New Phase 2 REC-4881 Data Presented at CGA-IGC Show Deep, Durable Polyp Burden Reductions in FAP, with Activity Across the GI Tract and in Larger, Higher-Risk Polyps

November 2, 2026

- ***Updated TUPELO results featured in a Presidential Plenary at CGA-IGC:*** *Lisa Boardman, M.D., Professor of Medicine at Mayo Clinic, presented updated findings from the Phase 1b/2 TUPELO trial in familial adenomatous polyposis (FAP) at the Collaborative Group of the Americas on Inherited Gastrointestinal Cancer (CGA-IGC) Annual Meeting.*
- ***Deep reductions sustained off treatment:*** *In an expanded adult population aged 18 years and older, after 12 weeks of treatment, patients achieved a 47% median reduction in total polyp burden, with approximately 1 in 3 achieving reductions of ≥65%. Twelve weeks after stopping treatment, 85% of evaluable patients remained below baseline.*
- ***Activity throughout the upper and lower GI tract, including near-clearance****: After 12 weeks of treatment, 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%. Two patients achieved ≥98% reductions in upper GI polyp burden.*
- ***Substantial reductions in larger, higher-risk polyps:*** *Six of eight patients with polyps >5 mm at baseline had reductions in the number of these polyps after 12 weeks of treatment. Four achieved reductions of ≥80%, including two whose larger-polyp counts fell from more than 90 polyps to one.*
- ***No new safety signals observed:*** *Favorable chronic dosing safety profile, consistent with the MEK inhibitor class. The highest-grade treatment-related adverse event (TRAE) was Grade 1 or 2 in 21 of 26 patients (81%) and Grade 3 in four patients (15%); one patient experienced no TRAEs. No Grade 4 or 5 TRAEs were reported. No additional discontinuations were reported since the previous data cutoff.*
- ***Registrational trial:*** *The Company anticipates initiating a registrational trial in the second half of 2027, pending ongoing FDA discussions, and will provide additional details later this year.*

Denver, Colorado, Nov. 02, 2026 (GLOBE NEWSWIRE) -- Recursion (Nasdaq: RXRX), a leading clinical-stage company pioneering AI-enabled drug discovery and development, today announced new positive Phase 2 data from the ongoing TUPELO trial of REC-4881, an investigational, oral MEK1/2 inhibitor for familial adenomatous polyposis (FAP). The new analyses show that most patients had reductions in both the number of larger, higher-risk polyps and in lower GI polyp burden, building on the upper GI results announced on October 15, 2026. Together, these findings support the potential of REC-4881 as an oral therapy to address FAP across the GI tract. Lisa Boardman, M.D., a gastroenterologist and Professor of Medicine at Mayo Clinic, presented the results in a Presidential Plenary at the Collaborative Group of the Americas on Inherited Gastrointestinal Cancer (CGA-IGC) Annual Meeting in Denver, Colorado.

“People have been doing research in the chemoprevention space in FAP for decades, and at least in the United States, we still don’t have an agent that is FDA approved. We’re still having to send FAP patients for major surgeries and we’re still doing frequent scopes on these patients. The need for effective chemoprevention in FAP is very large, and it’s only going to increase over time as the number of FAP patients continues to increase,” said Bryson Katona, M.D., Ph.D., Director of the GI Cancer Genetics Program, University of Pennsylvania Perelman School of Medicine, and TUPELO study investigator.

“We recently shared data that showed deep, durable reductions in polyps with REC-4881, particularly in the upper GI, where patients with FAP face the greatest risk and the fewest options. Today's update goes a layer deeper. REC-4881 is reducing the larger polyps that often drive much of the surgery for these patients, across the GI tract from a single oral therapy,” said Najat Khan, Ph.D., President and Chief Executive Officer of Recursion. “This is a lifelong disease with no approved pharmacologic therapies, and REC-4881 is the clearest proof point yet of what we built Recursion to do. Our priority now is to align with the FDA on a registrational path and move with focus and discipline toward a trial in the second half of 2027.”

