Lyell Immunopharma Announces Positive New Clinical Data Demonstrating High Rates of Durable Complete Responses from the Phase 1/2 Trial of LYL314 for the Treatment of Aggressive Large B-cell Lymphoma

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- LYL314 demonstrated robust clinical responses, with an 88% overall response rate and a 72% complete response rate in patients treated in the third- or later-line setting (N = 25)
- 71% of patients with complete response remained in complete response at ≥ 6 months
- Manageable safety profile appropriate for outpatient administration with no Grade ≥ 3 cytokine release syndrome and low rates of Grade ≥ 3 ICANS with rapid resolution
- Pivotal single-arm PiNACLE trial is underway in CAR T-naïve patients with large B-cell lymphoma treated in the third- or later-line setting
- Lyell to host an investor webcast at 8:00 AM ET today

SOUTH SAN FRANCISCO, Calif., June 17, 2025 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage company advancing next-generation CAR T-cell therapies for patients with cancer, today announced positive new clinical data from the multi-center Phase 1/2 trial of LYL314, including data from patients with large B-cell lymphoma (LBCL) treated in the third- or later-line (3L+) setting. LYL314 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 FDA that is in development for patients with relapsed and/or refractory (R/R) LBCL. In patients treated in the 3L+ setting (N = 25), LYL314 continued to demonstrate robust clinical responses, with an 88% overall response rate and a 72% complete response rate. Of the 3L+ patients who achieved a complete response, 71% remained in complete response at ≥ 6 months. The single-arm pivotal PiNACLE trial, a seamless expansion of the Phase 1/2 trial of patients with R/R LBCL being treated in the 3L+ setting, is underway.

“Based on the LYL314 data to be presented at the International Conference on Malignant Lymphoma and my personal experience treating patients in the clinical trial, I believe that LYL314 has the potential to provide differentiated benefit for patients with relapsed/refractory large B-cell lymphoma in both the complete response rate and durability of response,” stated 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, and an investigator in the Phase 1/2 clinical trial. “We look forward to completing enrollment in the ongoing single-arm pivotal trial evaluating LYL314 in patients in the third- or later-line setting.”

Fifty-one CAR T-naive patients with R/R LBCL received LYL314 as of April 15, 2025 (the data cutoff date for the presentation). The efficacy evaluable population consisted of 36 patients with Day 84 assessments or prior disease progression or death. Patient demographics and baseline disease characteristics were consistent with high-risk patient populations: median ages of 65 and 69 years in the 3L+ and 2L, respectively, 41% of 3L+ and 65% of 2L patients had Stage IV disease at trial entry, and 47% of 3L+ and 82% of 2L patients had primary refractory disease. There were 49 patients who received the recommended Phase 2 dose of 100 x 10^6 CAR T cells; two patients received a dose of 300 x 10^6 CAR T cells. CD19/CD20 screening was not required prior to enrollment.

In efficacy-evaluable 3L+ patients, with a median follow up of 9 months (N = 25):

- The overall response rate was 88% (22/25 patients), with 72% (18/25) of patients achieving a complete response
- 71% (10/14) of patients with complete response remained in complete response at ≥ 6 months

In initial data from efficacy-evaluable 2L patients, with a median follow up of 5 months (N = 11):

- The overall response rate was 91% (10/11 patients), with 64% (7/11) achieving a complete response
- 100% (7/7) of patients with complete response were in complete response at last assessment, including 3/3 at ≥ 6 months

- In patients with primary refractory disease, a difficult to treat population, 70% (7/10) achieved a complete response
- These patients had high-risk features, including primary refractory disease (91%), stage IV disease (64%), and older age (27% > 75 years; median age 73 years)

In 51 patients, including patients from both the 3L+ and the 2L cohorts, a manageable safety profile appropriate for outpatient administration was observed. No Grade ≥ 3 and low rates of Grade 1 (22%) or Grade 2 (35%) cytokine release syndrome (CRS) were reported. Immune effector cell-associated neurotoxicity syndrome (ICANS) was reported in 6% (Grade 1), 2% (Grade 2), and 14% (Grade ≥ 3) of patients. The median time to complete resolution of all reports of ICANS was 5 days, with rapid improvement (median of 2 days) to Grade 2 or lower with standard therapy. No deaths were related to LYL314 administration. LYL314 demonstrated robust expansion with a time to peak of 10 days (N = 51). The final drug product contained the desired CD62L positive naïve T-cell phenotype (median, 95%). Rapid and durable depletion of B cells was demonstrated through month 6 and up to the month 12 assessment using a highly sensitive and robust method.

“Based on these robust data, and our recent End-of-Phase 1 meeting with the FDA, we have initiated PiNACLE, a single-arm pivotal trial of LYL314 in patients with large B-cell lymphoma in the third- or later-line setting and remain on track to initiate a pivotal trial to evaluate LYL314 in the second-line setting by the beginning of 2026,” said Lynn Seely, MD, Lyell’s President and Chief Executive Officer.

The data will be presented on Wednesday, June 18, 2025 in an oral session at the International Conference on Malignant Lymphoma in Lugano, Switzerland 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, and will be available as a presentation in the Investors’ section of the Company’s website.

Conference Call Details

Lyell’s management will host an investor conference call and webcast beginning at 8:00 AM ET today. The Webcast registration link 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.

About LYL314

LYL314 (formerly IMPT-314) 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 large B-cell lymphoma.

LYL314 is designed with an ‘OR’ logic gate to target B cells that express either CD19, CD20 or both. LYL314 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.

LYL314 has received Regenerative Medicine Advanced Therapy (RMAT) designation, as well as Fast Track Designation, from the U.S. Food and Drug Administration for the treatment of patients with relapsed and/or refractory aggressive B-cell lymphoma in the third- or later-line setting.

About the PiNACLE Trial

PiNACLE is a single-arm pivotal trial of LYL314, 100 x 10^6 CAR T cells, in patients with large B-cell lymphoma treated in the third- or later-line setting. The trial is expected to enroll approximately 120 patients with relapsed and/or refractory diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, high grade B-cell lymphoma, grade 3B follicular lymphoma, or transformed follicular lymphoma who have not previously received CAR T-cell therapy. Patients may be treated with LYL314 in either the inpatient or outpatient setting. The primary endpoint of the trial is the overall response rate. More information about the PiNACLE trial can be found on clinicaltrials.gov (NCT05826535) here.

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 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. The Lyell 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 LYL314 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; expectations around enrollment and timing of Lyell's ongoing single-arm pivotal trial evaluating LYL314 in patients in the 3L+setting and the initiation of a pivotal trial to evaluate LYL314 in the 2L setting; the potential of Lyell's manufacturing process to generate CAR T cells with enhanced antitumor activity; the sufficiency of the capacity of LyFE to manufacture drug supply for Lyell's ongoing and planned pivotal trials and through potential commercial launch; Lyell's anticipated progress, business plans, business strategy and clinical trials; Lyell's advancement of its pipeline, technology platform and research, development and clinical capabilities; 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 March 31, 2025, filed with the Securities and Exchange Commission on May 13, 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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