Lyell Immunopharma Announces FDA Clearance of its IND for LYL845, a TIL Product Candidate Enhanced with its Novel Epigenetic Reprogramming Technology for Solid Tumors

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- Autologous TIL therapy enhanced with Lyell's Epi-R™ reprogramming technology designed to create polyclonal T cell populations with properties of durable stemness and improved function
- Phase 1 trial to initially enroll patients with relapsed and/or refractory metastatic or locally advanced melanoma and subsequently expand into non-small cell lung cancer and colorectal cancer
- Initial data presentation expected in 2024

SOUTH SAN FRANCISCO, Calif., Oct. 06, 2022 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage T-cell reprogramming company dedicated to developing curative cell therapies for patients with solid tumors, announced today that the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND) application to initiate a Phase 1 clinical trial for LYL845. LYL845 is an investigational tumor infiltrating lymphocyte (TIL) therapy enhanced with Lyell's Epi-R™ technology for patients with relapsed and/or refractory metastatic or locally advanced melanoma and other select solid tumors. In preclinical studies, Epi-R creates polyclonal populations of T cells that demonstrate properties of durable stemness and anti-tumor functionality. Durable stemness is the quality that enables T cells to self-renew, proliferate, persist and generate differentiated effector cell progeny.

LYL845 is Lyell's first TIL product candidate and second wholly owned product candidate to receive IND clearance within the past year. Patient screening for the Phase 1 trial is set to begin over the coming months, and initial clinical data is expected in 2024.

"Advancing LYL845 into the clinic represents steady progression of our mission to develop T-cell therapies that can outlast and eradicate solid tumors," said Liz Homans, chief executive officer of Lyell. "Our goal is to develop LYL845 as an effective TIL therapy for patients with solid tumor cancers such as melanoma, as well as for indications where TIL therapy has not yet been widely effective such as non-small cell lung and colorectal cancer."

"We have developed our epigenetic reprogramming technology to produce T-cell populations with more favorable attributes than those generated by standard manufacturing approaches," stated Rick Klausner, MD, chair of Lyell's Board of Directors. "LYL845 T cells are highly polyclonal and exhibit qualities of durable stemness that have been linked with the anti-tumor functionality and improved outcomes in previous TIL clinical trials, and we look forward to clinically evaluating LYL845 and the role of these qualities in cell therapy for solid tumors."

"While TILs have previously shown clinical benefit in patients with melanoma and limited other solid tumors, we believe that TIL with properties of durable stemness and increased polyclonality are needed for adoptive cell therapies to have curative potential," said Tina Albertson, MD, PhD, chief medical officer and head of development of Lyell.

Phase 1 Trial Design

The Phase 1 clinical trial is an open-label, dose-escalation trial for patients with relapsed and/or refractory metastatic or locally advanced melanoma with expansion cohorts for patients with melanoma, non-small cell lung cancer (NSCLC), and colorectal cancer (CRC). The primary objective of the trial is to determine safety, tolerability and a recommended phase 2 dose range of LYL845. The secondary objective is to determine antitumor activity as evaluated by response rates, duration of response, progression free survival and overall survival. Exploratory biomarkers of T-cell stemness will also be assessed.

About Melanoma, NSCLC and CRC

Melanoma accounts for only ~1% of all skin cancers but is responsible for ~80% of skin cancer-related deaths. Only ~14% of patients with metastatic melanoma survive for five years.

Lung cancer is the second most common cancer and is the leading cause of cancer mortality worldwide. NSCLC accounts for 84% of all lung cancers. For localized NSCLC, the overall 5-year survival rate is ~60%. For regional NSCLC, the 5-year survival rate is ~35%. Based on current data, when NSCLC metastasizes, the 5-year survival rate is 6%.

Colorectal cancer is the second most common cause of cancer deaths in the United States. For localized CRC, the overall 5-year survival rate is ~90% but for metastatic disease, the 5-year survival rate is 14%. Approximately 25% of patients have metastatic disease at diagnosis, and ~50% of patients with colorectal cancer will eventually develop metastases.

About LYL845

LYL845 is an autologous tumor infiltrating lymphocyte (TIL) product candidate enhanced with Epi-R reprogramming technology for patients with relapsed and/or refractory metastatic or locally advanced melanoma and select solid tumors. In preclinical studies, Epi-R creates polyclonal populations of T cells that demonstrate properties of durable stemness and anti-tumor functionality. Durable stemness is the quality that enables T cells to self-renew, proliferate, persist and generate differentiated effector cell progeny.

TIL products are created by expanding T cells taken from the patient's own tumor. Previous clinical experiences suggest that the efficacy of adoptive transfer of ex vivo expanded TILs is largely driven by specific recognition of mutated tumor neoantigens specific to each patient. To date, broad efficacy of TIL therapies has been limited by variable and often poor product quality, lack of stemness or potential durability of expanded TILs, failure to maintain polyclonality of TILs during production, and failure to enrich the TIL product with tumor-reactive T cells.

TIL products manufactured using Lyell's Epi-R reprogramming technology aim to overcome these challenges. Preclinical studies supporting the development of LYL845 suggest Epi-R technology improves TIL products by maintaining properties of durable stemness, which leads to superior ex vivo cell expansion and product qualities, maintenance of tumor reactive clones, and enhanced polyclonality.

About Lyell Immunopharma, Inc.

Lyell is a clinical-stage T-cell reprogramming company dedicated to developing curative cell therapies for patients with solid tumors. The Company is advancing a pipeline of therapies designed to address what it believes are the primary barriers that limit consistent, reliable and curative responses to adoptive T-cell therapy: T-cell exhaustion and lack of durable stemness, which includes the ability to proliferate, persist and self-renew, as well as generate differentiated effector cell progenies to provide durable anti-tumor functionality. Lyell is applying its proprietary *ex vivo* genetic and epigenetic reprogramming technologies to address these barriers in order to develop new medicines with improved, durable and potentially curative clinical outcomes. Lyell is based in South San Francisco, California with facilities in 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: Lyell's expectation to begin screening patients for the Phase 1 clinical trial of LYL845 and the timing thereof and to present initial data and the timing thereof; LYL845 and ability to develop T-cell therapies that can outlast and eradicate solid tumors; LYL797 and LYL845 and their ability to overcome T-cell exhaustion and promote durable stemness; Lyell's plans to screen patients with relapsed/refractory metastatic or locally advanced melanoma with expansion cohorts for patients with melanoma, non-small cell lung cancer (NSCLC), and colorectal cancer (CRC); potential increased polyclonality of Lyell product candidates; Lyell's plans to recommended Phase 2 dose range of LYL845 based on outcomes of the Phase 1 clinical trial; Lyell's vision of curing patients with solid tumors; the therapeutic potential of Lyell's product candidates; 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 effects of the COVID-19 pandemic; geopolitical instability; Lyell's ability to submit planned INDs or initiate and execute clinical trials on the anticipated timelines, if at all; Lyell's ability to manufacture and supply its product candidates for its clinical trials; the preclinical profiles of Lyell's product candidates not translating in clinical trials; the potential for results from clinical trials to differ from preclinical, 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; Lyell's reliance on GSK to advance the development of its NY-ESO-1 programs; 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 most recently filed periodic reports on Form 10-K and Form 10-Q and in Lyell's future reports to be filed with the Securities and Exchange Commission. 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.

Contact:
Ellen Rose
Senior Vice President, Communications and Investor Relations
erose@lyell.com