Lyell Immunopharma Presents New Clinical Data from Ongoing Trial of Ronde-Cel Showing High Rates of Durable Complete Responses in Patients with Large B-cell Lymphoma at the 67th ASH Annual Meeting and Exposition

December 7, 2025

- 93% overall response and 76% complete response rates with median progression-free survival of 18 months in patients with large B-cell lymphoma in the 3L+ setting
- 83% overall response and 61% complete response rates in cohort comprised predominantly of patients with primary refractory large B-cell lymphoma in the 2L setting
- Manageable safety profile appropriate for outpatient administration; no high-grade CRS and ≤ 5% of patients with Grade ≥ 3 ICANS following dexamethasone prophylaxis
- Lyell management will host an investor webcast with presenting author and ronde-cel investigator Sarah M. Larson, MD, Associate Professor at the David Geffen School of Medicine, University of California, Los Angeles, at 8:30 AM ET on Monday, December 8th

SOUTH SAN FRANCISCO, Calif., Dec. 07, 2025 (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 new clinical and translational data from the ongoing clinical trial of rondecabtagene autoleucel (ronde-cel, also known as LYL314) in patients with large B-cell lymphoma (LBCL), which were presented today in two oral presentations at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition. As of the data cutoff date of September 5, 2025, ronde-cel continued to demonstrate robust clinical responses with a manageable safety profile appropriate for outpatient administration. A 93% overall response rate, a 76% complete response rate, and median progression-free survival of 18 months were reported for patients with relapsed and/or refractory (R/R) LBCL in the third- or later-line (3L+) setting. Patients evaluated in the second-line (2L) setting (94% with difficult-to-treat primary refractory disease) achieved an 83% overall response rate and a 61% complete response rate, and 70% of patients with a complete response remained in complete response at 6 months or longer.

Ronde-cel is an autologous dual-targeting CD19/CD20 CAR T-cell product candidate in pivotal development for patients with R/R LBCL. Ronde-cel CAR T cells are designed to have enhanced antitumor activity through a proprietary manufacturing process that enriches for CD62L-positive cells to produce a CAR T-cell product with a higher proportion of naïve and central memory T cells. The United States Food and Drug Administration (FDA) has granted ronde-cel Regenerative Medicine Advanced Therapy (RMAT) designation for the treatment of patients with R/R LBCL in the 3L+ and 2L settings.

“These data from the ongoing clinical trial showing high rates of durable complete responses along with a manageable safety profile in patients with high-risk large B-cell lymphoma represent the potential of ronde-cel to improve patient outcomes,” commented Sarah M. Larson, MD, Associate Professor, Department of Medicine, Medical Director, Immune Effector Cell Therapy Program, Division of Hematology/Oncology, David Geffen School of Medicine at UCLA. “The two pivotal trials underway, including the first-of-its kind head-to-head CAR T-cell trial, are expected to provide a comprehensive and robust evaluation of the potential for ronde-cel to demonstrate differentiated benefit over approved CD19 CAR T-cell therapies.”

Sixty-nine CAR T-cell naïve patients with R/R LBCL received ronde-cel as of the data cutoff date for the presentation. The efficacy evaluable population, defined as those patients with Day 84 assessments or prior disease progression or death, consisted of 47 patients (29 in the 3L+ and 18 in the 2L settings). Imaging assessments were performed locally by the sites. Patient demographics and baseline disease characteristics were consistent with a high-risk, heavily pre-treated patient population, particularly as compared to historical trials of CD19 CAR T-cell products: median ages of 64 and 65 years with 20% (9/45) and 21% (5/24) of patients being 75 years or older in the 3L+ and 2L settings, respectively; and primary refractory disease in 49% (22/45) and 92% (22/24) of patients in the 3L+ and 2L settings, respectively.

Patients Evaluated in the 3L+ Setting

There were 29 efficacy-evaluable 3L+ patients with R/R LBCL (diffuse large B-cell lymphoma, primary mediastinal B-cell

lymphoma, Grade 3B follicular lymphoma, or transformed follicular lymphoma) with a median follow up time of 12 months as of the data cutoff date. In these patients:

- The overall response rate was 93% (27/29 patients), with 76% (22/29) of patients achieving a complete response
- 72% (13/18) of patients with complete response remained in complete response at 6 months or longer
- Median progression-free survival was 18 months

Patients Evaluated in the 2L Setting

There were 18 efficacy-evaluable patients enrolled in the 2L setting with a median follow-up time of 9 months as of the data cutoff date. Of these efficacy-evaluable patients, 94% had primary refractory disease. In these patients:

- The overall response rate was 83% (15/18 patients), with 61% (11/18) achieving a complete response
- 70% (7/10) of patients with complete response remained in complete response at 6 months or longer
- The median duration of complete response was not reached

Safety Data

In 69 patients, including patients from both the 3L+ and the 2L cohorts, a manageable safety profile appropriate for outpatient administration was observed. No Grade 3 or greater cytokine release syndrome (CRS) was observed in any patient. Twenty-five of the 69 patients received protocol-directed dexamethasone prophylaxis (10 mg/day for 3 days). One case (4%) of Grade 3 or greater ICANS was reported in a patient with high disease burden; no case of Grade 2 ICANS was reported.

In all 69 patients, as of the data cutoff date, low rates of Grade 1 (32%) or Grade 2 (29%) CRS were reported; ICANS rates were reported as follows: Grade 1 (9%), Grade 2 (3%), and Grade 3 or greater (12%) of patients. The median time to complete resolution of all reports of ICANS was 4 days. Cell pharmacodynamic data demonstrated robust CAR T-cell expansion and persistence that were similar in patients with or without dexamethasone prophylaxis. No deaths were determined to be related to ronde-cel administration.

Pivotal Clinical Trials

Lyell has initiated two pivotal clinical trials of ronde-cel: PiNACLE – H2H and PiNACLE.

PiNACLE – H2H is a Phase 3 head-to-head CAR T-cell therapy randomized controlled clinical trial of ronde-cel versus investigator's choice of either lisocabtagene maraleucel (liso-cel) or axicabtagene ciloleucel (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 the trial is event-free survival and the trial is expected 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.

PiNACLE is a single-arm trial of ronde-cel that is enrolling up to 120 patients receiving treatment in the 3L+ setting. This registration trial is a seamless expansion of the 3L+ cohort from the Phase 1/2 trial. The dose is 100 x 10^6 CAR+ 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.

Ronde-cel Translational Data

Translational data from the ongoing Phase 1/2 clinical trial showed that ronde-cel manufactured with CD62L enrichment achieved robust expansion and high expression of memory-related genes after infusion in patients with LBCL. An evaluation of ronde-cel and published data for CD19 CAR T-cell products demonstrated that ronde-cel had a higher proportion of CD62L-positive T cells with a higher proportion of memory-cell phenotype prior to infusion (ronde-cel, N = 34; axi-cel, N = 110 and tisagenlecleucel (tisa-cel), N = 31). In addition, ronde-cel had up to a three-fold higher expansion in patients after infusion compared to the expansion of approved CD19 CAR T-cell products. The product memory-cell phenotype was positively correlated with expansion. Peripheral blood samples collected from patients one month after infusion (N = 9) also had a higher proportion of CAR T cells with a memory phenotype compared to cells from axi-cel-treated patients (N = 4). Ronde-cel CAR-positive T cells collected from patients one (N = 7) and two months (N = 3) after infusion demonstrated sustained capacity to proliferate, kill tumor cells over 72 hours, and secrete cytokines (N = 3).

The clinical data were highlighted in an oral presentation by Sarah M. Larson, MD, Associate Professor, Department of Medicine, Medical Director, Immune Effector Cell Therapy Program, Division of Hematology/Oncology, David Geffen School of Medicine at UCLA, Los Angeles, CA. Translational data were presented in a separate oral presentation by Akil Merchant, MD, Associate Professor and Co-Director of the Lymphoma Program at the Samuel Oschin Cancer Center, Cedars-Sinai Medical Center, Los Angeles, CA.

Conference Call Details

Lyell's management will host an investor conference call and webcast to review these data at 8:30 AM ET on Monday, December 8th. The webcast registration link can be accessed here. A replay of the event and presentation materials will be available on the Investor page of the Lyell Website following the end of the event.

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 RMAT designation from the FDA for the treatment of patients with R/R LBCL in the 3L+ and 2L settings, as well as Fast Track Designation for the treatment of patients with R/R LBCL in the 3L+ setting.

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; 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: interim results of a clinical trial as of the data cutoff are not necessarily indicative of final results and one or more of the clinical and safety outcomes may 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 becomes available; 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; 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; the translational data presented above is not based on a head-to-head trial and differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials; Lyell's ability to submit planned Investigational New Drug Applications 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 its product candidate 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; 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 our 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 Exchange Commission (SEC) on March 11, 2025, and Lyell's Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, filed with the SEC 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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