Latest Data from Phase 2 Trial of REC-4881

Deep reductions in total polyp burden, sustained off treatment

The TUPELO study was designed to study polyp burden reduction after 12 weeks on REC-4881 (4 mg QD) and again after 12 weeks off-treatment. Results show a rapid and durable treatment effect across the GI tract. Trial results have strengthened since the November 2025 data cut, including expanded adult FAP population ages 18 years and older:

- 87% of patients (13 of 15) had a reduction in total polyp burden after 12 weeks of treatment, with a 47% median reduction. One in three patients achieved reductions of 65% or more.
- All patients added since the November 2025 data cut (n=4) had a reduction in total polyp burden, including two patients with 89% and 98% reduction, respectively. At Week 25, after 12 weeks off-treatment, 85% of patients (11 of 13) remained below baseline.
- The persistence of polyp burden reduction below baseline in most patients may allow for dosing flexibility, which could matter in the long-term management of a chronic disease.

“The durability of a reduction in polyp burden is an important metric to understand for any type of chemopreventive agent in FAP. The dream chemopreventive agent for FAP is one that a patient doesn’t have to take lifelong and that potentially could be taken for a shorter amount of time or with an intermittent dosing pattern. Seeing durability over a twelve-week course is certainly encouraging. In longer trials we’ll see exactly how long that durability lasts, but I think it is a very encouraging first sign for this drug,” said Dr. Katona.

Activity across the upper and lower GI tract, including near-clearance

For post-colectomy patients, upper GI disease represents the highest unmet need in FAP, due to risks of bleeding and perforation from polyp removal, high complication rates from surgery, and high cancer risk. When endoscopic management is no longer sufficient to control duodenal disease, patients may require major surgery, including removal of the duodenum. Lower GI disease also remains a concern after colectomy, as polyps can continue to develop in the remaining rectum or ileal pouch, posing an ongoing cancer risk and potential need for additional surgery. REC-4881 has now shown polyp burden reductions in both regions.

Upper GI findings:

- 92% of patients (12 of 13) had reductions in polyp burden after 12 weeks of treatment, with a 55% median reduction. Nearly 1 in 2 patients achieved reductions of ≥65%, and two patients achieved reductions of ≥98%.
- Half (6 of 12) improved by at least one Spigelman stage at Week 13, a widely used system clinicians use to grade duodenal polyposis and decide how often patients need endoscopy and when surgery is recommended.
- 92% (11 of 12) remained below baseline at Week 25, after 12 weeks off-treatment, and 6 of 11 had equal or greater reductions during the off-treatment period than during treatment.

Lower GI findings:

- 9 of 11 patients (82%) with measurable polyp burden at baseline had reductions after 12 weeks of treatment, with a 50% median reduction, and 1 in 3 achieved reductions of 65% or more.
- At Week 25, after 12 weeks off-treatment, 70% of evaluable patients remained below baseline.

Substantial reductions in larger, higher-risk polyps

Polyp size is one of the primary risk factors in FAP. The chance that a polyp contains high-grade dysplasia or cancer increases with polyp size, and clinical guidelines use size to decide which polyps to remove and how often patients need endoscopy. In a new analysis, REC-4881 reduced the number of polyps >5 mm in most patients who had them at baseline:

- Six of eight patients had fewer polyps >5 mm after 12 weeks of treatment, and in four patients the count fell by ≥80%.
- In two patients, more than 90 larger polyps were reduced to a single polyp. In both of those patients, all of the larger polyps were in the upper GI.
- The highest Week 13 responder went from 1,344 mm of total polyp burden to 32 mm, a 98% reduction, and from 96 upper GI polyps >5 mm to one. This is a single patient and is not representative of the overall population.
- Six of the eight patients assessed at Week 25 were below their baseline count after 12 weeks off-treatment. Most of the larger polyps at baseline were in the upper GI.

Note that the study collected polyp counts using >5 mm as the largest size category, which is inclusive of all polyps above this threshold; separate counts for polyps >10 mm were not collected.

