Lyell Presents Positive Initial Clinical Data from the Phase 1-2 Clinical Trial of IMPT-314 for the Treatment of B-cell Lymphoma at the 2024 ASH Annual Meeting

December 9, 2024

- Objective response rate (ORR) of 94% and a complete response (CR) rate of 71% demonstrated after IMPT-314 treatment in CAR T-naïve patients with large B-cell lymphoma who had received at least 2 prior lines of therapy
- Manageable safety profile with no high-grade cytokine release syndrome (CRS) and low rates of Grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS); adverse events were resolved with standard treatment protocols
- Initial clinical data are consistent with clinical experience from UCLA trial of CART19/20, a product candidate with the same CAR construct as IMPT-314 that has demonstrated durable responses in a Phase 1 trial of patients with non-Hodgkin lymphoma

SOUTH SAN FRANCISCO, Calif., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage company advancing a pipeline of next-generation CAR T-cell therapies for patients with solid tumors or hematologic malignancies, today announced initial positive clinical data from the multi-center Phase 1-2 study of IMPT-314 in patients with large B-cell lymphoma that is being presented at the 66th American Society of Hematology (ASH) Annual Meeting. IMPT-314 is an autologous dual-targeting CD19/CD20 chimeric antigen receptor (CAR) T-cell product candidate being developed for patients with aggressive B-cell non-Hodgkin lymphoma.

As of October 22, 2024 (the data cutoff for the presentation), 23 patients with relapsed or refractory (R/R), CAR T-naive large B-cell lymphoma received IMPT-314. The efficacy evaluable population consisted of 17 patients. The ORR was 94% (16/17 patients), with 71% (12/17 patients) achieving a CR by three months. The median follow up was 6.3 months (range 1.2 – 12.5 months) and 71% of patients were in response at last follow-up). In the safety evaluable population of 23 patients, no Grade 3+ CRS was reported. Grade 3 ICANS was reported in 13% (3/23) of patients with a median time to complete ICANS resolution of 5 days, and rapid improvement to Grade 2 or lower with standard therapy. In the efficacy evaluable set, 16 patients were evaluable for pharmacokinetics. IMPT-314 demonstrated robust expansion and peak cell expansion occurred between Days 7 – 28 post IMPT-314 infusion (median T_{max} = 10 days). Additionally, the final drug product contained the desired naïve and central memory cell phenotype (median, 91%; range, 82 – 99%) that has been associated with improved overall survival in other CAR T cell clinical studies.

The data are being presented today at the 2024 ASH Annual Meeting by Sarah M. Larson, M.D., Associate Professor, Department of Medicine, Medical Director, Immune Effector Cell Therapy Program, Division of Hematology/Oncology, David Geffen School of Medicine at UCLA, and the poster is available in the Investors' section of the Company's website.

"The high rate of complete responses with a favorable safety profile support the strong potential of IMPT-314, Lyell's next-generation dual-targeting CAR T-cell therapy enriched for naïve and central memory T cells. This product candidate was designed to maximize durable responses by overcoming heterogeneous CD19 antigen density and antigen escape, enhance CAR T cell persistence, and reduce exhaustion," said Lynn Seely, M.D., Lyell's President and Chief Executive Officer. "Based on these strong data, we remain on track to initiate a pivotal trial in 2025 of IMPT-314 in CAR T-naive patients with large B-cell lymphoma in the 3rd-line+ setting and are continuing to evaluate IMPT-314 in the 2nd-line setting in the ongoing Phase 1-2 trial."

"The data presented today from IMPT-314 suggest the potent targeting of both CD19 and CD20 coupled with CD62L+ cell enrichment has the potential to provide differentiated benefit in objective and complete response rates over first-generation CD19 CAR therapies in patients with aggressive large B-cell lymphoma," stated Sarah M. Larson, M.D., Associate Professor, Department of Medicine, Medical Director, Immune Effector Cell Therapy Program, Division of Hematology/Oncology, David Geffen School of Medicine at UCLA. "IMPT-314 incorporates the same CAR construct as CART19/20 which was evaluated in a Phase 1 trial at UCLA, and I am pleased that the IMPT-314 data are consistent with our experience at UCLA."

About IMPT-314

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 response as compared to the approved CD19-targeted CAR therapies for the treatment of

large B-cell lymphoma.

IMPT-314 is designed with an ‘OR’ logic gate to target B cells that express either CD19, CD20 or both. IMPT-314 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.

IMPT-314 has received Fast Track Designation from the U.S. Food and Drug Administration for the treatment of relapsed/refractory aggressive B-cell lymphoma.

About Lyell

Lyell is a clinical-stage company advancing a pipeline of next-generation CAR T-cell therapies for patients with cancer. Lyell’s product candidates are designed to generate T cells that resist exhaustion and have qualities of durable stemness in order to drive durable tumor cytotoxicity and achieve consistent and long-lasting clinical response. Lyell is based in South San Francisco, California with facilities in West Hills, California and Seattle and Bothell, Washington. 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 IMPT-314, including its potential to maximize durable responses by overcoming heterogeneous CD19 antigen density and antigen escape, enhancing CAR T cell persistence and reducing exhaustion; the continued clinical progress of the IMPT-314 trials and expectations around the timing of updated clinical data and the timing and design of a pivotal trial of IMPT-314; the potential of IMPT-314 to provide differentiated benefit in objective and complete response rates over first-generation CD19 CAR therapies; the ability of Lyell’s technology to generate T cells that resist exhaustion and have qualities of durable stemness in order to drive durable tumor cytotoxicity and achieve consistent and long-lasting clinical response; 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 Lyell’s recent acquisition of ImmPACT Bio and successful integration of ImmPACT Bio’s business with Lyell’s, including manufacturing IMPT-314 in Lyell’s LyFE manufacturing facility; the effects of macroeconomic conditions, including any geopolitical instability and actual or perceived changes in interest rates and economic inflation; 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, 2023, filed with the Securities and Exchange Commission (SEC) on February 28, 2024, and the Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed with the SEC on November 7, 2024. 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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