Lyell Immunopharma Receives Regenerative Medicine Advanced Therapy (RMAT) Designation for LYL314 for the Treatment of Relapsed and/or Refractory Large B-Cell Lymphoma

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- RMAT designation was granted based on promising clinical data from the ongoing Phase 1/2 trial of LYL314 in patients with relapsed and/or refractory large B-cell lymphoma.
- RMAT designation recognizes the potential of LYL314 to address significant unmet needs of patients with relapsed and/or refractory large B-cell lymphoma and enables an increased frequency of communications with FDA on the development of LYL314
- Additional clinical data to be presented this year from the Phase 1/2 trial, including data from patients being treated in the 3rd or later line and 2nd line settings

SOUTH SAN FRANCISCO, Calif., April 15, 2025 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage company advancing a pipeline of next-generation CAR T-cell therapies for patients with cancer, today announced that the U.S. Food and Drug Administration (FDA) granted Regenerative Medicine Advanced Therapy (RMAT) designation to LYL314 (formerly IMPT-314) for the treatment of adult patients with relapsed and/or refractory large B-cell lymphoma after two or more prior lines of therapy. 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 response as compared to the approved CD19-targeted CAR T-cell therapies for the treatment of aggressive large B-cell lymphoma (LBCL).

RMAT designation provides all the benefits of the Fast Track and Breakthrough Therapy designation programs, including early interactions with the FDA. LYL314's RMAT designation was granted based on promising early data from the ongoing Phase 1/2 clinical trial.

"The RMAT designation for LYL314, is based on promising clinical data from our ongoing Phase 1/2 trial and highlights the transformative potential of this next-generation CAR T-cell therapy to address the unmet needs of patients with aggressive large B-cell lymphoma," said Lynn Seely, M.D., president and chief executive officer of Lyell. "We believe that by targeting both CD19 and CD20 with equal potency and manufacturing with a process that enriches for more naïve and central memory CAR T cells, LYL314 has the potential to offer patients with aggressive B-cell lymphoma more complete responses and longer duration of response than first-generation CAR T-cell therapies that only target CD19. LYL314 has now received both Fast Track Designation and RMAT designation in the 3rd or later line setting and we look forward to working closely with the FDA as we continue to accelerate this promising CAR T-cell therapy into two pivotal programs for patients."

Initial data from the Phase 1/2 trial of LYL314 were presented at the American Society for Hematology 2024 Annual Meeting in December 2024, including data from 23 patients with relapsed or refractory LBCL in the 3rd or later line setting who received LYL314. The efficacy evaluable population consisted of 17 patients. The overall response rate was 94% (16/17) of patients, with 71% (12/17) of patients achieving a complete response by three months. The median follow up was 6.3 months (range 1.2 – 12.5 months) and 71% of patients were experiencing a response at last follow-up. In the safety evaluable population of 23 patients, no Grade 3 or greater cytokine release syndrome (CRS) was reported. Grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS) was reported in 13% (3/23) of patients with a median time to ICANS resolution of 5 days, and rapid improvement to Grade 2 or lower with standard therapy.

Additional clinical updates from the Phase 1/2 trial of LYL314 are planned for 2025. The company expects to present more mature data from the ongoing Phase 1/2 trial from patients being treated in the 3rd or later line setting and initial data from patients in the 2nd line setting in mid-2025 and to present more mature data from patients treated in the 2nd line setting in late 2025. Two pivotal programs for LBCL are planned, including one for patients treated in the 3rd or later line setting expected to be initiated in mid-2025 and another for patients treated in the 2nd line setting expected to be initiated by early 2026.

The RMAT designation is a program under the 21st Century Cures Act that is intended to expedite the development and review of regenerative medicine therapies for serious or life-threatening diseases or conditions. A regenerative medicine therapy is eligible

for RMAT designation if it is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such disease or condition.

RMAT designation provides all Breakthrough Therapy designation features, including early interactions to discuss any potential surrogate or intermediate endpoints. RMATs may be eligible for accelerated approval based on previously agreed-upon surrogate or intermediate endpoints that are reasonably likely to predict long-term clinical benefit.

About LYL314

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 response as compared to the approved CD19-targeted CAR therapies for the treatment of LBCL. LYL314 is designed as a true CD19/CD20 “OR” logic-gated CAR targeting either CD19 or CD20 with full potency, and the cell therapy product is manufactured with a process that enriches for CD62L+ cells to generate more naïve and central memory CAR T cells with enhanced stemlike features and antitumor activity.

In addition to RMAT, LYL314 has received Fast Track Designation from the U.S. Food and Drug Administration for the treatment of relapsed and/or refractory LBCL in the 3rd or later line setting.

About Lyell Immunopharma, Inc.

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. 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 anticipated benefits of the RMAT designation, including frequency of communications with the FDA; the anticipated benefits LYL314, including its potential to address significant unmet needs of patients with relapsed and/or refractory LBCL and to increase complete response rates and prolong the duration of response as compared to approved CD19-targeted CAR T-cell therapies for the treatment of LBCL; the acceleration of clinical progress of the LYL314 trials and expectations around the timing and scope of updated clinical data and the timing and design of pivotal programs of LYL314; the ability of Lyell’s 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 anticipated progress, business plans, business strategy and clinical trials; 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 inability to recognize the anticipated benefits of the RMAT designation; the effects of macroeconomic conditions, including the effects of disruption between the U.S. and its trading partners due to tariffs or other policies, any geopolitical instability, inflationary pressures, fluctuations in the interest rate environment and other challenges; Lyell’s ability to submit planned INDs or initiate or progress clinical trials on the anticipated timelines, if at all; Lyell’s limited experience as a company in enrolling and conducting clinical trials, and lack of experience in completing clinical trials; Lyell’s ability to manufacture and supply its product candidates for its 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; 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; 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; and other risks, including those described under the heading “Risk Factors” in Lyell’s Annual Report on Form 10-K for the year ended December 31, 2024, filed with the Securities and Exchange Commission on March 11, 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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