Recursion announces first patient dosed in Phase 2 clinical study of REC-3964, a potential first-in-class, oral, non-antibiotic small molecule for recurrent Clostridioides difficile infection

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- REC-3964 is Recursion's first new chemical entity developed using the RecursionOS.
- REC-3964 represents a novel, non-antibiotic approach with a unique mechanism of action that binds and blocks catalytic activity of the toxin's innate glucosyltransferase in order to inhibit the toxin produced by *C. diff.* in the gastrointestinal tract.
- There are up to 175,000 cases of recurrent *C. diff.* each year and more than 29,000 patients die in the U.S. from *C. diff.* annually. Rates of recurrent *C. diff.* have increased significantly in recent years, representing a major public health challenge.

SALT LAKE CITY, Oct. 22, 2024 (GLOBE NEWSWIRE) -- Recursion (NASDAQ: RXRX), a leading clinical stage TechBio company decoding biology to radically improve lives, today announced that the first patient has been dosed in its Phase 2 clinical trial of REC-3964, a potential first-in-class, oral small molecule and new chemical entity for the treatment of recurrent *Clostridioides difficile* infection. *C. diff* is a toxin producing bacteria that causes diarrhea and colitis, and can be life threatening. Up to 730,000 cases are estimated to occur in the U.S. and EU5 annually, and the infection is responsible for an estimated 29,000 deaths in the U.S. each year. Recursion's study will initially address the recurrent *C. diff.* (up to 175,000 cases in the United States per year) population, which costs the healthcare system approximately two billion dollars per year.

Increasing cases of recurrent *C. diff.* infections pose significant public health challenges. Antibiotics, the standard treatment for *C. diff.* infections, disturb the gut microbiome due to their non-selective nature. Despite initial success, antibiotics fail to prevent recurrence in 20-30% of primary cases. Further, the risk of subsequent recurrence rises to 40% after the first and 45-65% after two or more.

REC-3964 is the first novel small molecule developed through Recursion's Operating System, and selectively inhibits the glucosyltransferase activity of toxin B produced by *C. diff* in the gastrointestinal tract, offering a unique mechanism of action. Unlike antibiotics, which disrupt the gut microbiome, REC-3964 precisely targets the bacterial toxin while sparing healthy tissue, potentially minimizing adverse events. It is being studied as part of a treatment regimen to prevent recurrent *C. diff* infections, a leading cause of antibiotic-associated diarrhea that can lead to significant morbidity and mortality.

Presented at the 6th Edition of World Congress on Infectious Diseases, preclinical studies demonstrated its superiority over bezlotoxumab in a human disease-relevant *C. diff.* hamster model. Additionally, Phase 1 studies in healthy volunteers showed REC-3964 was well tolerated with no serious adverse events (SAEs), underscoring its potential safety and tolerability.

"There's a significant unmet need for new treatment options for patients with *C. diff.* infection that are easier to use and more cost effective," said Chris Gibson, Ph.D., Co-Founder and CEO of Recursion. "We are encouraged by the progress of REC-3964, the first new chemical entity from our platform to advance to Phase 2 clinical trials, and now, to the first patient dosed. We look forward to continuing to advance this trial to help patients in need and drive down billions in costs to the healthcare system for treatment."

Christian John Lillis, Co-Founder and CEO of the Peggy Lillis Foundation, shared: "We are so pleased to learn that our partner Recursion has initiated its ALDER trial. All new therapies that can be added to the known standard of care have the potential to decrease the physical and emotional suffering of recurrent *C. diff*. on patients and the significant burden to the health care system."

"Patients with *C. diff* face significant challenges, with 20-30% of initial infections recurring after standard treatment and a 40% chance of further recurrence, often leading to severe complications and a diminished quality of life," said Najat Khan, Ph.D., Chief Commercial Officer and Chief R&D Officer at Recursion. "For these patients and their families, the need for safe, effective, non-antibiotic treatment options is critical. REC-3964 offers a novel, targeted approach by selectively inhibiting the bacterial toxin while sparing the host. With encouraging preclinical data and strong tolerability demonstrated in Phase 1 studies, it's particularly rewarding to see the first drug developed using the RecursionOS and advancing to Phase 2 trials."

