Lyell Immunopharma Announces the Initiation of a Phase 3 Head-to-Head CAR T-Cell Therapy Clinical Trial in Aggressive Large B-Cell Lymphoma and Formation of Expert Steering Committee

September 3, 2025

- PiNACLE - H2H will evaluate 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 (2L) setting
- Ronde-cel is Lyell's next-generation, dual-targeting CD19/CD20 CAR T-cell therapy designed to deliver improved complete response rates and longer duration of responses over currently approved CD19 CAR T-cell therapies
- Steering Committee of distinguished lymphoma experts established to advise on the design and conduct of this first-of-its-kind CAR T-cell clinical trial

SOUTH SAN FRANCISCO, Calif., Sept. 03, 2025 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a late-stage clinical company advancing next-generation CAR T-cell therapies for patients with cancer, today announced the initiation of PiNACLE - H2H, a Phase 3 head-to-head CAR T-cell therapy randomized controlled trial and the formation of a Steering Committee of preeminent lymphoma experts. The trial is 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 2L setting. Ronde-cel is an autologous dual-targeting CD19/CD20 chimeric antigen receptor (CAR) T-cell product candidate with Regenerative Medicine Advanced Therapy (RMAT) and Fast Track designations from the U.S. Food and Drug Administration (FDA) for development in patients with R/R LBCL. Ronde-cel targets B cells that express either CD19, CD20, or both, and is manufactured to produce a product with higher proportions of naïve and central memory T cells – features that are designed to deliver improved complete response rates and durability for patients.

"We believe, based on the robust emerging clinical profile demonstrated by ronde-cel in the Phase 1/2 trial, that targeting both CD19 and CD20 with full potency can deliver more complete responses and prolong the duration of remission as compared to the single antigen-targeting CD19 CAR T-cell therapies currently approved for patients with aggressive large B-cell lymphoma," said David Shook, MD, Lyell's Chief Medical Officer. "We are delighted to be collaborating with a distinguished group of lymphoma and cell therapy experts on the design and conduct of our ground-breaking head-to-head clinical trial and expect to begin enrolling patients by early 2026."

"Lyell is undertaking a well-designed and innovative Phase 3 trial to provide patients and their physicians with the data needed to demonstrate the potential clinical benefit of ronde-cel, a dual-targeting CD19/CD20 CAR T-cell therapy, over and above that of the currently approved CD19 CAR T-cell therapies," said Michael Jain, MD, PhD, PiNACLE - H2H Steering Committee member and Immune Cell Therapy Medical Director in the Moffitt Cancer Center Department of Blood and Marrow Transplant and Cellular Immunotherapy. "I am encouraged by the promising data from the Phase 1/2 clinical trial of ronde-cel and believe this innovative cell therapy can improve clinical outcomes for patients."

"Lyell is leading the field with the announcement of the first Phase 3 head-to-head CAR T-cell therapy trial for patients with large B-cell lymphoma," said Matthew Lunning, DO, PiNACLE - H2H Steering Committee member and Professor in the Division of Hematology/Oncology at the University of Nebraska Medical Center. "We have designed this trial evaluating ronde-cel to include the spectrum of patients who are currently receiving CD19 CAR T-cell therapy in the large B-cell lymphoma setting, as well as to provide the option for treatment in the outpatient setting based on the safety profile observed to date."

Members of the PiNACLE - H2H Steering Committee include:

- **Michael Bishop, MD,** Professor of Medicine and Director, Hematology/Oncology Cellular Therapy Program, University of Chicago, Chicago, IL
- **Michael Jain, MD, PhD,** Immune Cell Therapy Medical Director in the Moffitt Cancer Center Department of Blood and Marrow Transplant and Cellular Immunotherapy, Tampa, FL
- **Manali Kamdar, MD,** Associate Professor of Medicine and Hematology and Clinical Director of Lymphoma Services,

University of Colorado, Denver, CO

- **Matthew Lunning, DO,** Professor in the Division of Hematology/Oncology and Medical Director of Cellular Therapy at the University of Nebraska Medical Center, Omaha, NE
- **Krish Patel**, **MD**, Director of Lymphoma Research at Sarah Cannon Research Institute (SCRI), Nashville, TN
- **Jason Westin, MD,** Professor, Department of Lymphoma/Myeloma, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Lyell is advancing two pivotal trials for patients with R/R LBCL:

- **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 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. The primary endpoint of the trial is event-free survival. The trial is expected to enroll approximately 400 patients 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 and are required to remain near the treating center for 14 days. Clinical site initiation is underway in the United States and Australia, and the first patient is expected to be enrolled by early 2026.
- **PiNACLE** is a single-arm pivotal trial of ronde-cel that is enrolling patients with R/R LBCL receiving treatment in the third- or later-line (3L+) setting. This trial is a seamless expansion of the 3L+ cohort of the Phase 1/2 trial of ronde-cel and is expected to enroll approximately 120 patients. The primary endpoint is overall response rate.

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

About Lyell

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 endow CAR T cells with attributes 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 for patients with R/R LBCL, including its potential to increase complete response rates and prolong the duration of responses as compared to approved CD19-targeted CAR T-cell therapies for the treatment of LBCL; the potential benefits, if any, from the RMAT and Fast Track designations from the FDA for the treatment of patients with R/R LBCL in the 3L+ setting; statements made by our Chief Medical Officer and members of the PiNACLE – H2H Steering Committee; expectations around enrollment, trial design, dosing and timing of -PiNACLE and PiNACLE H2H; the sufficiency of the capacity of LyFE to manufacture drug supply for Lyell's ongoing and planned pivotal trials and 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: the potential for results from clinical trials to differ from nonclinical, early clinical, preliminary or expected results; Lyell's limited experience as a company in enrolling and conducting clinical trials and lack of experience in completing clinical trials; significant adverse events, toxicities or other undesirable side effects associated with Lyell's product candidates; Lyell's ability to 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 does 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; 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; and other risks, including general economic conditions and regulatory developments, not within our control; and other risks described under the heading "Risk Factors" in Lyell's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, 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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