Fractyl Health Presents New Mechanistic Data on Revita® DMR in Type 2 Diabetes

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- *Patients treated with Revita experienced a 0.8%-point reduction in HbA1c along with a 33% improvement in markers of insulin sensitivity three months after undergoing the procedure*
- *Markers of insulin production capacity in the pancreas also improved, with a 25% increase in insulin secretion rate and a 37% improvement in Disposition Index*

LEXINGTON, MA., May 22, 2022 – Fractyl Health, an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes (T2D), announced today new data from its Revita-1 and Revita-2 studies. Prior publications from these open-label and sham-controlled studies have shown improvements in glycemic control and weight in subjects with inadequately controlled type 2 diabetes. New data presented at this week's Digestive Disease Week® (DDW) 2022 build on this earlier evidence to assess the effect of Revita on insulin resistance, insulin production capacity, and key metabolic hormones via a mixed meal tolerance test.

In the current investigation presented at DDW 2022, a pooled, post-hoc mechanistic analysis of insulin sensitivity, beta cell function, and metabolic hormone assessment was performed in all patients who were treated in the Revita-1 and Revita-2 open-label training phase studies in whom mixed meal tolerance tests were performed at baseline and three months post-intervention. Results in these subjects (n=28) exhibited the following findings at three months after a single outpatient procedure:

- **Glycemic control:** 8%-point reduction in HbA1c (from baseline of 8.2%; p=0.002) and 36 mg/dL reduction in fasting plasma glucose (from baseline 198 mg/dL; p<0.001)
- **Weight loss:** 3 kg reduction in weight (4.7% total body weight loss; p<0.001)
- **Insulin resistance:** 33% improvement in HOMA-IR and 32% improvement in the Matsuda Index, two measures of insulin resistance that have been associated with a heightened risk of T2D progression (p=0.005 for each)
- **Beta cell function:** 25% improvement in insulin secretion rate and 37% improvement in Disposition Index, two measures of pancreatic beta cell function that reflect an improvement in the pancreas' ability to produce and secrete insulin in response to a meal (p=0.002 and p=0.001, respectively)
- **Gut hormones:** The response of two key gut hormones known to regulate blood sugar (GIP and GLP-1) in response to a meal was unchanged after treatment with Revita

"The current data suggest that Revita may be the first investigational therapy to offer the potential for improvements in insulin sensitivity and pancreatic beta cell function months after a single minimally invasive, outpatient intervention," said Juan Carlos Lopez-Talavera, M.D. Ph.D., Chief Medical Officer, Fractyl Health. "These results raise intriguing questions about the potential for therapeutic interventions targeting the duodenum to help address underlying root causes of metabolic dysfunction in people with T2D."

About Revita®

Fractyl Health's lead product candidate, Revita, is based on the company's insights surrounding the potential role of the gut in metabolic diseases. 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 diseases. In April 2016, Revita received a CE mark from the European Union. In the United States, Revita is for investigational use only and has received Breakthrough Device designation from the FDA to improve glycemic control and eliminate insulin needs in T2D patients who are inadequately controlled on long-acting insulin.

About the Revitalize T2D Clinical Development Program

The Revitalize T2D program is a series of ongoing and planned clinical studies sponsored by Fractyl Health to investigate the potential utility of Revita in patients with, or at high risk for, T2D. The company's ongoing pivotal clinical study, Revitalize-1, is designed as a randomized, double-blind crossover, sham-controlled, multi-center study in patients with inadequately controlled T2D despite being on metformin, up to two additional ADAs, and long-acting insulin. The Revitalize-2 study is an ongoing pivotal study in patients with T2D who are inadequately controlled on two or three ADAs for whom insulin would be the next step in therapy. The Revitalize-3 proof-of-concept pilot study is a planned study in patients with high-risk prediabetes to evaluate the effects of hydrothermal ablation of the duodenal mucosa using Revita to reduce the risk of developing T2D.

About Fractyl Health

Fractyl Health is focused on pioneering a new approach to the treatment of T2D. Despite advances in treatment over the last 50 years, metabolic diseases in general, and T2D in particular, continue to be a principal and rapidly growing driver of morbidity and mortality in the 21st century. Fractyl Health's goal is to transform T2D treatment from chronic blood glucose management to disease-modifying therapies that target the organ-level root causes of the disease. Fractyl Health's lead product candidate, Revita, is designed to remodel the duodenal lining via hydrothermal ablation (i.e., duodenal mucosal resurfacing) in order to edit abnormal intestinal nutrient sensing and signaling mechanisms that are a potential root cause of metabolic diseases. Fractyl Health is a private organ-editing metabolic therapeutics company based in Lexington, MA. For more information, visit www.fractyl.com or www.twitter.com/FractylHealth

About Digestive Disease Week®

Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and virtual meeting from May 21-24, 2022. The meeting showcases more than 3,100 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

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