Lyell Immunopharma Provides Update on Safety Profile of LYL273 in Relapsed or Refractory Metastatic Colorectal Cancer and Amends Phase 1 Trial to Phase 1/2 Expansion

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- Gastrointestinal prophylaxis reduced Grade ≥ 2 diarrhea/colitis from 55% without prophylaxis to 10% with prophylaxis
- The maximum tolerated dose has not yet been determined
- No difference is observed in GCC CAR T-cell expansion kinetics in patients with or without GI prophylaxis
- Ongoing U.S. Phase 1 trial amended to enable seamless expansion into a potential pivotal single-arm Phase 2 trial pending regulatory alignment
- Amendment of ongoing U.S. Phase 1 trial adds new cohorts, including a second-line cohort and a cohort evaluating a combination strategy with radiotherapy
- Additional Phase 1 clinical data, including clinical outcomes, and End-of-Phase 1 FDA meeting expected in second half of 2026

SOUTH SAN FRANCISCO, Calif., June 08, 2026 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a late-stage clinical company advancing a pipeline of next-generation chimeric antigen receptor (CAR) T-cell therapies for patients with cancer, today provided an update on the safety profile of LYL273 in its ongoing U.S. Phase 1 clinical trial in patients with relapsed or refractory metastatic colorectal cancer (mCRC), and announced the Phase 1 trial has been amended to enable seamless expansion into a potential pivotal single-arm Phase 2 trial pending regulatory alignment.

LYL273 is a guanylyl cyclase C (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. A 50% overall response rate across Dose Levels 1 and 2 has been previously reported (data cutoff date of October 28, 2025) in third- or later-line (3L+) relapsed or refractory mCRC patients in the U.S. Phase 1 clinical trial. The FDA has granted LYL273 Fast Track designation for the treatment of mCRC.

“The substantial reduction of Grade 2 or higher diarrhea or colitis, and absence of Grade 3 or higher CRS and ICANS in patients treated under our gastrointestinal prophylaxis and standardized safety management plan suggest we can manage the safety profile of LYL273 in patients with relapsed or refractory metastatic colorectal cancer,” said Lynn Seely, M.D., President and Chief Executive Officer of Lyell. “We are continuing to move forward to selection of the recommended Phase 2 dose and are on track for an End-of-Phase 1 meeting with the FDA by the end of the year.”

Updated Safety Data from U.S. Phase 1 Clinical Trial Evaluating LYL273 in Patients with Relapsed or Refractory Third- or Later-Line mCRC

Nineteen patients have been enrolled in the U.S. Phase 1 clinical trial across Dose Levels 1 and 2 (1 and 2 x 10^6 CAR+ cells/kg) as of the data cutoff date of May 5, 2026. Ten of these patients were enrolled under the new gastrointestinal (GI) prophylaxis regimen including infliximab, vedolizumab and budesonide, along with a standardized safety management plan. Notably, the GI prophylaxis and standardized safety management plan reduced Grade $\geq$ 2 diarrhea or colitis from 55% to 10% in patients without (N = 9) and with (N = 10) GI prophylaxis, respectively. These ten patients did not experience Grade ≥ 3 cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS). No additional adverse events of interest have been identified. There was no difference observed in GCC-CAR+ cell expansion either in terms of maximum cell expansion or area under the curve in those patients who received GI prophylaxis and those who did not.

Dose escalation continues in the U.S. Phase 1 clinical trial; the maximum tolerated dose has not been determined.

Phase 1 Clinical Trial Amended to Phase 1/2 Design

The U.S. Phase 1 clinical trial evaluating LYL273 in relapsed or refractory 3L+ mCRC has been amended to a Phase 1/2 design

(CARABINER). The amended design enables seamless expansion into a potential pivotal single-arm Phase 2 trial once the recommended Phase 2 dose has been determined, subject to discussions with the U.S. Food and Drug Administration (FDA). New centers are being added to the trial in preparation for initiating the dose expansion portion of the Phase 1/2 trial.

The Phase 1 portion of the clinical trial includes four dose-escalation cohorts at Dose Levels 1 through 4 (1, 2, 3, 4 x 10^6 CAR+ cells/kg). Each dose-escalation cohort is designed to include three or six patients, with up to twenty-four patients across the four dose-escalation cohorts.

In addition to the existing 3L+ cohorts, the amendment adds new cohorts, including a second-line cohort and a cohort evaluating a combination strategy with radiotherapy. Up to sixty patients are expected to be enrolled across the new cohorts. The Phase 2 portion will expand enrollment at the recommended Phase 2 dose in an open-label, single-arm cohort.

Upcoming LYL273 Milestones

In the second half of 2026, additional Phase 1 clinical data, including clinical outcomes, and an End-of-Phase 1 meeting with the FDA are expected.

About Lyell Immunopharma, Inc.

Lyell is a late-stage clinical company advancing a pipeline of next-generation CAR T-cell therapies for patients with hematologic malignancies and solid tumors. To realize the potential of cell therapy for cancer, Lyell utilizes a suite of technologies to arm CAR T cells with enhancements needed to drive durable tumor cytotoxicity and achieve consistent and long-lasting clinical responses, including the ability to resist exhaustion, maintain qualities of durable stemness and function in the hostile tumor microenvironment. LyFE has commercial launch capability and is expected to have the capacity to manufacture more than 1,200 CAR T-cell doses per year. To learn more, please visit www.lyell.com.

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: Lyell's intention for the amended ongoing U.S. Phase 1 trial to enable seamless expansion into a potential pivotal single-arm Phase 2 trial pending regulatory alignment; the potential clinical benefits and therapeutic potential of Lyell's product candidates; Lyell's expected timing for an End-of-Phase 1 meeting with the FDA and for reporting additional Phase 1 data, including clinical outcomes; the number of patients expected to be enrolled across the new cohorts of the amended ongoing U.S. Phase 1 trial; and the sufficiency of the capacity of LyFE to manufacture drug supply through potential commercial launch. 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 ability to successfully develop, manufacture and commercialize product candidates or its experiencing significant delays in doing so; Lyell's dependence on the enrollment and retention of patients in its current and planned clinical trials for its product candidates; the potential for results of Lyell's research, nonclinical studies or earlier clinical trials to not be predictive of future results; clinical development involving a lengthy and expensive process with uncertain outcomes; Lyell's product candidates and technologies being based on novel technologies that are unproven and may not result in approvable or marketable products; significant adverse events, toxicities or other undesirable side effects associated with Lyell's product candidates; Lyell facing substantial competition in a rapidly changing industry, which may result in others discovering, developing or commercializing products before or more successfully than it does; the complexity of manufacturing cellular therapies; Lyell's ability to manufacture drug products for its clinical trials itself and any potential delays in further qualifying or in receiving regulatory approvals for any manufacturing facility or product candidates or in expanding its manufacturing capacity; Lyell's reliance on third parties; implementation of Lyell's strategic plans for its business and product candidates and Lyell's realization of the expected benefits of such plans; 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 sufficiency of Lyell's capital resources and need for additional capital to achieve its goals; and other risks, including those described under the heading "Risk Factors" in Lyell's Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, filed with the Securities and Exchange Commission on May 6, 2026. 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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