Fractyl Health Authorized to Initiate First-in-Human Trial of RJVA-001 in the Netherlands: First Gene Therapy Candidate to Enter Clinical Development for Type 2 Diabetes

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Authorization advances Fractyl Health to a dual clinical-stage company, with Revita® in pivotal development for post-GLP-1 weight maintenance and Rejuva® entering first-in-human studies for type 2 diabetes

First-in-human dosing and preliminary data expected in the second half of 2026, subject to site activation

Rejuva® clinical development funded within existing cash runway into early 2027, beyond anticipated REMAIN-1 Pivotal data readout; no change to capital plans

BURLINGTON, Mass., May 11, 2026 (GLOBE NEWSWIRE) -- Fractyl Health, Inc. (Nasdaq: GUTS) (the Company or Fractyl), a clinical-stage metabolic therapeutics company focused on pioneering novel approaches to treat obesity and type 2 diabetes (T2D), today announced that it has received Clinical Trial Application authorization in the Netherlands to initiate the Phase 1/2 first-in-human study of RJVA-001, the first clinical candidate from the Company's Rejuva ® Smart GLP-1™ gene therapy platform. With this authorization, Fractyl believes RJVA-001 is the first adeno-associated virus (AAV)-based gene therapy candidate to enter clinical development for T2D, and Fractyl now advances to a dual clinical-stage company, with Revita® in pivotal development for post-GLP-1 weight maintenance and Rejuva entering first-in-human studies for T2D in the Netherlands. Pending site activation, Fractyl expects to dose the first patient with RJVA-001 and report preliminary data in the second half of 2026.

RJVA-001 is a one-time, beta-cell–targeted gene therapy designed to enable nutrient-responsive, physiologic GLP-1 expression within the pancreas, potentially avoiding the high circulating drug levels that contribute to side effects seen with systemic GLP-1 therapy. RJVA-001 is delivered via a minimally invasive endoscopic ultrasound-guided infusion directly into the pancreas, where it harnesses a proprietary, engineered version of the human insulin promoter and trafficking signals to drive nutrient-triggered secretion of GLP-1 from transduced pancreatic beta cells.

"GLP-1 medicines have changed what is possible in obesity and type 2 diabetes, but they require chronic, high-dose systemic exposure that many patients cannot or do not sustain. RJVA-001 takes a different path: a potential one-time, pancreas-targeted gene therapy designed to enable the body to produce GLP-1 in response to meals: physiology, not pharmacology," said Harith Rajagopalan, MD PhD, Co-Founder and CEO of Fractyl Health. "With this authorization, RJVA-001 becomes the first AAV gene therapy candidate to enter clinical development for type 2 diabetes. We are funding Rejuva's clinical development within our existing cash runway, beyond the anticipated REMAIN-1 Pivotal readout, with no change to our capital plans. We expect to dose the first patient and report initial data in the second half of 2026."

"For decades, we have managed T2D as a chronic, progressive disease that inevitably worsens over time. With this authorization, we are preparing to test, for the first time in humans, whether a one-time, pancreas-targeted gene therapy delivered via a routine endoscopic procedure could provide durable metabolic control by enabling physiologic, nutrient-responsive GLP-1 expression at the source of disease," said Professor Jacques Bergman, M.D., Ph.D., Professor of Gastrointestinal Endoscopy and Deputy Chair, Department of Gastroenterology & Hepatology at Amsterdam UMC, and a Principal Investigator of the RJVA-001 first-in-human study. "Patients who remain inadequately controlled despite maximally tolerated GLP-1 receptor agonists (GLP-1RAs) and multiple oral agents represent a population with significant unmet need. If successful, RJVA-001 could transform how we think about T2D, from a chronic disease you manage every day to one that could potentially be treated once."

