Fractyl Health Announces Increased Focus on Groundbreaking Revita® Weight Maintenance and Rejuva® Pancreatic Gene Therapy Programs with Potential to Deliver Key Clinical Milestones Across Multiple Studies in 2025

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Prioritizing Revita's clinical development on weight maintenance post-GLP-1 withdrawal in response to significant patient and physician demand in ongoing REMAIN-1 pivotal study; anticipate midpoint data analysis in Q2 2025 and full pivotal study enrollment in summer 2025

RJVA-001, first clinical candidate in Rejuva gene therapy program, has completed key preclinical in vivo studies; on-track to initiate first-in-human studies in H1 2025

Streamlined focus expected to extend cash runway into 2026

BURLINGTON, Mass., Jan. 31, 2025 (GLOBE NEWSWIRE) -- Fractyl Health, Inc. (Nasdaq: GUTS) (the "Company"), a metabolic therapeutics company focused on pioneering pattern breaking approaches for the treatment of obesity and type 2 diabetes (T2D), today announced it is prioritizing its REMAIN-1 pivotal study, addressing the demand for an off-ramp to GLP-1 drugs, while advancing its novel Rejuva gene therapy platform into first-in-human studies. This decision is driven by positive initial feedback from the REVEAL-1 cohort, significant demand for participation in the REMAIN-1 study, and strong patient and physician feedback on the urgent need for durable weight maintenance solutions. Fractyl will pause investment in its Revita programs for T2D, which consist of the REVITALIZE-1 study and the German Real-World Registry. These measures are expected to extend the Company's cash runway into 2026, through multiple key clinical milestones.

"The real challenge in obesity is no longer losing weight, it is keeping the weight off. The strong response from patients and physicians to the REMAIN-1 study highlights the urgent need for durable weight maintenance solutions, and we are doubling down on our efforts in this space," said Harith Rajagopalan, Co-Founder and CEO of Fractyl Health. "Revita is the first therapeutic candidate to receive Breakthrough Device designation for weight maintenance, and we are uniquely positioned to address this critical gap. By prioritizing REMAIN-1 and advancing our groundbreaking Rejuva gene therapy platform, we are channeling our resources toward what we believe are the most impactful and differentiated opportunities. Given the rapidly evolving obesity landscape, we are pausing investment in our Revita programs for T2D and sharpening our focus. We believe these strategic steps will enable us to execute on our mission of delivering truly transformative solutions for patients with obesity and metabolic disease."

Revita Update: Promising Early Data and Midpoint Data Analysis in Q2 2025

- Earlier this month, Fractyl reported positive preliminary results from the REVEAL-1 open-label cohort of the REMAIN-1 study. Initial findings from the first patient showed successful weight maintenance following GLP-1 drug discontinuation and Revita procedure. Additional data from the REVEAL-1 cohort is anticipated to be presented in Q1 2025.
- The Company also announced significant progress in its ongoing REMAIN-1 pivotal study, which is evaluating weight maintenance after discontinuation of GLP-1 drugs. Recruitment for the REMAIN-1 study has generated significant interest, with over 145 patients enrolled across 10 clinical study sites in 5 months since first site activation, reflecting strong engagement from both patients and physicians. This momentum underscores the urgent need for effective post-GLP-1 weight maintenance solutions. The Company has completed enrollment of a sufficient number of patients for the midpoint analysis of the study, which is on track and expected in Q2 2025. Full enrollment in the study is expected in the summer of 2025.
- The Company will pause investment in Revita for T2D, which includes the REVITALIZE-1 study and the German Real-World Registry.

Rejuva Update: Pioneering Gene Therapy Progress into First-in-Human Studies

- After garnering significant scientific recognition over the past 12 months, Fractyl has completed key preclinical in vivo studies to support a Clinical Trial Application (CTA) for RJVA-001. The Company is on track to initiate first-in-human studies for RJVA-001 in H1 2025.

Corporate Update

- The Company is streamlining resources, including a 17% workforce reduction, which is expected to extend its cash runway

into 2026.

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.

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. Revita is designed to remodel the duodenal lining via hydrothermal ablation (i.e. duodenal mucosal resurfacing) to reverse damage to intestinal nutrient sensing and signaling mechanisms caused by chronic high-fat and high-sugar diets that are a root cause of metabolic disease. In the U.S., Revita is for investigational use only under U.S. law. Revita has U.S. FDA Breakthrough Device designation in weight maintenance for people with obesity who discontinue GLP-1 based drugs. A pivotal study of Revita in patients with obesity after discontinuation of GLP-1 based drugs, called REMAIN-1, was initiated in the third quarter of 2024 and is currently enrolling.

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 intends to initiate its first-in-human study for RJVA-001, the Company's first nominated GLP-1 pancreatic gene therapy candidate designed for the treatment of T2D, in the first half of 2025.

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 our anticipated financial performance, including cash and cash equivalents, for any period of time, our strategic reprioritization and related workforce reduction, including its implementation and the expected costs and benefits, if any, the promise and potential impact of our preclinical or clinical trial data, the design, initiation, timing and results of clinical enrollment and any clinical studies or readouts, the content, information used for, timing or results of any IND-enabling studies, IND applications or Clinical Trial Applications, 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, 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 November 12, 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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