



Fractyl Health Announces Nomination of RJVA-001 as First Clinical Candidate in its Rejuva® GLP-1 Gene Therapy Platform

Jan 5, 2024

RJVA-001 is the first GLP-1 pancreatic gene therapy (GLP1 PGTx) candidate to be nominated by the Company and is designed to improve upon known issues of treatment discontinuation and metabolic rebound typically seen with existing GLP-1 based therapies

Fractyl Health further announces successful meeting with European regulators to align on clinical trial-enabling path for RJVA-001 leading to a first-in-human (FIH) study in Type 2 Diabetes (T2D)

The Company anticipates completing IND-enabling studies, or its equivalent, for RJVA-001 in the second half of 2024

LEXINGTON, Mass., Jan. 05, 2024 (GLOBE NEWSWIRE) — Fractyl Health, a metabolic therapeutics company focused on pioneering new approaches for the treatment of T2D and obesity, announced the nomination of RJVA-001 as the first clinical T2D candidate in its Rejuva gene therapy platform. This milestone marks the Company's first GLP1 gene therapy candidate to emerge from the platform, setting the stage for a potentially transformative approach to treating metabolic diseases, including obesity and T2D.

The goal of the Rejuva platform is to achieve the durable remission of obesity and T2D, and it is designed to deliver locally administered genetic medicines to the pancreas to enable the durable production of nutrient-responsive hormones. We believe the Rejuva platform represents a major leap forward in the GLP-1 therapy landscape because pancreatic production and secretion of nutrient-responsive hormones have the potential to exhibit several key advantages over systemic GLP-1 therapies. Benefits may include the potential for a high local concentration of GLP-1 in the pancreas without high circulating levels and the potential for durable efficacy from sustained transgene expression within islets. RJVA-001, the platform's first clinical candidate, combines a novel, proprietary Rejuva catheter for delivery, an AAV9 serotype vector, and a proprietary transgene construct, which features a modified human insulin promoter and a modified human GLP-1 coding sequence.

Encouraging head-to-head proof-of-concept studies versus semaglutide in well-validated disease models have shown that a single administration of a GLP1 PGTx candidate may achieve superior glucose-lowering potency in the db/db rodent model of T2D and durable weight loss in the diet-induced obesity (DIO) rodent model.¹

"Our goal is to drive a major advance in metabolic care by developing therapies that aim to eradicate T2D and obesity. We're excited by the potential of the Rejuva platform, led by RJVA-001, to redefine the treatment landscape for patients by offering sustained, physiologic GLP-1 from the pancreas. Successful demonstration of safety, feasibility, and activity of RJVA-001 in humans may open the door to a suite of genetic medicines targeting the pancreas that aim to durably remit metabolic diseases altogether," said Harith Rajagopalan MD PhD, co-founder and CEO of Fractyl Health. "In addition, our Revita[®] candidate is currently being tested in a pivotal study for glucose control in advanced T2D, and we plan to test it for maintenance of weight loss after GLP-1 drug discontinuation for patients who cannot remain on GLP-1 therapies."

Fractyl Health has engaged with European regulators to align on an IND-enabling path for RJVA-001 for the treatment of T2D. The Company anticipates completing IND-enabling studies, or its equivalent, for RJVA-001 in the second half of 2024.

About Fractyl

Fractyl Health is a metabolic therapeutics company focused on pioneering new approaches to the treatment of metabolic diseases, including T2D and obesity. Despite advances in treatment over the last 50 years, T2D and obesity continue to be rapidly growing drivers of morbidity and mortality in the 21st century. Fractyl Health's goal is to transform metabolic disease treatment from chronic symptomatic management to durable disease-modifying therapies that target the organ-level root causes of disease. Fractyl Health is 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 obesity. 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 Revita

Fractyl Health's lead product candidate, Revita, is based on the company's insights surrounding the potential role of the gut in obesity and T2D. 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 disease. Revita has received a CE mark in Europe and, in January 2022, received reimbursement authorization through NUB in Germany. In the United States, Revita is for investigational use only under US law. A pivotal study of Revita in patients with inadequately controlled T2D despite multiple medicines and insulin, called Revitalize-1, is currently enrolling in the United States and Europe.

[1] https://www.fractyl.com/wp-content/uploads/2023/12/Fractyl-Health_WCIRDC-2023_Rejuva_FINAL.pdf

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