Lyell Immunopharma Announces FDA Clearance of IND for LYL132, a T-Cell Receptor Therapy for Solid Tumors Being Developed in Collaboration with GSK

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LYL132 is an NY-ESO-1-targeted TCR therapy that incorporates Epi-R™, Lyell's novel epigenetic reprogramming technology designed to create populations of T cells with properties of durable stemness

SOUTH SAN FRANCISCO, Calif., Jan. 24, 2022 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc., (Nasdaq: LYEL), a T-cell reprogramming company dedicated to the mastery of T cells to cure patients with solid tumors, announced today that the U.S. Food and Drug Administration (FDA) has cleared an Investigational New Drug (IND) application to initiate a Phase 1 clinical trial for LYL132, an investigational T-cell receptor (TCR) therapy for patients with solid tumors expressing New York esophageal squamous cell carcinoma 1 (NY-ESO-1) that the company is developing in collaboration with GSK. LYL132 incorporates Epi-R, Lyell's epigenetic reprogramming technology and is under investigation as a potential next-generation enhancement to letetresgene autoleucel (lete-cel), a GSK TCR therapy targeting NY-ESO-1 currently in pivotal clinical development. The cell surface antigen NY-ESO-1 is a clinically validated target present on many aggressive solid tumors. Lyell's Epi-R technology is designed to address a major barrier to successful Adoptive Cell Therapy (ACT) by creating populations of T cells with properties of durable stemness. T cells with properties of durable stemness are able to proliferate, persist, and self-renew with anti-tumor functionality.

"Clearance of the second IND incorporating Lyell's novel reprogramming technologies is another important milestone for Lyell, especially coming within a month of FDA clearance of an IND for LYL797, our lead CAR program," said Liz Homans, Chief Executive Officer of Lyell. "We are eager to start multiple clinical trials that utilize our technologies to assess the potential benefits for patients with solid tumor cancers and also remain on track for two additional INDs by the end of this year."

"Clinically assessing, in a validated target, the potential benefit of reprogrammed T cells designed to have properties of durable stemness is a profoundly important and exciting milestone for Lyell and cancer drug development," stated Rick Klausner, MD, Chair of Lyell's Board of Directors. "We believe lack of durable stemness is a major barrier to successful ACT in solid tumors and expect our Epi-R technology platform will offer a path forward to better outcomes for patients."

The planned Phase 1 trial will assess LYL132 in patients with NY-ESO-1+ advanced synovial sarcoma (SS) or myxoid/round cell liposarcoma (MRCLS). Lyell will manufacture LYL132 in its LyFE™ Manufacturing Center and GSK will conduct the Phase 1 trial.

About NY-ESO-1, Synovial Sarcoma (SS) and Myxoid/Round Cell Liposarcoma (MRCLS)

NY-ESO-1 is a member of the cancer testis-antigen (CTA) family of tumor-associated antigens and has been previously validated as a therapeutic target in clinical trials. NY-ESO-1 has low or no expression in healthy adult tissues but is detectable in multiple solid tumor cancer types including non-small cell lung cancer, bladder cancer, melanoma, liver cancer, SS and MRCLS. SS is a rare yet highly malignant tumor occurring in soft tissue and accounts for approximately 5-10% of all soft tissue sarcomas, with approximately 650 to 1,300 cases per year. It is more common in adolescents and young adults than in older individuals. Patients often develop metastases, particularly to the lungs, resulting in 10-year survival rates of <50%. MRCLS is a type of liposarcoma, a rare soft connective tissue tumor that grows in cells that store fat in the body, typically in the arms and legs. MRCLS is one of the most common types of liposarcoma and makes up approximately 30% of all cases, with 2,000 diagnosed occurrences in the United States each year. When this type of cancer metastasizes, the 5-year survival rate is approximately 40%.

About LYL132 and the GSK Collaboration

LYL132 is a novel, NY-ESO-1-targeted TCR product that incorporates Epi-R, Lyell's proprietary epigenetic reprogramming technology designed to create populations of T cells which have the properties of durable stemness – the quality that enables T cells to proliferate, persist, and self-renew with anti-tumor functionality.

Preclinical in vitro and in vivo experiments of LYL132 have demonstrated that LYL132 has T cells with qualities consistent with T

cell stemness, including enhanced metabolic fitness and proliferation. We believe these qualities could be associated with improved clinical responses that could further improve first generation approaches.

In 2019 Lyell and GSK entered into a collaboration agreement to research and develop potential T-cell therapies that apply Lyell's platform technologies and cell therapy innovations to TCRs or chimeric antigen receptor (CAR) therapies under distinct programs for a specified number of targets. Lyell received $250 million in the form of a combined upfront payment and equity investment and is eligible for technology validation payments totaling approximately $200 million and up to approximately $400 million in additional aggregate development and sales milestones for LYL132. In addition to LYL132, a separate GSK-sponsored program evaluating an NY-ESO-1-targeted TCR that incorporates Lyell's Gen-R genetic reprogramming technology is planned. These programs could represent a single future product opportunity for GSK utilizing one or both of Lyell's platform technologies.

About Lyell Immunopharma, Inc.

Lyell is a T-cell reprogramming company dedicated to the mastery of T cells to cure patients with solid tumors. The Company focuses on addressing 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 proliferative capacity and the ability to self-renew, differentiate and eliminate solid tumors. Lyell is applying its proprietary *ex vivo* genetic and epigenetic reprogramming technology platforms, Gen-R and Epi-R, 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 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: initiation of the LYL132 Phase 1 clinical trial; the Epi-R technology designed to address a major barrier to successful Adoptive Cell Therapy (ACT) by creating populations of T cells with properties of durable stemness; initiation of clinical trials and the timing thereof; Lyell's plans to submit two additional INDs for our TIL and partnered TCR program and the timing thereof; durable stemness as a major barrier to successful ACT in solid tumors; the potential for the Epi-R technology platform to offer a path forward to better outcomes for patients; 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 evolving COVID-19 pandemic; Lyell's ability to submit planned INDs on the anticipated timing or at all; initiation of planned clinical trials and enrollment of patients in its future clinical trials; Lyell's ability to manufacture and supply its product candidates for its future 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; 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 and Lyell's future reports to be filed with the SEC. 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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