Recursion Announces Alignment with FDA on Registrational Phase 3 Trial Design for REC-4881 in Familial Adenomatous Polyposis

November 18, 2026

- *REC-4881 is among the first AI-enabled programs to advance a registrational Phase 3 trial design for a disease with no approved pharmacologic therapies. Its potential as a first-in-class oral therapy for FAP was identified through unbiased phenotypic screening using Recursion's AI foundation models.*
- *Achieved a key regulatory milestone with FDA alignment on including excision of adenomas ≥10 mm throughout the GI as a novel and clinically meaningful event in the composite event-free survival primary endpoint. Adenomas of this size are associated with an increased risk of high-grade dysplasia, and cancer.*
- *Modified Spigelman stage progression and total polyp burden will be included among secondary endpoints.*
- *The trial is expected to enroll approximately 200 adults with FAP following colectomy or proctocolectomy and is on track to begin in the second half of 2027.*

Salt Lake City, UT, Nov. 18, 2026 (GLOBE NEWSWIRE) -- Recursion (Nasdaq: RXRX), a leading clinical-stage company pioneering AI-enabled drug discovery and development, today announced that it has aligned with the FDA on the design of its registrational Phase 3 trial of REC-4881, an investigational oral MEK1/2 inhibitor for the treatment of familial adenomatous polyposis (FAP). The alignment includes a composite event-free survival primary endpoint with a novel, clinically meaningful component: excision of an adenoma 10 mm or larger in either the upper or lower gastrointestinal (GI) tract. The trial is on track to begin in the second half of 2027.

REC-4881 is among the first AI-enabled programs to advance a registrational Phase 3 trial design for a disease with no approved pharmacologic therapies. Its potential as a first-in-class oral therapy for FAP was identified through unbiased phenotypic screening using Recursion's AI foundation models.

"Adenomas 10 millimeters and larger are associated with increased cancer risk and are nowadays routinely removed in patients with FAP. However, removal carries risks of bleeding and perforation, alongside the burden of repeated procedures and intensive surveillance," said Dr. Evelien Dekker, Head of Expert Clinic for Familial and Hereditary Polyposis and Colorectal Cancer, and Professor of Gastrointestinal Oncology, Amsterdam University Medical Center. "There is a substantial unmet need for a therapy that could prevent adenomas from reaching this size or developing in cancer. Reducing the need for these interventions could provide a meaningful benefit to patients."

"Patients with familial adenomatous polyposis face a lifelong burden of endoscopic surveillance, repeated interventions, and frequently major surgery. A medical therapy that could safely and durably prevent the progression of adenomas, reduce the need for endoscopic interventions, and potentially delay or avoid major surgery would represent a significant advance in the management of FAP," said Dr. Robert Hüneburg, MD, Senior Gastroenterologist and Head of the Hereditary Tumor Clinic, National Center for Hereditary Tumor Syndromes, Department of Internal Medicine I, University Hospital Bonn, Germany.

"For people living with FAP, colectomy does not end the disease. Patients continue to face decades of lifelong surveillance, repeated polyp removal and, for some, further major surgery," said Najat Khan, Ph.D., President and Chief Executive Officer of Recursion. "Our Phase 2 TUPELO results showed substantial and rapid reductions in polyp burden across the GI tract, including larger, higher-risk polyps, supporting our advancement toward a registrational trial. Securing FDA alignment on a novel component of our primary endpoint - counting the removal of adenomas 10 mm or larger across both the upper and lower GI tract as events - is a key milestone, reflecting an important and clinically meaningful intervention in FAP care. We appreciate the FDA's constructive engagement and look forward to starting the trial in the second half of 2027, with the goal of bringing a much-needed treatment option to people living with FAP."

About the Phase 3 registrational trial

The registrational Phase 3 trial is a randomized, double-blind, placebo-controlled, event-driven study expected to enroll approximately 200 patients with FAP aged 18 and older who have had a colectomy or proctocolectomy. The trial will evaluate REC-4881 at a dose of 4 mg, with the dosing schedule that will be determined based on data emerging from the ongoing TUPELO trial. Patients in both arms will be monitored with comprehensive endoscopic surveillance.

The primary endpoint is event-free survival, measured from randomization to the first occurrence of any of the following events: excision of an adenoma ≥10 mm in either the upper or lower GI tract, meeting prespecified criteria for multiple types of FAP-related surgery, development of high-grade dysplasia or cancer, or death from any cause. Modified Spigelman stage progression and total polyp burden will be included among secondary endpoints. The trial design will include a prespecified interim analysis.

Adenoma size is one of the main measures clinicians use to assess risk in FAP. Adenomas 10 mm or larger are associated with an increased risk of high-grade dysplasia and cancer, and their removal may require advanced endoscopic techniques that carry risks of bleeding, intestinal perforation and incomplete resection requiring repeat intervention. Once an adenoma reaches this size, patients typically require more frequent surveillance, repeated endoscopic interventions, and additional complicated and life altering procedures. Adenomas of this size occur regularly over the course of the disease in both the upper and lower GI tract. By counting qualifying excisions in either region as events, the primary endpoint captures a common and consequential intervention across FAP care. These events are expected to contribute meaningfully to the trial's event rate while reflecting decisions that directly shape clinical care.

