Recursion Announces Two Key Investigational Oncology Drugs Advancing to Clinical Trials, Targeting High Unmet Needs in Hematologic Malignancies, Small-Cell Lung Cancer, & More

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- REC-3565 is a potential best-in-class MALT1 inhibitor for multiple hematology indications, designed to reduce the risk of hyperbilirubinemia, a common side effect of other MALT1 inhibitors
- REC-4539, a potential best-in-class LSD1 inhibitor, is the first designed to be reversible and CNS penetrant for small-cell lung cancer

Salt Lake City, UT, Jan. 07, 2025 (GLOBE NEWSWIRE) -- Recursion (NASDAQ: RXRX), a leading clinical stage TechBio company decoding biology to industrialize drug discovery, announced today that the UK Medicines and Healthcare Products Regulatory Agency (MHRA) has cleared a clinical trial application (CTA) for a Phase 1 clinical trial of REC-3565, a potential best-in-class MALT1 inhibitor for B-cell malignancies. For REC-3565, the total addressable population could include a range of hematological indications, with approximately 41,000 relapsed and/or refractory (R/R) patients with chronic lymphocytic leukemia (CLL) and B-cell lymphomas in the US+EU5 annually.

Recursion also announced that the U.S. Food and Drug Administration (FDA) has cleared an investigational new drug (IND) application for a Phase 1/2 clinical trial of REC-4539, a potential best-in-class LSD1 inhibitor for small-cell lung cancer (SCLC) and other potential indications. For REC-4539, the total addressable population in the US+EU5 for extensive stage SCLC is approximately 45,000 patients annually.

Chris Gibson, Ph.D., Co-Founder and CEO of Recursion said, “We are excited to add REC-4539 and REC-3565 to our clinical stage portfolio as we explore first- and best-in-class oncology medicines and build momentum and value through our pipeline. These are prime examples of how precision design, powered by the Recursion OS platform with advanced AI capabilities, enables us to identify and optimize molecules with unique properties.”

“For REC-4539, we’ve developed a reversible LSD1 inhibitor that not only targets peripheral disease, but is also designed to penetrate the brain, potentially addressing a critical unmet need in small-cell lung cancer. Similarly, REC-3565 is a highly selective MALT1 inhibitor without significant off-target inhibition of UGT1A1, which could enhance combination therapy by mitigating potential risks of drug-drug interaction and hyperbilirubinaemia,” said Najat Khan, Ph.D., Chief R&D Officer and Chief Commercial Officer, of Recursion. “As we expand our platform in the development space, we aim to leverage multimodal data and causal AI models to advance precision medicine through optimized patient selection —ensuring the right drug for the right patient.”

About REC-3565

In December 2024, a CTA was approved for a Phase 1 clinical trial of REC-3565, a potential best-in-class MALT1 inhibitor for B-cell malignancies, including CLL. The total addressable population could include a range of hematological indications, with approximately 41,000 relapsed and/or refractory (R/R) patients with CLL and B-cell lymphomas in the US+EU5 annually.

MALT1 is a central regulator of NF-kB signaling, supporting the uncontrolled proliferation of malignant B and T cells in a number of hematological cancers, specifically B-cell malignancies. Inhibiting MALT1 in these cancer types has the potential to block the NF-kB signaling in immune cells. Within B-cell lymphomas, Bruton's tyrosine kinase inhibitors (BTKi) have revolutionized the treatment landscape; however, drug resistance compromises treatment outcomes and needs to be solved urgently. Combining REC-3565 with BTKi (or BCL inhibitors) could potentially overcome resistance, as well as providing deeper and more durable efficacy, to drive improved patient outcomes.

Current MALT1 inhibitors in clinical development have demonstrated off-target inhibition of UDP glucuronosyltransferase 1A1 (UGT1A1), an enzyme involved in bilirubin disposition, resulting in hyperbilirubinaemia. In contrast, REC-3565 does not significantly inhibit UGT1A1, which may mitigate potential risks of drug-drug interaction/hyperbilirubinaemia that could limit dose escalation and the level of target engagement necessary to achieve clinical efficacy.

In in vivo studies, REC-3565 has shown:

- Tumor growth inhibition in a range of hematological xenograft models as both a single agent, and in combination with BTK inhibitors. Notably, durable tumor eradication was observed in combination with zanubrutinib in an ABC-DLBCL xenograft model (Payne et al. ESMO 2023 & Payne et al. ENA 2024)
- Precision design as an allosteric inhibitor to achieve potency and selectivity over UGT1A1 for low predicted risk of hyperbilirubinemia, creating the potential for better combination profile with drugs that have known liver toxicity issues (BTK & BCL2 inhibitors) and a potential safety benefit compared with other MALT1 inhibitors in development (Payne et al. ESMO 2023)
- Favorable absorption, distribution, metabolism, and excretion (ADME) profile, well-balanced molecular properties, potentially enabling daily dosing for an orally administered drug, and potency and selectivity to potentially reduce off-target toxicity (Payne et al. ESMO 2023)

The first patient is expected to be dosed in the Phase 1 EXCELERIZE clinical trial in Q1 2025. The trial will evaluate the safety/tolerability of REC-3565 and provide a recommendation for dosing in later combination studies with standard of care agents for B-cell malignancies.

About REC-4539

In January 2025, the U.S. Food and Drug Administration (FDA) cleared an investigational new drug (IND) application for a Phase 1/2 clinical trial of REC-4539, a potential best-in-class brain penetrant LSD1 inhibitor. Initial clinical investigation will focus on small cell lung cancer (SCLC) while also exploring several other solid tumor indications. The total addressable population in the US+EU5 for extensive stage SCLC is approximately 45,000 patients annually.

Overexpression of LSD1 occurs in several tumor types, including SCLC where it drives cancer cell proliferation and survival. Inhibiting LSD1 in these cancer types has the potential to provide a superior patient solution - targeting both peripheral disease, but also enabling the potential treatment of the brain metastases that are common at initial diagnosis and which subsequently develop in approximately half of all SCLC patients during treatment with current standard of care.

In in vivo studies, REC-4539 has shown:

- Dose-dependent tumor inhibition in SCLC xenograft model with brain penetration & a reversible mechanism (Payne et al. AACR 2023)
- Potency and selectivity to potentially reduce off-target toxicity with favorable ADME profile and shorter human half-life than other LSD1 inhibitors currently in clinical trials (Payne et al. AACR 2023)
- Limited platelet level effects (Okumara et al. ENA 2024), highlighting its potential to maximise anti-tumor activity while limiting thrombocytopenia

The first patient is expected to be dosed in the Phase 1/2 ENLYGHT clinical trial in H1 2025. The trial willevaluate REC-4539 as monotherapy and in combination with durvalumab in patients with SCLC.

About Recursion

Recursion (NASDAQ: RXRX) is a clinical stage TechBio company decoding biology to industrialize drug discovery. Enabling its mission is the Recursion OS, a platform built across diverse technologies that continuously expands 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-4539 and REC-3565; timing of and plans to initiate clinical trials of REC-4539 and REC-3565; the potential size of the market opportunity for our drug candidates; the relevance of pre-clinical data; early and late stage discovery, preclinical, and clinical programs; licenses and collaborations; prospective products and their potential future indications; 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.

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