Fractyl Health Announces FDA IDE Approval to Begin Revitalize-2 Pivotal Study Designed for Patients with Type 2 Diabetes (T2D) Who Are Not Yet on Insulin

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- *Revitalize-2 is the second pivotal study for the Revita DMR® system (Revita®) in Fractyl Health's Revitalize T2D clinical development program*
- *Revitalize T2D is designed to evaluate the potential of Revita in over 1,000 patients across the spectrum of T2D and prediabetes*

LEXINGTON, MA., April 4, 2022 – Fractyl Health, an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes (T2D), announced that the company has received approval from the U.S. Food and Drug Administration (FDA) for an Investigational Device Exemption (IDE) to begin its Revitalize-2 pivotal study. This new pivotal study of Revita is designed for patients with T2D whose disease is inadequately controlled despite treatment with at least two antidiabetic agents (ADAs) and who are not yet on insulin. Revitalize-2 is a prospective, randomized, double-blind, sham-controlled study enrolling up to 510 patients at up to 35 sites around the world, with approximately 25 sites in the United States. This pivotal study aims to examine the effect of Revita on improving glycemic control and preventing the need for insulin therapy. The primary endpoint of the study will be change in HbA1c (reflecting degree of glycemic control), comparing Revita to a sham treatment arm.

"We are delighted the FDA has granted this IDE allowing Fractyl Health to begin a second pivotal clinical study evaluating Revita DMR in a high unmet need T2D patient population that is looking for an alternative to insulin therapy. Alongside our ongoing Revitalize-1 study for patients who are already on insulin, Revitalize-2 has potential for patients whose disease is inadequately controlled on multiple antidiabetic agents and who may benefit from a non-drug option to address the root cause of their disease," said Juan Carlos Lopez-Talavera M.D., Ph.D., Fractyl Health's Chief Medical Officer.

Revita has been tested in early pilot clinical studies in approximately 300 patients with various stages of T2D. The Revitalize T2D clinical development program is designed to encompass multiple parallel ongoing and planned clinical studies aiming to test the use of Revita in different populations ranging from patients with prediabetes to those with T2D on long-acting insulin. The Revitalize-1 pivotal study is the first of these clinical studies and is actively enrolling insulin-treated patients in multiple centers in the U.S. and Europe.

"We believe there is considerable potential to intervene in gut dysfunction in a manner that may prevent disease progression or the development of T2D altogether," said Harith Rajagopalan, M.D., Ph.D., Fractyl Health's Co-Founder and Chief Executive Officer. "We see the Revitalize-2 pivotal study as an important step in the journey for Revita in patients with T2D and potentially prediabetes as well."

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. Revita has received a CE mark in Europe and in January 2022 received reimbursement authorization in Germany. 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 or multiple ADAs, and long-acting insulin. The Revitalize-2 study is an FDA IDE approved pivotal study in T2D patients who qualify for insulin and are failing guideline-directed 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.

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