Recursion Reports Interim Phase 1 Clinical Data for REC-617 Monotherapy, a Potential Best-in-Class CDK7 Inhibitor, With Encouraging Patient Response and Favorable Tolerability

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- *REC-617, a precision designed molecule, demonstrated dose-linear pharmacokinetics (PK) with rapid absorption and robust pharmacodynamic (PD) biomarker modulation, suggesting substantial target engagement*
- *Confirmed partial response (PR) observed during monotherapy dose-escalation in a patient with platinum-resistant ovarian cancer, treated with 4 lines of prior therapy in advanced setting, durable response ongoing after more than 6 months of treatment*
- *Additional 4 patients demonstrated a best response of stable disease (SD) for up to 6 months of treatment*
- *Plans to continue monotherapy dose escalation and initiate combination studies in 1H 2025*

SALT LAKE CITY, Dec. 09, 2024 (GLOBE NEWSWIRE) -- Recursion (Nasdaq: RXRX) reported initial monotherapy dose-escalation data from the Phase 1/2 study (ELUCIDATE) of REC-617, a selective CDK7 inhibitor, in advanced solid tumors.

These results were presented today after market close at an AACR Special Conference in Cancer Research. The company will also hold a webinar on December 10 at 6:30 AM MT / 8:30 AM ET / 1:30 PM GMT to present the preliminary data broadcast from Recursion's X (formerly Twitter), LinkedIn, and YouTube accounts with an opportunity to submit questions here.

"Cell cycle dysregulation and transcriptional 'addiction' are both hallmarks of many aggressive cancers," said David Hallett, Ph.D., Chief Scientific Officer of Recursion. "By inhibiting CDK7, we have the potential to target both mechanisms while fine tuning the therapeutic index. Using our precision design platform, we created a molecule with rapid oral absorption to reduce GI tissue exposure, a suitable half life to manage side effects, and target engagement covering the IC80 level."

ELUCIDATE is an ongoing Phase 1/2 study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and maximum tolerated dose (MTD) of REC-617 in patients with advanced solid tumors. As of the November 15, 2024 data cutoff, preliminary findings include 18 patients with advanced solid tumors who were response evaluable in the monotherapy dose-escalation phase. Doses ranged from 2 mg to 20 mg once daily (QD) and 1 mg twice daily (BID).

REC-617 was generally well-tolerated across all dose levels, with no discontinuations due to adverse events (AEs). Adverse events to date were predominately Grade 1-2, on-target, and reversible. An MTD has not yet been reached.

While efficacy was not an endpoint in this Phase 1 study, or anticipated in monotherapy, a confirmed durable partial response (PR) by RECIST on REC-617 monotherapy was achieved in a patient with metastatic, platinum-resistant ovarian cancer. The response is on-going after more than 6 months of treatment. This patient had progressed following 4 lines of prior therapy in the advanced setting. In addition, four patients achieved a best response of stable disease (SD) across multiple dose levels for up to 6 months of treatment.

"These initial findings for REC-617 represent an exciting step forward in the development of CDK7 inhibitors, with a favorable PK/PD profile and a durable confirmed partial response observed in dose escalation in a highly pre-treated patient population," said Najat Khan, Ph.D., Chief R&D Officer and Chief Commercial Officer, Recursion. "Designed using our AI-powered OS platform, REC-617 reflects our focus on enhancing the therapeutic index to deliver more effective and safer treatment options for patients. We are eager to continue this momentum in dose escalation and to initiate the next phase of the program next year."

In parallel to the ongoing monotherapy dose escalation (QD and BID), combination studies are expected to initiate for ELUCIDATE in H1, 2025. The company expects to present additional ELUCIDATE as well as preclinical REC-617 data at future medical meetings.

Summary of Interim REC-617 Monotherapy Dose Escalation Results

Study Design & Demographics

- Phase 1 monotherapy dose escalation in advanced solid tumors
- Data cutoff as of November 15, 2024 - 19 patients enrolled (18 response evaluable)
- Heavily pre-treated population (median of 4 prior lines of therapy in the advanced setting)
- Antiemetics and anti-diarrheals not mandated prophylaxis for nausea/vomiting/diarrhea

PK/PD Summary

- REC-617 exceeds CDK7 IC_{80} with rapid absorption (Tmax 0.5–2 hours) with a half-life of 5-6 hours
- Early POLR2A 3-4x modulation suggests ~80–90% target engagement
- Quick, time-limited target engagement with POLR2A normalization in 24 hours
- Twice-daily (BID) dosing under investigation

Safety Profile/AE Summary

- Adverse events (AEs) were predominantly low grade, on-target, and reversible upon treatment cessation
- Early data indicates a favorable safety profile – maximum tolerated dose (MTD) not reached
- No treatment discontinuations due to AEs
- 3 treatment related serious adverse events (SAE)s reported in 2/19 patients
- Events resolved and treatment continued after dose reduction
- Antiemetics and anti-diarrheals not mandated prophylaxis for nausea/vomiting/diarrhea

Confirmed Partial Response & Stable Disease Summary

- One confirmed partial response (PR) by RECIST 1.1 (decrease of more than 30% in the sum of the longest diameters of target lesions + no new lesions + no progression of non target lesions)
    - Partial response (-34%) achieved with reduction of 2 lymph nodes (para-aortic and mesenteric) at Week 16 with normalization of LDH
    - Reduction of tumor marker CA125 from 1249 to 694 kU/L (-44%)
    - Reduction of tumor marker TK1 from 174 to 56 DuA (-68%)
    - Response ongoing after more than 6 months of treatment
    - Patient continues study therapy without need for antiemetics
- Four additional patients achieved durable (up to 6 months of treatment) response of stable disease (SD) as best response across multiple dose levels
    - All four patients progressed prior to entering the study
    - Three CRC patients (6L-7L) and one NSCLC patient (4L)
    - One patient on 2mg QD and three patients on 10mg QD

About REC-617
REC-617 is a potential best-in-class CDK7 inhibitor, precision designed using AI-led approaches, with only 136 novel molecule synthesized from hit to candidate identification in less than 12 months. The molecule is designed to maximize its therapeutic index by enabling the tight control of both the extent and duration of target inhibition. CDK7 inhibition combines many potential benefits such as transcription inhibition, reduction of aberrant kinome activation, cell cycle inhibition, and modulation of estrogen receptor activity. This makes it an attractive target to overcome common resistance pathways associated with CDK4/6 inhibition, which only targets the cell cycle.

About ELUCIDATE
REC-617 is currently being evaluated as a monotherapy in the ELUCIDATE trial. ELUCIDATE is a multicenter, open-label, two-stage clinical trial to evaluate safety, pharmacokinetics, pharmacodynamics, and efficacy of REC-617 in advanced solid tumors, including non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer.

Both the monotherapy and combination therapy dose escalation portion of the trial will enroll patients across multiple dose levels to determine the optimal biological dose (OBD). The dose expansion phase of the trial will commence upon identification of the OBD. The primary efficacy endpoint of the expansion phase is objective response rate (ORR).

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, New York, London, Oxford area, 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-617; timing of the Phase 1/2 clinical trial of REC-617; 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.