Fractyl Health Announced Positive Proof-of-Concept Data of Pancreatic GLP-1 Gene Therapy in a Type 2 Diabetes Animal Model at the 20th World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease

Dec 5, 2022

- *POC efficacy data in rodents shows that a novel adeno-associated virus (AAV) pancreatic gene therapy platform can confer dose-dependent effects on improving insulin production and reducing blood sugar*
- *Dose-dependent metabolic benefits were sustained through 2 months of follow up after a single dose islet-targeted gene therapy administration in a rodent model of T2D and obesity*

LEXINGTON, MA., December 5, 2022 – Fractyl Health, an organ-editing metabolic therapeutics company focused on pioneering new approaches for the treatment of type 2 diabetes (T2D), today announces that positive new preclinical proof-of-concept data was presented at the World Congress of Insulin Resistance, Diabetes & Cardiovascular Disease (WCIRDC) that took place in Los Angeles, from Dec 1-3, 2022. At WCIRDC, the Company shared new data from its Rejuva program, a novel device and AAV-mediated delivery platform for gene therapy directly targeting the pancreas to potentially embed multiple different pharmacologies to address serious metabolic diseases, including T2D and obesity.

The Rejuva platform encompasses both AAV-delivered transgenes and device-based delivery systems that have the potential to deliver these novel gene therapies directly to the pancreas. Data presented in the current study includes new dose-dependent *in vivo* pharmacology and efficacy data for an AAV-mediated gene therapy of a GLP-1 receptor agonist candidate in a db/db rodent model of T2D. The Company also announces today that it plans to present encouraging large animal procedure feasibility data from its novel Rejuva delivery device system at an international congress in 2023.

"Today's Rejuva program preclinical results represent the first demonstration of sustained, dose-dependent efficacy of a gene therapy targeting the GLP-1 receptor pathway in the pancreas in a rodent model of type 2 diabetes and obesity," said Harith Rajagopalan, M.D, Ph.D., Co-Founder and Chief Executive Officer of Fractyl Health. "Results show that a single dose islet-targeted GLP-1 receptor agonist gene therapy candidate can induce sustained production of the transgene in pancreatic islets, delay disease progression, improve insulin production, and reduce blood glucose levels for up to ten weeks of follow-up."

Dr. Rajagopalan continued, "The deterioration of insulin production in the pancreas is the *sine qua non* of hyperglycemia in T2D, and despite advancements in the field, progressive loss of beta cell function has not been resolved with current therapies. We are developing not only an AAV vector platform, but also local delivery devices and methods to potentially enable pancreatic gene therapy to become a reality for the first time. In many gene therapy programs, local delivery is demonstrating the potential to reduce viral load and associated risk of systemic administration, and we believe the same could be true for the pancreas. Taken together, our Revita and Rejuva programs have the potential to address root cause pathology in two organs that are diseased in T2D: the gut and the pancreas."

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) 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 under US law 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. 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 World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease (WCIRDC)

WCIRDC is a global meeting dedicated to diabetes, obesity, lipids, cardiovascular-kidney, and liver disease. The Congress links basic research to clinical practice in pursuit of the theme: Exploring New Frontiers in Metabolism — Tomorrow's Clinical Science Today.

WCIRDC 2022 is a virtual and in-person meeting that took place in Los Angeles on December 1-3, 2022. More information can be found at https://www.wcir.org.

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