About FAP

FAP is a rare, inherited disease that affects more than 50,000 patients in the US and EU5, with no approved pharmacologic therapies. It is caused by mutations in the APC gene, and without surgery to remove the colon, the lifetime risk of colorectal cancer approaches 100%. Colectomy does not stop the disease, as polyps continue to form in the remaining rectum or ileal pouch and in the upper GI tract, so patients face lifelong endoscopic surveillance, repeated polyp removal and, for some, further major surgery. Based on Company estimates, FAP represents a potential $15 billion opportunity.

Among the approximately 35,000 post-colectomy patients, upper GI disease is the area of greatest unmet need. Nearly all patients develop adenomas in the duodenum, and duodenal or ampullary cancer is a leading cause of cancer-related death after colectomy. The thin duodenal wall raises the risk of bleeding and perforation when these polyps are removed. When endoscopy can no longer control the disease, patients may need major surgery, such as removal of the duodenum or a Whipple procedure, which carries significant morbidity and a long recovery.

About REC-4881 and the TUPELO trial

REC-4881 is an investigational, oral, allosteric MEK1/2 inhibitor with FDA Orphan Drug and Fast Track designations for FAP. It is designed to address both the Wnt/β-catenin and MAPK pathways and was identified through unbiased phenotypic screening using Recursion's AI foundation models. REC-4881 is currently being evaluated in the ongoing Phase 1b/2 TUPELO trial (NCT05552755) in post-colectomy patients aged 18 and older, and its registrational Phase 3 trial is expected to begin in the second half of 2027.

In updated TUPELO data presented at CGA-IGC on November 2, 2026, patients had a 47% median reduction in total polyp burden after 12 weeks of treatment with REC-4881 4 mg once daily, with approximately 1 in 3 achieving reductions of 65% or more. Activity was seen throughout the GI tract. Nearly 1 in 2 patients in the upper GI and more than 1 in 3 in the lower GI achieved polyp burden reductions of 65% or more, two patients achieved reductions of 98% or more in the upper GI, and half improved by at least one Spigelman stage. Twelve weeks after stopping treatment, 85% of evaluable patients remained below baseline. Six of eight patients with polyps larger than 5 mm at baseline had fewer of these polyps after 12 weeks, including two whose counts fell from more than 90 to one. No new safety signals were observed. The highest-grade treatment-related adverse event was Grade 1 or 2 in 81% of patients and Grade 3 in 15%, with no Grade 4 or 5 events.

About Recursion

Recursion (Nasdaq: RXRX) is a leading clinical-stage company pioneering AI-enabled drug discovery and development decoding biology to radically improve lives. Recursion is advancing a portfolio of differentiated investigational medicines across its wholly owned and partnered pipeline in oncology, rare disease, neuroscience, immunology, and other therapeutic areas with significant unmet need. Enabling its mission is the Recursion OS, an AI-native, end-to-end drug discovery and development platform integrating biology, chemistry, and clinical development into a unified intelligence system. Powered by proprietary multimodal data, purpose-built AI models, and bilingual teams fluent in both science and AI, the Recursion OS is designed to translate complex science into medicines that matter — faster, better, and at scale — for patients who are waiting.

Recursion's platform infrastructure is anchored in Salt Lake City, Utah and Milton Park, Oxfordshire, where its automated biology and chemistry laboratories generate proprietary data at industrial scale. Recursion also maintains offices in New York and London, two global hubs for talent and leadership at the intersection of AI and scientific innovation. Learn more at www.recursion.com, or connect on X and LinkedIn.

Forward-Looking Statements

This document contains information that includes or is based upon “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, without limitation, those regarding the design, endpoints, expected enrollment, interim analysis, and dosing of the registrational Phase 3 trial of REC-4881 in FAP; the expected timing of initiation of the Phase 3 trial in the second half of 2027; the potential of REC-4881 to address unmet need in FAP; the potential for the Phase 3 trial, including its composite primary endpoint, to support regulatory approval of REC-4881; estimates of the FAP patient population and market opportunity; Recursion OS and other technologies; business and financial plans and performance; and all other statements that are not historical facts. Forward-looking statements may or may not include identifying words such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “plan,” “potential,” “project,” “seek,” “should,” “target,” “will,” “would,” and similar terms, or the negative of these terms. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements, including but not limited to: challenges inherent in pharmaceutical research and development, including the timing and results of preclinical and clinical programs, where the risk of failure is high; the risk that interim or preliminary clinical data may change or may not be indicative of final results; the risk that alignment with the FDA on the Phase 3 trial design, including its novel primary endpoint, does not ensure trial success or regulatory approval; the timing of trial initiation and enrollment; our ability to leverage and enhance our drug discovery platform; risks related to our development and use of artificial intelligence, including evolving regulation; our reliance on third parties for clinical trials and manufacturing; competition from other companies pursuing similar technologies or drug candidates; our ability to obtain financing for development activities and other corporate purposes; the success of our collaboration activities; our ability to obtain regulatory approval of, and ultimately commercialize, drug candidates; our ability to obtain, maintain, and enforce intellectual property protections; cyberattacks or other disruptions to our technology systems; our ability to attract, motivate, and retain key employees and manage our growth; inflation and other macroeconomic issues; and other risks and uncertainties such as those described under the heading “Risk Factors” in our filings with the U.S. Securities and Exchange Commission, including our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q. All forward-looking statements are based on management’s current estimates, projections, and assumptions and speak only as of the date of this document. Recursion undertakes no obligation to correct or update any such statements, whether as a result of new information, future developments, or otherwise, except to the extent required by applicable law.

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