# Lyell Immunopharma Acquires Exclusive Global Rights to a Next-Generation CAR T-Cell Product Candidate in Clinical Development for Metastatic Colorectal Cancer

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- LYL273 has demonstrated a 67% overall response rate, an 83% disease control rate, and a manageable safety profile at the highest dose level studied to date in patients with refractory metastatic colorectal cancer enrolled in an ongoing U.S. Phase 1 clinical trial
- LYL273 is a GCC-targeted CAR T-cell product candidate armed with enhancements designed to improve CAR T-cell expansion and cancer cell killing
- Lyell management will host an investor webcast at 8:30 AM ET today

SOUTH SAN FRANCISCO, Calif., Nov. 10, 2025 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a late-stage clinical company advancing next-generation chimeric antigen receptor (CAR) T-cell therapies for patients with cancer, today announced it has strengthened its solid tumor pipeline by acquiring global rights to LYL273 (formerly GCC19CART), a novel autologous guanylyl cyclase-C (GCC)-targeted CAR T-cell product candidate for the treatment of metastatic colorectal cancer (mCRC) and other GCC-expressing cancers, from Innovative Cellular Therapeutics (ICT). Patients with refractory mCRC treated with LYL273 in a Phase 1 clinical trial conducted in the United States (U.S.) achieved a 67% overall response rate and an 83% disease control rate (complete and partial response plus stable disease) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 with a manageable safety profile at the highest dose level studied to date. LYL273 is a GCC-targeted CAR T-cell product candidate enhanced with CD19 CAR expression and controlled cytokine release designed to improve CAR T-cell expansion, immune cell infiltration and cancer cell killing in the hostile solid tumor microenvironment.

"We rarely see such deep and durable responses in colorectal cancer patients treated with multiple prior lines of chemotherapy. The outcomes in this initial cohort of heavily pre-treated patients are very encouraging," said Benjamin L. Schlechter, MD, Senior Physician in the Gastrointestinal Cancer Center, Dana-Farber Cancer Institute and Assistant Professor of Medicine at Harvard Medical School, Boston, MA, and lead investigator in the Phase 1 clinical trial. "Patients with metastatic colorectal cancer have a tremendous need for innovations like LYL273, and I look forward to partnering with the Lyell team as we work to rapidly deliver on the potential of this innovative cellular therapy for patients with advanced colorectal cancer."

"The ability to treat solid tumors with an acceptable safety profile has become the holy grail for CAR T-cell therapy for cancer," said Richard Klausner, MD, Lyell co-founder and Board Chairman, former Director of the National Cancer Institute and co-founder and former Director of Juno Therapeutics. "These impressive early results suggest we may be on the path to finally breaking the barrier for solid cancer."

Colorectal cancer (CRC) is the second leading cause of cancer deaths worldwide, and the incidence of colorectal cancer is rising in people younger than 55 years old. Approximately 53,000 people are expected to die from CRC in the U.S. in 2025. With approved therapies, only six percent of patients with mCRC in the third- or later-line setting achieve partial or complete responses to their next line of therapy, and median overall survival is generally less than 12 months. GCC is a receptor that plays a key role in the regulation of intestinal electrolyte homeostasis. It is expressed on more than 95% of colorectal cancers and a majority of pancreatic adenocarcinomas. Its expression in healthy tissue is limited to the gastrointestinal tract, where it is sequestered by tight junctions from the circulation.

**U.S. Phase 1 Clinical Trial Data**

Dose-dependent clinical activity in 12 patients enrolled in a Phase 1 clinical trial in the U.S. are reported as of an October 28, 2025 data cutoff date. Six patients were treated at Dose Level 1 ($1 \times 10^6$ CAR T cells/kg) and six patients were treated at Dose Level 2 ($2 \times 10^6$ CAR T cells/kg). All patients received a single dose of lymphodepleting chemotherapy on Day -3, including cyclophosphamide, 300 mg/m$^2$, and fludarabine, 30 mg/m$^2$. RECIST 1.1 classification of imaging results is per local site review.

Across both dose levels, the overall response rate was 50% (6 of 12 patients) and the disease control rate was 83%. At the highest dose tested, Dose Level 2, the overall response rate was 67% (4 of 6 patients), including one patient with a pathological complete response, one patient with complete reduction in tumor volume of the target lesions (100% partial response), and two

additional patients with confirmed partial responses. For patients treated at Dose Level 2, the disease control rate was 83%, and the median progression-free survival was 7.8 months.

The incidence and severity of treatment-related adverse events were higher at Dose Level 2 than at Dose Level 1. The most common treatment-related adverse events at Dose Level 2 were cytokine release syndrome in 83% (5/6) of patients (Grade 1, 67%; Grade 2, 17%) and diarrhea in 83% (5/6) of patients (Grade 1, 33%; Grade 2, 33%; Grade 3, 17%). Immune effector cell-associated neurotoxicity syndrome occurred in 33% (2/6) of patients (Grade 2, 17%; Grade 3, 17%) and resolved rapidly with treatment. One patient experienced a dose-limiting toxicity at Dose Level 2, including Grade 3 diarrhea, Grade 4 enterocolitis and death from fungal sepsis 48 days post-infusion. No Grade 3 or higher diarrhea has occurred in the last three patients treated since establishing an optimized management protocol for diarrhea, including prophylaxis.

