significant weight loss after discontinuing tirzepatide therapy.

"We believe there is substantial clinical and economic value in new approaches to obesity that can enable durable weight

maintenance after stopping GLP-1 based drugs," said Dr. Harith Rajagopalan, CEO of Fractyl Health. "We were very happy to work collaboratively with key advisors in obesity and gastrointestinal endoscopy by rapidly developing this protocol to address a huge, emergent unmet need in the field."

About Fractyl Health
Fractyl Health is a metabolic therapeutics company focused on pioneering new approaches to the treatment of metabolic diseases, including T2D and obesity. Despite advances in treatment over the last 50 years, T2D and obesity continue to be rapidly growing drivers of morbidity and mortality in the 21st century. Fractyl Health's goal is to transform metabolic disease treatment from chronic symptomatic management to durable disease-modifying therapies that target the organ-level root causes of disease. Fractyl Health is based in Burlington, MA. For more information, visit **www.fractyl.com** or **www.twitter.com/FractylHealth**.

About Revita
Fractyl Health's lead product candidate, Revita, is based on the company's insights surrounding the potential role of the gut in obesity and T2D. Revita is designed to remodel the duodenal lining via hydrothermal ablation (i.e., duodenal mucosal resurfacing) to edit abnormal intestinal nutrient sensing and signaling mechanisms that are a potential root cause of metabolic disease. Revita has received a CE mark in Europe and, in January 2022, received reimbursement authorization through NUB in Germany for the treatment of T2D. In the United States, Revita is for investigational use only under US law. A pivotal study of Revita in patients with inadequately controlled T2D despite multiple medicines and insulin, called Revitalize-1, is currently enrolling in the United States and Europe.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause the Company's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the Company's limited operating history; the incurrence of significant net losses and the fact that the Company expects to continue to incur significant net losses for the foreseeable future; the Company's need for substantial additional financing; the Company's ability to continue as a going concern; the restrictive and financial covenants in the Company's credit agreement; the lengthy and unpredictable regulatory approval process for the Company's product candidates; uncertainty regarding its clinical studies; the fact that the Company's product candidates may cause serious adverse events or undesirable side effects or have other properties that may cause it to suspend or discontinue clinical studies, delay or prevent regulatory development, prevent their regulatory approval, limit the commercial profile, or result in significant negative consequences; the Company's reliance on third parties to conduct certain aspects of the Company's preclinical studies and clinical studies; the regulatory approval process of the FDA, comparable foreign regulatory authorities and notified bodies, are lengthy, time-consuming and inherently unpredictable, and even if we complete the necessary clinical studies, we cannot predict when, or if, we will obtain regulatory approval or certification for any of our product candidates, and any such regulatory approval or certification may be for a more narrow indication than we seek; and the potential launch or commercialization of any of product candidates or products and our strategic and product development objectives and goals. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including the factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, and in our other filings with the SEC. These forward-looking statements are based on management's current estimates and expectations. While the Company may elect to update such forward-looking statements at some point in the future, the Company disclaims any obligation to do so, even if subsequent events cause its views to change.

Contacts
Corporate Contact
Lisa Davidson, Chief Financial Officer
ir@fractyl.com, 781.902.8800

Media Contact
Beth Brett, Corporate Communications
Bbrett@fractyl.com, 720.656.6544

Investor Contact
Stephen Jasper
Gilmartin Group
stephen@gilmartinir.com, 619.949.3681