The Phase 2 ALDER clinical trial is a multi-center randomized study to investigate the safety, tolerability, pharmacokinetics (PK) and efficacy of REC-3964 at doses of either 250 mg or 500 mg for the reduction of *C. diff.* and will include an observation only arm. Approximately 80 individuals will ultimately be enrolled in the study across the U.S. and Europe.

About *Clostridioides difficile* infection

Clostridioides difficile (*C. diff.*) infection is a bacterial disease that impacts more than 730,000 people in the U.S. and EU5 every year. Rates of recurrent *C. diff.* have increased significantly in recent years, representing a major public health challenge, with people 7 to 10 times more likely to get *C. diff.* infection while taking an antibiotic and the subsequent month. About 20-30% patients who have *C. diff.* infection will have it again in the subsequent 2 to 8 weeks. After the first recurrence, there's a 40% likelihood of a second recurrence, and a 45-65% likelihood of recurrence among patients who have recurred more than twice. In total *C. diff.* infection is estimated to cause 29,300 deaths in the U.S. each year. More than 80% of *C. diff.* infection deaths occur in people aged 65 and older. On average, one in 11 patients older than 65 years diagnosed with healthcare-associated *C. diff.* infection will die within a month. Extended stays in healthcare settings, such as hospitals and nursing homes, also increase risk.

About REC-3964

REC-3964 is a potential first-in-class, orally bioavailable non-antibiotic small molecule that is being investigated for the potential treatment of recurrent *Clostridioides difficile* (*C. diff.*) infection. This selective inhibitor is Recursion's first new chemical entity to reach the clinic, and binds and blocks

catalytic activity of the toxin's innate glucosyltransferase. In preclinical studies, REC-3964 was found to be superior to bezlotoxumab in a human disease relevant *C. diff*. hamster model, with significant difference in probability of survival versus bezlotoxumab alone at the end of treatment. REC-3964 was also well tolerated in Phase 1 healthy volunteer studies, demonstrating potential safety and tolerability with no serious adverse events (SAEs).

About the Trial
Our Phase 2 ALDER clinical trial is a multi-center, open-label study to investigate the safety, tolerability, pharmacokinetics (PK) and efficacy of REC-3964 (doses of either 250 mg or 500 mg PO every 12 hours) for the reduction of *Clostridioides Difficile* infection (*C. diff.*). Approximately 80 individuals will be enrolled in this open-label Phase 2 study, randomized 1:2:1 to receive oral doses of REC-3964, 250 mg, 500 mg or observation. The purpose of this study is to investigate the safety, tolerability, pharmacokinetics (PK) and efficacy of REC-3964 for the reduction of recurrent *Clostridioides difficile* infection (rCDI) after initial cure with vancomycin. Participants will receive treatment with REC-3964 for 28 days.

About Recursion
Recursion (NASDAQ: RXRX) is a clinical stage TechBio company leading the space by decoding biology to radically improve lives. Enabling its mission is the Recursion OS, a platform built across diverse technologies that continuously generate one of the world's largest proprietary biological and chemical datasets. Recursion leverages sophisticated machine-learning algorithms to distill from its dataset a collection of trillions of searchable relationships across biology and chemistry unconstrained by human bias. By commanding massive experimental scale — up to millions of wet lab experiments weekly — and massive computational scale — owning and operating one of the most powerful supercomputers in the world, Recursion is uniting technology, biology and chemistry to advance the future of medicine.

Recursion is headquartered in Salt Lake City, where it is a founding member of BioHive, the Utah life sciences industry collective. Recursion also has offices in Toronto, Montréal, London, and the San Francisco Bay Area. Learn more at www.Recursion.com, or connect on X (formerly Twitter) and LinkedIn.

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Forward-Looking Statements

This document contains information that includes or is based upon "forward-looking statements" within the meaning of the Securities Litigation Reform Act of 1995, including, without limitation, those regarding the potential efficacy of REC-3964; timing of the Phase 2 clinical trial of REC-3964; early and late stage discovery, preclinical, and clinical programs; licenses and collaborations; prospective products and their potential future indications and market opportunities; 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 "plan," "will," "expect," "anticipate," "intend," "believe," "potential," "continue," and similar terms. These statements are subject to known or 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; our ability to leverage and enhance our drug discovery platform; 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 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.

Source: Recursion Pharmaceuticals, Inc.