"Lyell was founded to realize the full potential of cell therapy for solid tumors, which make up more than 90% of all cancers. We believe LYL273 has the potential to be a transformational advance in the treatment of colorectal cancer, an area of tremendous unmet need," said Lynn Seely, MD, Lyell's President and Chief Executive Officer. "We look forward to leveraging our expertise in T-cell biology and CAR T-cell clinical development to rapidly progress this program, as well as our two pivotal clinical trials evaluating ronde-cel for patients with relapsed or refractory large B-cell lymphoma."

LYL273 was granted Fast Track designation for the treatment of mCRC by the U.S. Food and Drug Administration. The Phase 1 clinical trial is continuing to enroll patients with refractory mCRC to determine the recommended Phase 2 dose. The next data update from this clinical trial is expected in the first half of 2026.

Clinical proof-of-concept was initially demonstrated in an investigator-sponsored clinical trial conducted in China. Data from this clinical trial in 15 patients with mCRC were published in *JAMA Oncology* (September 2024).

**Details of the Transaction**

Under the terms of the definitive license agreement, Lyell will receive exclusive global rights, outside of mainland China, Hong Kong, Macau and Taiwan, to research, develop, manufacture and commercialize LYL273. ICT will receive an upfront payment of $40 million and 1.9 million shares of Lyell common stock. ICT is also eligible to receive additional cash and equity consideration, as well as royalties on future net sales. Additional cash consideration consists of a potential $30 million clinical milestone, up to $115 million in late-stage regulatory milestones and up to $675 million in commercial sales milestones. Additional equity consideration consists of up to 1.85 million shares of Lyell common stock upon achievement of certain clinical and late-stage regulatory milestones. Tiered royalties range from mid-single digits up to 10% on annual net sales in the U.S. and low to mid-single-digit royalties on annual net sales in other countries within the licensed territory.

Following the close of the transaction, Lyell expects its cash will be adequate to fund operations into 2027 through data and progress updates from the rondecabtagene autoleucel (ronde-cel) clinical program for patients with large B-cell lymphoma and additional clinical data from the Phase 1 clinical trial of LYL273.

The transaction will have a modest impact on operating expenses for 2025. As a result of continued prudent expense management, Lyell now expects net cash use in 2025 to be between $155 million and $160 million, excluding the $40 million upfront payment from the transaction, below its previous net cash use guidance of between $175 million and $185 million.

Skadden, Arps, Slate, Meagher & Flom LLP served as legal counsel to Lyell.

**Conference Call Details**

Lyell's management will host an investor conference call and webcast beginning at 8:30 AM ET today. The webcast can be accessed here.

A replay of the event and presentation materials will be archived on the Investor page of the Lyell Website following the end of the event.

**Forward Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this press release include, but are not limited to, statements regarding: the potential clinical benefits and therapeutic potential of LYL273 and ronde-cel; statements made by our Chief Executive Officer and others; expectations around enrollment for, and the next data update from, the Phase 1 clinical trial of LYL273; Lyell's expectation that its cash will be adequate to fund operations into 2027 and through data and progress updates from the ronde-cel clinical program and additional clinical data from the Phase 1 clinical trial of LYL273; Lyell's estimated 2025 net cash use; Lyell's ability to rapidly move forward the development of LYL273; and other statements that are not historical fact. These statements are based on Lyell's current plans, objectives, estimates, expectations and intentions, are not guarantees of future performance and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, but are not limited to, risks and uncertainties related to: Lyell's limited experience as a company in initiating and conducting clinical trials, and lack of experience in completing clinical trials; the nonclinical profiles of Lyell's product candidates or technology not translating in clinical trials; the potential for results from clinical trials to differ from nonclinical, early clinical, preliminary or expected results; significant adverse events, toxicities or other undesirable side effects associated with Lyell's product candidates; Lyell's ability to submit

planned INDs or initiate or progress clinical trials on the anticipated timelines, if at all; RMAT and Fast Track designations may not actually lead to faster development, regulatory review or approval process, and do not assure ultimate FDA approval; the significant uncertainty associated with Lyell's product candidates ever receiving any regulatory approvals; Lyell's ability to obtain, maintain or protect intellectual property rights related to its product candidates; the complexity of manufacturing cellular therapies and Lyell's ability to manufacture and supply its product candidates for its clinical trials; implementation of Lyell's strategic plans for its business and product candidates; Lyell's realization of the expected benefits of its strategic plans for its business and product candidates, including the license of LYL273; the potential reduction of Lyell's cash resources and fluctuations in Lyell's operating results and financial condition as a result of Lyell's milestone, royalty and success payment obligations for LYL273; the sufficiency of Lyell's capital resources and need for additional capital to achieve its goals; the effects of macroeconomic conditions, including the effects of disruption between the U.S. and its trading partners due to tariffs or other policies, and any geopolitical instability; potential changes to U.S. drug pricing, including the potential for "most-favored nations" pricing limitations; other risks, including general economic conditions and regulatory developments, not within Lyell's control; and other risks, including those described under the heading "Risk Factors" in Lyell's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the Securities and Exchange Commission on March 11, 2025 and in Lyell's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, previously filed with the Securities and Exchange Commission on August 12, 2025. Forward-looking statements contained in this press release are made as of this date, and Lyell undertakes no duty to update such information except as required under applicable law.

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