Lyell Immunopharma Announces Initiation of Patient Dosing in First-of-Its-Kind Phase 3 Head-To-Head CAR T-Cell Clinical Trial in Aggressive Large B-Cell Lymphoma

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- PiNACLE – H2H will evaluate the efficacy and safety of rondecabtagene autoleucel (ronde-cel) versus Investigator's choice of approved CD19 CAR T-cell therapies in patients with aggressive large B-cell lymphoma receiving treatment in the second-line setting
- The pivotal single-arm trial, PiNACLE, evaluating ronde-cel in the third- or later-line setting is ongoing with BLA submission expected in 2027
- Site activation for both PiNACLE – H2H and PiNACLE are underway in the United States, Canada and Australia

SOUTH SAN FRANCISCO, Calif., Feb. 12, 2026 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage company advancing a pipeline of next-generation chimeric antigen receptor (CAR) T-cell therapies for patients with cancer, today announced that the first patient has been dosed in the PiNACLE – H2H Phase 3 trial evaluating rondecabtagene autoleucel (ronde-cel, also known as LYL314) compared to lisocabtagene maraleucel (liso-cel) or axicabtagene ciloleucel (axi-cel) for the treatment of patients with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) receiving treatment in the second-line (2L) setting.

"Ronde-cel is a dual-targeting CD19/CD20 CAR T-cell product candidate that has demonstrated impressive clinical data in patients with aggressive large B-cell lymphoma," said Krish Patel, MD, Director of Lymphoma Research at Sarah Cannon Research Institute (SCRI). "One of our SCRI CAR T-cell sites is the first to enroll in this important trial designed to provide physicians the data we need to make the best treatment decisions for our patients. Furthermore, this trial represents a milestone in the field of cellular therapy, being the first trial to randomize patients between different CAR T-cell therapies."

"Data from Lyell's single-arm pivotal PiNACLE trial in patients with later-stage large B-cell lymphoma are expected to be submitted for marketing approval to the FDA next year," said David Shook, MD, Lyell's Chief Medical Officer. "We are now pleased to have underway PiNACLE – H2H, the first-of-its-kind Phase 3 head-to-head randomized controlled CAR T-cell trial. This strategy demonstrates Lyell's confidence in ronde-cel's potential to be the best-in-class CAR T-cell treatment for patients with relapsed or refractory disease."

PiNACLE – H2H is a Phase 3 head-to-head CAR T-cell randomized controlled clinical trial of ronde-cel versus Investigator's choice of either liso-cel or axi-cel in patients with R/R LBCL receiving treatment in the 2L setting. Patients randomized to ronde-cel will be treated with a dose of 100 x 10^6 CAR T cells; patients in the control arm will be treated as per the product label. The primary endpoint of this superiority trial is event-free survival and the trial plans to enroll approximately 200 patients per arm (N = 400) with R/R LBCL, including diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, high grade B-cell lymphoma, Grade 3B follicular lymphoma, or transformed follicular or transformed mantle cell lymphoma who have not previously received CAR T-cell therapy. Patients may be treated with ronde-cel in either the inpatient or outpatient setting.

More information about the PiNACLE – H2H trial can be found on clinicaltrials.gov (NCT07188558) here.

Ronde-cel is also being studied in PiNACLE, a pivotal single-arm trial in the third- or later-line (3L+) setting. This registration trial is a seamless expansion of the 3L+ cohort from the multi-cohort multi-center Phase 1/2 trial and will enroll approximately 120 patients at approximately 25 sites. The dose is 100 x 10^6 CAR T cells and the primary endpoint is overall response rate. Patients may be treated with ronde-cel in either the inpatient or outpatient setting. More information about the PiNACLE trial can be found on clinicaltrials.gov (NCT05826535) here.

At the American Society of Hematology (ASH) Annual Meeting and Exposition in December 2025, Lyell reported positive updated clinical data in patients with aggressive LBCL in the 3L+ and 2L settings from the Phase 1/2 trial. The oral presentation included updated data from the 3L+ cohort (now the ongoing PiNACLE pivotal trial), including a best overall response rate of 93% and a complete response rate of 76% in 29 efficacy-evaluable patients with R/R LBCL. The median progression-free survival was 18

months as of the data cutoff date of September 5, 2025. Updated data were also presented from the 2L cohort, including 18 efficacy evaluable patients (94% with high-risk primary refractory disease), and demonstrated an 83% best overall response rate and a 61% complete response rate. The safety profile was appropriate for outpatient administration of ronde-cel. Data from 25 patients treated with ronde-cel and receiving dexamethasone prophylaxis revealed no reports of Grade 3 or higher cytokine release syndrome (CRS) and one case (4%) of Grade 3 or higher immune effector cell-associated neurotoxicity syndrome (ICANS).

About Rondecabtagene Autoleucel (Ronde-cel)

Rondecabtagene autoleucel (ronde-cel, also known as LYL314) is a next-generation dual-targeting CD19/CD20 CAR T-cell product candidate designed to increase complete response rates and prolong the duration of the responses as compared to the approved CD19-targeted CAR T-cell therapies for the treatment of R/R LBCL.

Ronde-cel is designed with an 'OR' logic gate to target B cells that express either CD19, CD20 or both, each with full potency. Ronde-cel is manufactured to produce a CAR T-cell product with higher proportions of naïve and central memory T cells through a proprietary process that enriches for CD62L-expressing cells. This manufacturing process is designed to generate CAR T cells with enhanced antitumor activity.

Ronde-cel has received Regenerative Medicine Advanced Therapy (RMAT) designation as well as Fast Track designation from the U.S. Food and Drug Administration (FDA) for the treatment of adults with R/R diffuse LBCL (DLBCL) in the 3L+ setting and has also received RMAT designation for the treatment of LBCL in the 2L setting. The FDA has also granted ronde-cel Orphan Drug Designation for the treatment of DLBCL/high grade B-cell lymphoma with MYC and BCL2 rearrangements.

About Lyell

Lyell is a clinical stage 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. Lyell's LyFE Manufacturing Center™ has commercial launch capability and can manufacture more than 1,200 CAR T-cell doses at full capacity. 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: the potential clinical benefits and therapeutic potential of ronde-cel; Lyell's expectations around the progress of the PiNACLE and PiNACLE – H2H trials, including expectations around enrollment, and the timing of regulatory submissions for ronde-cel; the sufficiency of the capacity of LyFE to manufacture drug supply through potential commercial launch; 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 enrolling 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; the potential for interim results from a clinical trial as of a data cutoff to not be necessarily indicative of final results and for one or more of the clinical and safety outcomes to materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues and as more patient or final data become available; significant adverse events, toxicities or other undesirable side effects associated with Lyell's product candidates, including the risk that the ultimate safety profile of ronde-cel may not support outpatient administration; Lyell's ability to submit planned regulatory submissions 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; 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, and Lyell's realization of the expected benefits of such plans, for its business and product candidates; 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 September 30, 2025, filed with the U.S. Securities and Exchange Commission on November 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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