No new safety signals observed

MEK1/2 inhibitors are an established class with a well-characterized side-effect profile. Across the 26 safety-evaluable patients dosed at 4 mg (five in Phase 1b and 21 in Phase 2), treatment was well tolerated, with a safety profile consistent with other MEK inhibitors and with previously reported results. No new safety signals were observed as of the data cutoff in the expanded patient population, which includes patients 18 and older.

- The majority of treatment-related adverse events (TRAE) were Grade 1 or 2 (21 of 26 patients, 80.8%). The highest-grade TRAE was Grade 3 in four patients (15.4%), and there were no Grade 4 or 5 TRAEs.
- The most common TRAEs were consistent with MEK1/2 inhibition, including dermatitis acneiform, rash, CPK increase, diarrhea, and asymptomatic LVEF decrease. Adverse events were manageable, and most resolved within 12 weeks off-treatment.
- Four patients discontinued for Grade 1 or 2 TRAEs, with no discontinuations for a Grade 3 event. No additional discontinuations were reported since the previous data cutoff.

Next steps

The Company anticipates initiating a registrational trial in the second half of 2027, pending ongoing FDA discussions, and will provide additional details later this year.

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 keep forming 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.

Natural History of FAP

To better understand the natural history of FAP and to put the single-arm results of TUPELO in context, the Company collaborated with Amsterdam University Medical Center to analyze a registry of approximately 200 patients with FAP. In 47 patients matched to the original TUPELO eligibility criteria, polyp burden increased over time in both the upper and lower GI. In the 35 patients with upper GI involvement, mean annualized polyp burden increased by 33%. In the 28 patients with lower GI involvement, mean annualized polyp burden increased by 88%. These results help to contextualize the polyp burden reduction observed after 12 weeks of REC-4881 treatment.

REC-4881 Background and Dual Mechanism

REC-4881, a potential first-in-class oral therapy granted FDA Orphan Drug and Fast Track designations, is an allosteric inhibitor of MEK1 and MEK2 designed to address both Wnt/β-catenin initiation and MAPK evolution pathways. The opportunity was identified through unbiased phenotypic screening using Recursion's AI foundation models, which showed that MEK1/2 inhibition could potentially reverse the cellular effects of APC loss. This dual mechanism differentiates REC-4881 from other single-agent therapies studied in FAP, which have each been directed at a single pathway, and provides the potential to suppress both pathways and reduce polyp burden across the GI tract.

About the TUPELO Trial of REC-4881

REC-4881 is being evaluated in the Phase 1b/2 TUPELO open label study (NCT05552755) assessing its safety, tolerability, pharmacokinetics (PK), and efficacy as a monotherapy in post-colectomy patients aged 18+ years with familial adenomatous polyposis (FAP).

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, Montréal, and London, three global hubs for talent and leadership at the intersection of AI and scientific innovation.

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 potential efficacy, safety, tolerability, and durability of response of REC-4881; the clinical relevance of the TUPELO trial data and the natural history analysis, and the potential for additional data to confirm such results; the outcome and timing of Recursion's ongoing discussions with the FDA regarding a registrational path for REC-4881; the design, timing of initiation, and outcomes of a registrational trial of REC-4881, including anticipated initiation in the second half of 2027, and the timing of additional details regarding such trial; the potential for REC-4881 to be a first-in-class therapy for FAP and to address unmet need in FAP; the potential benefits of REC-4881's Orphan Drug and Fast Track designations; the estimated 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 and failure can occur at any stage prior to or after regulatory approval due to lack of sufficient efficacy, safety considerations, or other factors; the risk that preliminary or interim data from the TUPELO trial, which are based on a limited number of patients, may change as additional data become available or may not be predictive of results in later-stage trials, and that comparisons to natural history data may not be indicative of results in controlled trials; the risk that the FDA may not agree with our proposed registrational path or may require additional data or trials; our ability to leverage and enhance our drug discovery platform; risks related to our development and use of artificial intelligence and machine learning models, including the quality, sufficiency, and integrity of the data on which such models are trained and evolving laws and regulations governing artificial intelligence; our reliance on third parties, including contract research and contract manufacturing organizations, for the conduct of preclinical studies, 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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