About the RJVA-001 First-in-Human Study

The Phase 1/2 study is an open-label, multicenter, single-ascending-dose, first-in-human trial evaluating the safety, tolerability, and preliminary efficacy of RJVA-001 in adults with inadequately controlled T2D despite use of multiple glucose-lowering agents, including GLP-1RAs. Fractyl also plans to conduct the study at sites in Australia, where a clinical trial application has been submitted and regulatory feedback is expected in the third quarter of 2026.

Participants will undergo a standardized medication run-in and GLP-1 washout before receiving RJVA-001 delivered via endoscopic ultrasound-guided intrapancreatic infusion. Three escalating dose cohorts (3 participants each) will be followed by an optional expansion cohort of up to 20 additional participants treated at the selected optimal dose. Participants will be monitored for 12 months for safety, glucose control, immune response, and GLP-1 expression, and enrolled in a long-term follow-up study for up

to 5 years.

Key inclusion criteria:

- Adults aged 35–70 with T2D
- HbA1c between 7.0–10.0%, inclusive
- BMI 27–40 kg/m²
- On stable background therapy with GLP-1RAs and up to 3 non-insulin oral agents
- Demonstrated tolerance and benefit from prior use of GLP-1RAs

Primary endpoints include safety and tolerability. Secondary endpoints assess preliminary efficacy through continuous glucose monitoring, including time-in-range and other glycemic control measures. Exploratory endpoints assess beta-cell function, metabolic biomarkers, cardiovascular risk markers, and transgene expression.

About Fractyl Health

Fractyl Health is a clinical stage metabolic therapeutics company advancing two differentiated candidates designed to target the root causes of obesity and T2D: Revita, a procedural therapy in pivotal development for post-GLP-1 weight maintenance, and Rejuva, an AAV-based gene therapy platform with its lead candidate RJVA-001 entering first-in-human clinical studies. Fractyl's goal is to advance metabolic disease treatment from chronic management toward prevention and reversal of disease. Fractyl is headquartered in Burlington, Massachusetts.

About Rejuva

Fractyl Health's Rejuva platform is developing next-generation AAV-based, locally delivered gene therapies for the treatment of obesity and T2D. Rejuva leverages advanced delivery systems and proprietary screening methods to identify and develop metabolically active gene therapy candidates targeting the pancreas, with the goal of offering novel, disease-modifying therapies that address the underlying root causes of disease.

The platform's lead candidate, RJVA-001, has received Clinical Trial Authorization in the Netherlands to initiate a Phase 1/2 first-in-human clinical trial in T2D, the first clinical-stage program from the Rejuva platform. Fractyl expects to dose the first patient with RJVA-001 and report preliminary data in the second half of 2026, subject to site activation. Additional Rejuva candidates, including RJVA-002 (a dual GIP/GLP-1 gene therapy candidate designed to treat obesity), remain in preclinical development. In the United States, Rejuva is in preclinical development. No Investigational New Drug (IND) application has been filed with the U.S. Food and Drug Administration (the FDA), and Rejuva has not been approved or authorized by the FDA for use in humans.

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 are forward-looking statements. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, without limitation, statements regarding: the expected initiation, timing, design, endpoints, site activation, and conduct of the RJVA-001 first-in-human clinical trial; the timing and results of first-in-human dosing and reporting of preliminary data; our regulatory strategy, including submissions to and communications with regulators in the European Union, Australia, and other jurisdictions; the promise, potential impact, and mechanism of action of RJVA-001 and our Rejuva platform; our anticipated financial performance, including cash and cash equivalents, for any period of time; our expected cash runway; 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 for our other product candidates, including the REMAIN-1 Pivotal Cohort; the content, information used for, timing or results of any IND-enabling studies, IND applications or Clinical Trial Applications; our 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; our strategic and product development objectives and goals; 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. These and other risks are discussed more fully in our filings with the Securities and Exchange Commission (the SEC) including the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2025, filed with the SEC on March 24, 2026, and other documents we subsequently file with or furnish to 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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