Fractyl Announces FDA IDE Approval to Begin Pivotal Study of Revita DMR for Insulin-Treated Patients with Type 2 Diabetes

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Revita T2Di pivotal study to evaluate the ability of Revita DMR, the first non-drug, non-surgical, disease-modifying therapy, to eliminate need for insulin injections in T2D; enrollment expected to begin in late 2020

LEXINGTON, Mass., June 3, 2020 — Fractyl Laboratories Inc. (Fractyl) today announced that the company has received approval from the U.S. Food and Drug Administration (FDA) of an Investigational Device Exemption (IDE) to begin a pivotal study of Revita® DMR in type 2 diabetes (T2D) patients treated with insulin. This landmark pivotal study, called Revita T2Di, is a prospective, randomized, double-blind, sham-controlled study enrolling 300 patients at up to 35 sites around the world, with approximately 25 sites in the United States. Revita T2Di aims to examine the effect of Fractyl's Revita DMR (duodenal mucosal resurfacing) treatment on glycemic control and insulin requirements. The primary endpoint of the study will be the percentage of patients who are able to achieve target glycemic control (HbA1c less than or equal to 7%) without the need for insulin at 24 weeks, comparing Revita DMR to the sham arm.

"We are delighted the FDA has granted this IDE allowing Fractyl to begin a clinical study evaluating the ability of Revita DMR to not only improve glycemic (blood glucose) control but also eliminate or reduce insulin injections for patients with advanced type 2 diabetes," said Juan Carlos Lopez-Talavera, M.D., Ph.D., Fractyl's Chief Medical Officer. "We are grateful for the close collaboration with our scientific advisors and the productive partnership with the FDA that has led to the design of this pivotal study that aims to address the challenges and burden of insulin therapy with the use of Revita DMR."

The Revita T2Di pivotal study will enroll patients who have inadequately controlled T2D despite taking both oral drugs and insulin injections and adopting lifestyle changes. There are approximately 5 million people in the United States with T2D who are on insulin therapy, and more than half still do not achieve adequate glycemic targets.

"The Revita T2Di pivotal study addresses a significant challenge in today's treatment of type 2 diabetes, which is that most patients on insulin are still not able to achieve adequate glycemic (blood sugar) control. There is increasing evidence for the role of the gut in metabolic diseases, and data from earlier clinical studies of Revita DMR is encouraging. I am happy that the FDA has approved an IDE for this study that will evaluate a new approach to T2D that can potentially improve glycemic control and reduce insulin needs," said endocrinologist David Klonoff, M.D., Clinical Professor of Medicine, University of California, San Francisco.

"I am excited to partner with my endocrine colleagues in evaluating the role of Revita DMR as a potential treatment for type 2 diabetes," said Dr. Richard I. Rothstein, M.D., Professor of Medicine and Chair of Department of Medicine at Dartmouth-Hitchcock Medical Center in Lebanon, N.H. "Based on my experience in the U.S. pilot safety study, the Revita DMR technology is straightforward to learn, very well tolerated by patients, and can be performed in an outpatient setting in less than an hour. In addition to the glycemic benefits observed in type 2 diabetes in earlier studies, there was also significant improvement in liver disease parameters, including significant reduction in liver fat, and lipid profiles. This highlights the multifactorial and complicated nature of metabolic control and how achieving optimal clinical outcomes requires a multidisciplinary approach to correctly diagnose and treat patients with these conditions."

Revita is a first-in-class intervention designed to target insulin resistance and metabolic disease progression by resetting key pathways in the gut that drive metabolic disease. This minimally-invasive, outpatient, endoscopic procedure is a non-drug and non-surgical alternative that has been shown in clinical trials to enhance insulin sensitivity, lower HbA1c, and reduce liver fat to create long-lasting improvements in both blood sugar control and fatty liver disease to help patients with type 2 diabetes avoid further medication escalation.[1]

"The FDA's IDE approval for our pivotal study is an important and exciting milestone for Fractyl. Having first developed the science around the role of the gut in metabolic diseases and then establishing the proof of concept of Revita DMR as a treatment with the potential to reverse metabolic diseases, this pivotal study is now poised to evaluate the role of Revita DMR in addressing a critical need for patients and health systems in managing type 2 diabetes," said Harith Rajagopalan M.D. Ph.D., co-founder and CEO of Fractyl. "The clinical, economic, and patient burden of type 2 diabetes in society is already too large and growing too rapidly. Fractyl is committed to changing the trajectory of this disease for our patients and society. This pivotal study will be an important step in our journey toward developing and commercializing a therapy that has the potential to reverse the root cause of the disease."

Details on the trial will soon be posted on www.clinicaltrials.gov.

1. Van Baar, et al. Gut, 2020; 69:295-303.

About the Revita® DMR Treatment

The Revita DMR treatment harnesses breakthrough insights in intestinal biology and aims to reset key metabolic pathways, including insulin resistance, to prevent and even reverse metabolic disease progression. This same-day, outpatient endoscopic procedure uses heat to resurface the lining of the upper intestine (duodenal mucosa) in a minimally invasive, outpatient procedure. Data from clinical trials, involving close to 300 patients at over 20 centers across three continents, has demonstrated that one Revita treatment can create long-lasting improvements in both blood sugar control and fatty liver disease to help patients with type 2 diabetes avoid further medication escalation. Revita DMR has been shown to be safe and well tolerated with no long-term adverse events in clinical studies to date. In April 2016, the Revita DMR System received a CE mark in the European Union. In the United States, Revita is approved for investigational use only by the U.S. Food and Drug Administration. The Revita DMR System may be available for investigational use in other regions.

About Fractyl

Fractyl Laboratories is applying unparalleled insights into intestinal biology to advance treatments and potential cures for metabolic diseases. Fractyl is developing Revita DMR, a same-day, minimally invasive procedure to treat highly prevalent metabolic diseases, resulting from insulin resistance, including type 2 diabetes (T2D) and nonalcoholic fatty liver disease (NAFLD), of which the more serious condition is nonalcoholic steatohepatitis (NASH). The company's unique treatment approach offers the potential to restore health to millions of patients worldwide and reduce the global economic and healthcare burden of metabolic disease. Fractyl is a private biotechnology company based in Lexington, Mass. For more information, visit www.fractyl.com or www.twitter.com/FractylLabs.

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