Fractyl Health Reports Positive 3-Month REVEAL-1 Cohort Data Showing Revita® Sustained Weight Loss After GLP-1 Discontinuation, Supporting its Potential as a First-in-Class Weight Maintenance Therapy

12 of 13 participants maintained or lost weight at 3 months, with 6 of 13 losing additional weight after stopping GLP-1 therapy and undergoing Revita procedure

Median weight remained stable through 3 months (0.46% / ~ 1 pound weight change within the margin of error for daily weight measurement), compared to expected 5–6% weight regain (10–15 pounds) after stopping GLP-1 therapy

Revita continued to demonstrate excellent tolerability profile compared to GLP-1 drugs; treatment-emergent adverse effects were infrequent, mild, and transient

Randomized Midpoint Cohort data expected in Q3 2025; Pivotal Cohort data anticipated in H2 2026

BURLINGTON, Mass., June 23, 2025 (GLOBE NEWSWIRE) – Fractyl Health, Inc. (Nasdaq: GUTS) (the Company or Fractyl), a metabolic therapeutics company focused on pattern-breaking approaches that treat root causes of obesity and type 2 diabetes (T2D), today announced positive 3-month data from the REVEAL-1 Cohort of its ongoing REMAIN-1 pivotal study. These findings suggest Revita may help people stay at their target weight or lose additional weight, even after discontinuing GLP-1 drugs, offering a potential path to durable, drug-free weight maintenance.

3-Month Outcomes in REVEAL-1 Show Strong Early Signal for Durable Weight Maintenance

REVEAL-1 is the open-label cohort within the ongoing REMAIN-1 pivotal study, designed to evaluate the safety, tolerability, and early efficacy signals of Revita in individuals with obesity who have lost at least 15% of their total body weight on a recently discontinued GLP-1 therapy. This cohort serves as an early clinical window into Revita's potential to support durable weight maintenance following GLP-1 discontinuation, a period of time when patients are typically vulnerable to rapid weight regain. Participants undergo a single Revita procedure in an open-label setting and receive structured diet and lifestyle support consistent with the ongoing randomized, controlled, REMAIN-1 clinical study. The insights from REVEAL-1 are intended to inform and complement data from the randomized Midpoint and Pivotal Cohorts in REMAIN-1.

To date, 22 participants have been treated in the REVEAL-1 Cohort, with 3-month follow-up data available for 13 individuals. The profile of the REVEAL-1 Cohort closely mirrors that of the REMAIN-1 Midpoint and Pivotal Cohorts, with an average age of 49 and a gender distribution of 11 women and 2 men. All participants had previously been treated with a GLP-1 therapy for durations ranging from approximately 5 months to 3 years, with a median total body weight (TBW) loss of 20.9% while on therapy. Fifteen percent of participants had pre-diabetes at baseline.

- At 3 months, 12 of 13 participants either lost or maintained their weight after GLP-1 discontinuation and a single Revita procedure. Notably, 6 of 13 experienced further weight loss.
- Median weight remained stable through 3 months (TBW change of 0.46% / ~ 1 pound was within the margin of error for daily weight measurement), compared to the typical 5-6% (10–15 pounds) rebound seen in clinical studies such as SURMOUNT-4[1] [2]. Only one participant experienced weight regain similar to that seen after tirzepatide withdrawal.

[1] Aronne et al. JAMA. 2024;331(1):38–48. doi:10.1001/jama.2023.24945

[2] Wilding et al. Diabetes Obes Metab. 2022 Aug;24(8):1553-1564

- Early signs also point to excellent weight stability following Revita procedure, with essentially no weight change between 1 and 3 months (median weight gain at 1 month: 0.43% and 3 months: 0.46%).
- Consistent with prior studies of Revita, the procedure was well tolerated, with no unanticipated or serious adverse effects. No new safety concerns were observed.

“There is an extraordinary unmet need in obesity treatment, which is the ability for patients to stop GLP-1 drugs without regaining weight. Currently, if patients achieve successful weight loss, but stop these medications, they regain lost weight and typically report a significant return of hunger, cravings, and food noise even when switching to another agent in the same class,” said Shelby Sullivan, M.D., Professor of Medicine at the Geisel School of Medicine at Dartmouth University. “These early Revita data are better than I expected and suggest the potential to prevent the weight regain we see in practice. If these findings are sustained beyond 3 months and validated in the randomized cohort, this could become a viable solution for the many patients who would like to stop GLP-1 medications but currently can’t.”

Post-Revita TBW maintenance data at 3 months were as follows:

n=13	Pre-GLP-1Rx Weight (kg)	Post-GLP-1Rx TBW Change (%)	TBW Change 1-month Post-Procedure (%)	TBW Change 3 months Post-Procedure (%)
Mean	**104.6**	**-23.0**	**0.66**	**0.84**
Median	**100.2**	**-20.9**	**0.43**	**0.46**
IQR	**11.8**	**12.1**	**3.1**	**3.7**

“These REVEAL-1 Cohort data represent a powerful early signal of Revita’s ability to sustain weight loss after GLP-1 therapy ends, which is a significant challenge in the obesity treatment landscape,” said Harith Rajagopalan, M.D., Ph.D., Co-Founder and Chief Executive Officer of Fractyl Health. “With over 90 percent of patients maintaining or continuing to lose weight after a single Revita procedure, we believe Revita may be uniquely positioned to define a new therapeutic area in metabolic care: post-GLP-1 weight maintenance. We are encouraged by the consistent and robust signal of weight maintenance observed in this study, and these results strengthen our confidence in Revita’s potential and raise anticipation for the randomized data from the REMAIN-1 Midpoint Cohort expected in the third quarter. Alongside our Smart GLP-1™ Rejuva program, these advances underscore the depth of Fractyl’s innovation strategy focused on durable, disease modifying therapies for metabolic disease.”

Available safety data at the 3-month cutoff were as follows:

n=13	Patients, n (%)	Duration (days)
Grade ≥III TEAEs	**0 (0)**	**N/A**
Grade II TEAEs	**0 (0)**	**N/A**
Grade I TEAEs	**3 (23)**	**2-5**

Fractyl is advancing toward two key upcoming data readouts from its ongoing pivotal study of Revita: REMAIN-1 Midpoint Cohort data expected in the third quarter of 2025 and 6-month primary endpoint data from the REMAIN-1 Pivotal Cohort expected in the second half of 2026. Together, these clinical milestones are designed to demonstrate Revita's potential to help maintain weight loss after GLP-1 discontinuation and inform its possible role in supporting durable metabolic outcomes. Revita is being studied in an ongoing IDE-approved pivotal trial to evaluate its potential safety and efficacy in post-GLP-1 weight maintenance.

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 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 enrollment is now complete.

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 our anticipated financial performance, including cash and cash equivalents, for any period of time, 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 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 sub-assembly components for Revita and for 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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