Fractyl Announces New Clinical Data on the Mechanism of Revita DMR in Type 2 Diabetes

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Data presented at ENDO 2020 from the randomized, sham-controlled REVITA-2 study verifies that improvements in blood glucose control (HbA1C), insulin sensitivity, and other metabolic measures seen after one Revita treatment are also associated with improved pancreatic beta-cell function. Revita is the first non-drug, non-surgical, disease-modifying therapy in clinical trials in the U.S. and commercially available in the U.K. for the treatment of type 2 diabetes.

LEXINGTON, Mass., March 30, 2020 — Fractyl Laboratories Inc. (Fractyl) today announced clinical data that elucidate the mechanisms behind the beneficial effects and significant improvements in metabolic disease parameters for type 2 diabetes patients after one Revita® duodenal mucosal resurfacing (DMR) treatment. The data, including results from a mixed meal tolerance test, was accepted for presentation at the Endocrine Society's annual meeting, ENDO 2020 (cancelled due to the COVID-19 pandemic) and will be published in a special supplemental section of the *Journal of the Endocrine Society*. This clinical data was featured as a "Breakthrough in Diabetes" at today's webcast news conference hosted by the Endocrine Society.

Previous results from the REVITA-2 study, a randomized, sham-controlled clinical trial, presented at AASLD 2019 and recognized there as 'Best of the Liver 2019,' have shown that Revita treatment lowers blood glucose (HbA1c) and reduces liver fat in patients with type 2 diabetes and non-alcoholic fatty liver disease (NAFLD) compared to a sham procedure. For the sham, the Revita catheter was inserted into the intestine but no treatment was performed. All patients underwent a graduated diet for two weeks after the intervention per protocol. Neither the patients nor the endocrinologist knew which treatment the patients received.

As part of the REVITA-2 study, 70 patients with inadequately controlled type 2 diabetes on oral anti-diabetic medications (OADs) also took part in an additional evaluation called the mixed meal tolerance test (MMTT), which helps determine insulin sensitivity and pancreatic beta cell function. The MMTT was performed at baseline and three months after treatment in these patients. Compared with those receiving a sham procedure, patients who received the Revita treatment had significantly lowered glucose levels, primarily driven by decreased fasting blood glucose levels. The average fasting glucose level fell by 41 mg/dL in the Revita-treated group, whereas in the sham group, it only dropped by 15 mg/dL. Improvements in insulin sensitivity and pancreatic beta cell responsiveness to a meal were also observed in patients who received the Revita treatment compared to those that received the sham treatment.

David Hopkins, MB.Ch.B. (M.D.), director of the Institute of Diabetes, Endocrinology and Obesity, King's Health Partners in London, U.K. and REVITA-2 study investigator, said, "This data verifies the gut's critical role as a root cause of metabolic disease and as an important therapeutic target for type 2 diabetes. Revita leverages many of the benefits of bariatric surgery on glucose metabolism but as a minimally-invasive, outpatient procedure, it is a potential solution for millions of patients. With these data, we show that Revita can change the trajectory of disease by addressing the underlying insulin resistance that causes the progressive failure of the pancreatic beta cells. It's a major step forward in the development of a disease-modifying treatment for type 2 diabetes."

David Ehrmann, Professor of Medicine, University of Chicago, and a member of the Writing Committee for the Restoring Insulin Secretion (RISE) study, commented, "From the RISE study, it was disappointing to see that none of the drugs currently approved to treat type 2 diabetes could reverse pancreatic beta cell failure and, thus, could not stop disease progression. RISE results raise the question as to whether currently available pharmacologic agents will be able to fundamentally alter the trajectory of metabolic disease. These data from a completely innovative, minimally-invasive treatment provide hope that we will have the capability to help our patients improve and possibly mitigate the complications of diabetes instead of managing its symptoms with medications."

Harith Rajagopalan, M.D., Ph.D., co-founder and CEO of Fractyl, said, "The data from the REVITA-2 clinical study presented here builds on what we previously presented this past November at AASLD to show that one Revita treatment in the gut can improve the health and function of both the pancreas and the liver. It further confirms that by intervening in gut biology we can reverse both progressive beta cell deterioration and insulin resistance, which has implications for treating a number of metabolic diseases. Now, across hundreds of patients and several clinical studies in patients who have received Revita treatment, we have seen consistent and significant efficacy with an excellent safety profile. With two-year durability data, and now confirmation that Revita DMR is a disease-modifying therapy that can reverse insulin resistance, we are in a prime position to initiate our U.S. pivotal trial and accelerate global commercialization."

1. JAMA Internal Medicine, August 2019, doi:10.1001/jamainternmed.2019.2396

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. Revita is available to patients with type 2 diabetes in the United Kingdom (UK) via HCA Healthcare UK, which is the largest provider of privately funded healthcare in the UK and is part of the US-based HCA Healthcare, the world's largest private hospital group. 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 Type 2 Diabetes and NAFLD/NASH

Type 2 diabetes and NAFLD/NASH are two of the most prevalent metabolic diseases and have reached epidemic levels in the United States and around the world, affecting nearly a billion people. An estimated 18 million people in the United States have both conditions, which greatly increases their risk of negative health outcomes. While there is an increasing number of pharmacological treatments for type 2 diabetes, these have not translated into meaningful improvement in treatment outcomes for the patient and at the population level.[1] There are currently no FDA-approved treatments for NAFLD/NASH.

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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