Fractyl Health Unveils Groundbreaking Pre-Clinical Proof of Concept Results for its Rejuva® Pancreatic Gene Therapy Platform for Metabolic Diseases at the American Society of Gene & Cell Therapy Congress

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Rejuva device & procedure reliably and successfully targets pancreas with Adeno Associated Virus (AAV), potentially enabling gene therapy to address pancreatic diseases for the first time

Rejuva platform and genetic medicines offer potential for reversal of Type 2 Diabetes with a single point-in-time local administration of durable GLP-1-based genetic medicines

LEXINGTON, Mass.–(BUSINESS WIRE)– Fractyl Health today presented key findings from its preclinical Rejuva® program at the American Society of Gene & Cell Therapy (ASGCT) Congress. The oral presentation, "A Pancreatic Gene Therapy Delivery Platform for the Treatment of Type 2 Diabetes," highlighted proof-of-concept work of the Rejuva platform and its potential to revolutionize the treatment of type 2 diabetes (T2D) and obesity.

Importantly, the data presented today establishes the feasibility and proof-of-concept efficacy of AAV viral delivery to the pancreas and dose-dependent efficacy of GLP-1 based genetic medicines to restore the pancreas' ability to produce insulin and thereby dramatically improve blood sugar control and change the trajectory of diabetes – without any unexpected safety signals observed thus far.

"What is exciting to me about the Rejuva platform is that we now have substantial proof of concept in animal models that local delivery of AAV to the pancreas may not only be feasible, but could have profound effects on metabolic control," said Christopher C. Thompson, MD, Director of Endoscopy at Brigham and Women's Hospital and Professor at Harvard Medical School. "By targeting the pancreas, we may be able to reverse the pathology in that organ that drives T2D."

Rejuva is an AAV-based gene therapy platform designed to enable local and durable production of therapeutic proteins by the pancreas. The Rejuva platform combines three key therapeutic elements:

- a novel endoscopic device and route of administration to locally deliver gene therapy vectors directly to the pancreas,
- AAV-based gene therapy delivery vehicles designed to deliver genetic medicines targeting the pancreas, and
- tissue-restricted expression of potential genetic medicines within the pancreas itself.

Data presented today at ASGCT demonstrate that:

- the Rejuva device and approach can feasibly and reliably deliver AAV viral vectors to the pancreas via an endoscopic approach through the mouth (studies conducted in large animal models that are representative of human anatomy)
- AAV9 can target the pancreas with this local administration and successfully deliver genetic medicines to the pancreas at much lower doses than would be required through other approaches
- GLP-1 based gene therapy in the pancreas can durably improve blood sugar control and prevent progression of T2D (studies conducted in the db/db rodent model of T2D and obesity)

Together, the data presented today establish proof of concept for an AAV-based single administration of a genetic medicine delivering tissue-restricted expression of GLP-1RA within the pancreatic islet as a potentially potent and durable treatment for T2D.

"The progressive failure of the pancreas is the sine qua non of T2D. If we can protect the pancreas from failing, we can prevent the progression of T2D. Today's proof-of-concept findings show for the first time the potential that gene therapy has to protect the pancreas in T2D," said Dr. Harith Rajagopalan, CEO of Fractyl Health. "Our goal at Fractyl Health is to eradicate T2D for the millions of people living with the disease, and these results take us one step closer to that goal."

About Fractyl Health

Fractyl Health is focused on pioneering new approaches 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 is a private organediting

metabolic therapeutics company based in Lexington, MA. For more information, visit www.fractyl.com or www.twitter.com/FractylHealth

About Rejuva®

Fractyl Health's Rejuva platform focuses on developing next-generation adeno-associated virus (AAV)- based, locally delivered gene therapies for the treatment of T2D and other metabolic diseases. The Rejuva platform is in preclinical development and has not yet been evaluated by regulatory agencies for investigational or commercial use. Rejuva leverages advanced delivery systems and proprietary screening methods to identify and develop metabolically active gene therapy candidates targeting the pancreas. The program aims to transform the management of metabolic diseases by offering novel, disease-modifying therapies that address the underlying root causes of disease.

About ASGCT

The American Society of Gene & Cell Therapy (ASGCT) is a leading international organization for researchers, clinicians, and industry professionals dedicated to the advancement of gene and cell therapies. ASGCT's annual congress brings together experts from around the world to discuss the latest developments in gene editing, gene therapy, stem cell therapy, and cell therapy. The event offers a platform for sharing groundbreaking research, fostering collaborations, and shaping the future of these rapidly evolving fields. More information can be found at www.asgct.org.

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