# Fractyl Health Presents Compelling Preclinical Data from Single-Administration GLP-1 Pancreatic Gene Therapy Rejuva® at Digestive Disease Week 2024

May 20, 2024

*Results showed single-administration GLP-1 pancreatic gene therapy candidate reduced liver weight by 42% (p<0.01) and liver triglycerides by 67% (p<0.0001) compared to placebo two months after administration*

*Data also demonstrated reductions of 36% in total cholesterol and 51% in low density lipoprotein (LDL) cholesterol (both, p<0.0001) compared to placebo two months after administration*

*New results highlight potential for profound, durable, and broad metabolic benefit that can be achieved from single-administration GLP-1-based pancreatic gene therapy*

BURLINGTON, Mass., May 20, 2024 (GLOBE NEWSWIRE) -- Fractyl Health, Inc. (Nasdaq: GUTS) (the "Company"), a metabolic therapeutics company focused on pioneering new approaches for the treatment of obesity and type 2 diabetes (T2D), presented new data from its preclinical Rejuva pancreatic gene therapy program as part of an oral presentation (abstract number 4029196) on Sunday, May 19th, at Digestive Disease Week (DDW) 2024 in Washington, D.C.

"Metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction associated steatohepatitis (MASH) are the leading cause for liver transplant in the U.S. today. These diseases are caused by metabolic disease-associated accumulation of liver triglycerides and consequent liver inflammation. GLP-1-based drugs have demonstrated improved MASH in humans and are under investigation as a potential therapy for MASH. This is the first demonstration of a GLP-1-based pancreatic gene therapy (GLP-1 PGTx) on liver metabolic health in an obesity murine model – one that has strong potency, durable results, and a single administration," said Harith Rajagopalan, M.D., Ph.D., co-founder and Chief Executive Officer of Fractyl. "These data potentially open the door to a curative intervention for MASLD/MASH that is accessible to gastroenterologists to perform. Fractyl plans to nominate its first GLP-1 PGTx candidate for obesity in the second half of 2024 and is eager to explore potential effects on MASLD/MASH."

In the presentation titled "Single-Dose GLP-1-Based Pancreatic Gene Therapy Maintains Weight Loss After Semaglutide Withdrawal and Reduces Hepatic Triglycerides in a Murine Model of Obesity," data showed that Rejuva reduced liver weight by 42% (p<0.01) and liver triglyceride content by 67% (p<0.0001) compared to placebo two months after administration.

Data also showed a reduction of 36% in total cholesterol and 51% in LDL cholesterol compared to placebo two months after administration (both, p<0.0001). These results indicate the potential impact of this GLP-1 PGTx candidate to alleviate cardiovascular risk associated with increased levels of cholesterol.

Rejuva is the Company's modular, physiologic gene therapy platform with three key elements designed to enable successful pancreatic gene therapy: (1) a proprietary delivery catheter designed to enable local, low-dose, therapeutic delivery directly to the pancreas via endoscopic access, (2) vectors with tropism for the pancreatic islet to enable successful transduction and gene delivery with limited biodistribution, and (3) transgenes with tissue-restricted promoters and metabolically active peptides that can durably impact glucose and weight control.

**About Fractyl Health**
Fractyl Health is a metabolic therapeutics company focused on pioneering new approaches to the treatment of metabolic diseases, including obesity and T2D. Despite advances in treatment over the last 50 years, obesity and T2D 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 Burlington, MA. For more information, visit www.fractyl.com or https://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 obesity and T2D. 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 Digestive Disease Week®**
Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and online meeting from May 18-21, 2024. The meeting showcases more than 5,600 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

**Forward-Looking Statements**
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the promise and potential impact of our preclinical or clinical trial data, the design, initiation, timing and results of clinical enrollment and any clinical trials or readouts, the content, information used for, timing or results of any IND-enabling studies or IND applications, the potential launch or commercialization of any of our product candidates or products, the sufficiency of our cash, cash equivalents, and investments to fund our operating activities for any specific period of time, and our strategic and product development objectives and goals, including with respect to enabling long-term control over obesity and type 2 diabetes without the burden of chronic therapies. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause the Company's actual

results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the Company's limited operating history; the incurrence of significant net losses and the fact that the Company expects to continue to incur significant net losses for the foreseeable future; the Company's need for substantial additional financing; the Company's ability to continue as a going concern; the restrictive and financial covenants in the Company's credit agreement; the lengthy and unpredictable regulatory approval process for the Company's product candidates; uncertainty regarding its clinical studies; the fact that the Company's product candidates may cause serious adverse events or undesirable side effects or have other properties that may cause it to suspend or discontinue clinical studies, delay or prevent regulatory development, prevent their regulatory approval, limit the commercial profile, or result in significant negative consequences; additional time may be required to develop and obtain regulatory approval or certification for the Company's Rejuva gene therapy candidates; the Company's reliance on third parties to conduct certain aspects of the Company's preclinical studies and clinical studies; the Company's reliance on third parties for the manufacture of the materials for its Rejuva gene therapy platform for preclinical studies and its ongoing clinical studies; the regulatory approval process of the FDA, comparable foreign regulatory authorities and lengthy, time-consuming and inherently unpredictable, and even if we complete the necessary clinical studies, we cannot predict when, or if, we will obtain regulatory approval or certification for any of our product candidates, and any such regulatory approval or certification may be for a more narrow indication than we seek; and the potential launch or commercialization of any of Company's product candidates or products and our strategic and product development objectives and goals, and the other factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on May 13, 2024 and in our other filings with the SEC. These forward-looking statements are based on management's current estimates and expectations. While the Company may elect to update such forward-looking statements at some point in the future, the Company disclaims any obligation to do so, even if subsequent events cause its views to change.

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