Fractyl Health Presents New Data at the American Diabetes Association's 85th Scientific Sessions Demonstrating its Rejuva® Smart GLP-1™ Pancreatic Gene Therapy Platform Prevents Obesity and Type 2 Diabetes in Preclinical Models

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New findings demonstrated that a single dose of Rejuva was well tolerated in healthy animals, with no evidence of toxicity

Rejuva-treated healthy animals exposed to a high fat diet were protected from weight gain and hyperglycemia

Data reinforce advancement of RJVA-001 toward first-in-human studies; preliminary clinical data expected in 2026

BURLINGTON, Mass., June 23, 2025 (GLOBE NEWSWIRE) -- Fractyl Health, Inc. (Nasdaq: GUTS) (the Company), a metabolic therapeutics company focused on pattern-breaking approaches to treat the root causes of obesity and type 2 diabetes (T2D), today announced new preclinical data from its Rejuva Smart GLP-1 pancreatic gene therapy platform at the American Diabetes Association's (ADA) 85 th Scientific Sessions. The abstract, titled "Single-Dose GLP-1-Based Pancreatic Gene Therapy Prevents Obesity and Diabetes in High-Fat Fed Mice," demonstrated that a single dose of Rejuva was well-tolerated in healthy mice, and prevented weight gain and hyperglycemia following a switch to a high-fat diet.

These findings further validate Rejuva's potential as a one-time, durable therapy with strong activity in obesity and diabetes and a favorable toxicity profile across multiple preclinical models. Importantly, these data highlight Rejuva's distinct mechanism of action, setting it apart from systemic GLP-1 receptor agonists. The Smart GLP-1 design of Rejuva enables nutrient-responsive secretion, exerting no physiologic effect under healthy metabolic conditions and only activating in the presence of metabolic stress. This targeted activity, which mimics the body's endogenous GLP-1 physiology, highlights the potential for Rejuva to offer superior potency and tolerability.

"These results underscore the transformative potential of Rejuva to offer protection from obesity and diabetes in the setting of modern environmental exposure to unhealthy diets," said Harith Rajagopalan, M.D., Ph.D., Co-Founder and Chief Executive Officer of Fractyl Health. "Unlike chronic systemic GLP-1 therapy, our approach localizes treatment to the pancreas and enables nutrient-stimulated GLP-1 secretion from beta cells, mimicking natural hormone regulation. These data support our belief that Rejuva could offer a fundamentally different risk-benefit profile in our effort to defend humanity from the inevitable metabolic diseases of modernity."

Key Findings

The study evaluated Rejuva treatment using an AAV vector designed for beta-cell-specific expression of a GLP-1 analog in four groups of mice (n=8/group). Key results include:

- In a diet-induced obesity (DIO) model, Rejuva treatment resulted in a 20% reduction in body weight and a 38% decrease in blood glucose by day 21. These effects were maintained through the end of the study on day 37 despite continued exposure to a high-fat diet.
- In lean animals treated with Rejuva and then exposed to a high-fat diet, weight gain and hyperglycemia were fully prevented. By the end of the study, Rejuva treated animals maintained baseline body weight and showed an 8% reduction of blood glucose relative to baseline.
- Rejuva was well-tolerated across all treatment groups, with no signs of toxicity, excessive weight loss, or hypoglycemia in healthy animals. These findings reinforce the nutrient-responsive, self-limiting nature of Rejuva's mechanism of action, which activates only under metabolic stress and remains inactive under healthy conditions.

These new preclinical results complement previously reported data showing the durable impact of Rejuva in diabetes and obesity models and further establish the platform's potential as both a therapeutic and preventative approach to metabolic disease.

Momentum Toward the Clinic

Fractyl has completed key in vivo studies for RJVA-001, its first clinical candidate from the Rejuva platform targeting T2D. Pending regulatory authorization, Fractyl expects to dose the first patients with RJVA-001 and report preliminary data in 2026, which the Company believes could lead to a potentially first-in-class, smart, durable gene therapy designed to reprogram the pancreas to deliver natural metabolic control.

Scientific Validation Backed by Leading Experts

The new study was led by an accomplished team of researchers from Fractyl Health and the University of Michigan, including renowned metabolic experts Dr. Timothy Kieffer (University of British Columbia) and Dr. Randy Seeley (University of Michigan), who bring deep expertise in gut-brain-pancreas biology and obesity pharmacology. Their involvement underscores the growing scientific momentum behind Rejuva's differentiated approach, which aims to restore physiologic GLP-1 regulation by targeting the pancreas at the source.

"Systemic GLP-1 drugs have set a high bar, but their limitations are becoming increasingly evident," said Dr. Kieffer, Scientific Advisor to Fractyl Health. "There is a need to deliver the therapeutic benefit of GLP-1 in a more physiologic, durable manner. Rejuva has the potential to meet this need by enabling sustained metabolic benefit from a single treatment."

The poster is available via the Presentations & Publications section of the Fractyl website.

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'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. The Company has a robust and growing IP portfolio, with 31 granted U.S. patents and approximately 40 pending U.S. applications, along with numerous foreign issued patents and pending applications. Fractyl is based in Burlington, MA. For more information, visit www.fractyl.com.

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. The Company has submitted the first Clinical Trial Application (CTA) module for RJVA-001 in T2D to regulators, and if the CTA is authorized, the Company expects to dose the first patients with RJVA-001 and report preliminary data in 2026.

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, primary and secondary endpoints, and results of clinical enrollment and any clinical studies or readouts, the content, information used for, timing or results of any investigational new drug (IND)-enabling studies, IND applications or Clinical Trial Applications, communications with regulators, the potential launch or commercialization of any of our product candidates or products, the potential treatment population or benefits for any of our product candidates or products, 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, redefining the future of metabolic disease treatment, positioning our Company at the forefront of the global opportunity for metabolic care, and the timing of any of the foregoing. 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, 2025 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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