Fractyl Health Initiates Landmark Scientific Partnership to Study Root Cause Mechanisms Underlying Type 2 Diabetes

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- *Newly formed Erase T2D task force comprises leading scientists and pioneering scientific research to elucidate the role of the duodenum in type 2 diabetes and metabolic control*
- *Fractyl Health-supported research projects are now underway at Vanderbilt University and University of Michigan*

LEXINGTON, MA., November 1, 2022 – Fractyl Health, an organ-editing metabolic therapeutics company focused on pioneering a new approach to the treatment of type 2 diabetes (T2D), announced the creation of the Erase T2D task force, an academic-industry scientific partnership charged with advancing research on the role of the gut in metabolic disease to catalyze future discoveries that may inform how type 2 diabetes (T2D) can be better understood and hopefully 'erased.' Fractyl Health further announces that this partnership's first two research projects have now been initiated with Professor Alan Cherrington at Vanderbilt University and Professor Randy Seeley at University of Michigan. These two scientific research initiatives will establish a foundation of new evidence on nutrient sensing and signaling mechanisms in a segment of the intestine called the duodenum. The ambition is that this collaboration will lead to a deeper understanding of the possible causal relationship between a dysfunctional duodenum and the onset and progression of T2D.

The first of these studies, led by Alan Cherrington, Ph.D., Professor of Molecular Physiology & Biophysics, Professor of Medicine, and the Jacquelyn A. Turner and Dr. Dorothy J Turner Chair in Diabetes Research at Vanderbilt University School of Medicine, will focus on defining the gut-derived signaling pathways central to the development and progression of T2D. From Dr. Cherrington, "If the development of duodenal dysfunction as a consequence of high fat and sugar diets is an important event in the development of T2D, we need to try to understand which duodenal changes could represent key causal steps in metabolic dysregulation and diabetes pathogenesis."

The second study, led by Randy Seeley, Ph.D., Professor of Surgery and Director of Michigan Nutrition Obesity Research Center at the Elisabeth Weiser Caswell Diabetes Institute in the University of Michigan Medical School, will focus on establishing a rodent model of duodenal mucosal disruption to help better define the mechanism of action of therapies targeting the duodenal mucosa. "I am confident that we are taking the first steps in gaining a deeper understanding of the processes in the gut that lead to metabolic disease. This will enable us to identify precursors and therefore ultimately build increasingly effective therapeutic approaches that could lead to a metabolic reset in patients with T2D," notes Dr. Seeley.

These two studies will build upon a growing body of evidence by scientists around the world who have identified duodenal dysfunction as a potential root cause of metabolic disease (Aliluev et al; Duca et al). In spearheading this partnership, Fractyl Health is enthusiastic to begin this effort with academic partners who are icons in the field. "Our ambition is to support the deep science that will lead to a greater understanding of the root causes of T2D. We know these studies are the beginning of a journey and will lead to findings – and more questions – we can use to define our next steps in the process of discovery," says Harith Rajagopalan, M.D., Ph.D., Co-Founder and CEO of Fractyl Health.

About the Erase Task Force
The Erase Task Force is an academic-industry scientific partnership built on decades of scientific investigation which has identified the critical role of the gut as a regulator of metabolic disease. The signaling mechanisms between the gut and the rest of the body are numerous and not yet fully delineated. The Erase Task Force is charged with advancing research to catalyze future discoveries that may inform how T2D can be better understood and ultimately erased. Partnership members include: Alan Cherrington, Ph.D. (co-chair), Professor of Molecular Physiology & Biophysics, Professor of Medicine, and the Jacquelyn A. Turner and Dr. Dorothy J Turner Chair in Diabetes Research at Vanderbilt University School of Medicine; Harith Rajagopalan, M.D., Ph.D. (co-chair), Co-founder and CEO of Fractyl Health; Dave D'Alessio, M.D., Professor of Medicine and Chief of Division of Endocrinology and Metabolism at Duke University School of Medicine; Geltrude Mingrone, M.D., Ph.D., Professor of Diabetes and Nutrition at King's College, London, Associate Professor of Internal Medicine at Catholic University of Rome; Randy Seeley, Ph.D., Professor of Surgery and Director of Director of the Michigan Nutrition Obesity Research Center at University of Michigan Medical School.

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 principal and rapidly growing drivers 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 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 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.

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