Lyell Immunopharma Presents New Data at SITC Highlighting its Growing Pipeline of T – Cell Reprogramming Technologies and Product Candidates Targeting Solid Tumors

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- Preclinical data demonstrate genetic and epigenetic reprogramming can ameliorate T cell exhaustion and enhance stem-like qualities and potency of T cells in various modalities

SOUTH SAN FRANCISCO, Calif., Nov. 07, 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, is presenting preclinical data at the 37th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) on its product candidates and new genetic and epigenetic reprogramming technologies. This includes new preclinical research on the potential to generate more potent T cells to provide durable anti-tumor functions against certain aggressive solid tumor cancers.

"Our SITC presentations showcase compelling preclinical data underlying our lead TIL product candidate, LYL845, as well as the exciting progress Lyell's research team is making to advance our understanding of how to counter T-cell exhaustion and generate T cells with properties of durable stemness," said Gary Lee, Ph.D., chief scientific officer at Lyell. "We are applying this research to grow our pipeline by creating new stackable reprogramming technologies as we continue to work toward our mission of developing adoptive T-cell therapies that deliver consistent, reliable and durable responses in solid tumors."

Preclinical Data on LYL845

Two presentations on Friday, Nov. 11 highlight preclinical data on LYL845, Lyell's tumor-infiltrating lymphocyte (TIL) product candidate being evaluated for safety, tolerability and anti-tumor activity in a first-in-human Phase 1 clinical trial (NCT05573035). (Abstract Nos. 370 and 340).

The first presentation, titled "The Epi-R™ technology produces a polyclonal TIL product (LYL845) with a greater expansion success rate across hot and cold tumors, improved product phenotype, and maintenance of TCR diversity," showcases the ability of Epi-R technology to successfully expand TIL across three tumor types as compared to the standard (control) process. In this study, expanding TIL with Epi-R technology resulted in 100 percent success rate vs. 70 percent with control, including tumor samples collected from checkpoint inhibitor experienced melanoma patients. The study also includes colorectal tumor samples which have been considered more challenging to expand with standard processes. Further, in this study Epi-R technology yielded a product (LYL845) with a greater proportion of CD8+ T-cells and enriched for T-cells with stem-like profiles, better metabolic fitness, and preserved polyclonality compared to control TIL. These qualities have been linked with anti-tumor functionality and improved outcomes in previous TIL clinical trials.

The second presentation, titled "The Epi-R technology produces a polyclonal TIL product (LYL845) with diverse tumor-reactive clones that have stem-like qualities and anti-tumor function," highlights bioinformatic analyses demonstrating that LYL845 products expanded using Epi-R technology were highly polyclonal and retained putative tumor reactive clones with increased stemness and reduced exhaustion-associated genes compared to TIL products derived from the standard process. Moreover, tumor-specific reactivities of LYL845 were confirmed, and anti-tumor functions, including dose-dependent cytolytic activities and cytokine secretion, in tumor cell specific co-culture assays were demonstrated.

Stackable Genetic and Epigenetic Reprogramming Technologies in LYL119, a Second-Generation CAR T-cell therapy targeting ROR1+ solid tumors

Two presentations describe preclinical data on Lyell's new, stackable reprogramming technologies – NR4A3 knockout and Stim-R™ – being incorporated in LYL119, a second-generation ROR1 targeting CAR T-cell product candidate.

An abstract titled "NR4A3 gene editing and c-Jun overexpression synergize to limit exhaustion and enhance functional activity of ROR1 CAR T cells *in vitro* and *in vivo*" being presented on Thursday, Nov. 10 demonstrates that the combination of two genetic reprogramming technologies, NR4A3 gene knockout and c-Jun overexpression, enhances the functional activity of ROR1 CAR T cells. This is demonstrated by higher levels of cytokine production, increased CAR T-cell persistence and reduced surface

expression of inhibitory receptors after repetitive antigen stimulation, as well as significant improvement in tumor control *in vivo* (Abstract No. 243). NR4A3 and c-Jun both function within the activator protein 1 (AP-1) transcription factor pathway, which plays a key role in regulating T-cell function. This new research furthers the hypothesis that reprogramming of AP-1 transcription factor pathway in T cells may delay exhaustion and improve anti-tumor function. Lyell plans to incorporate these two stackable genetic reprogramming technologies in its new product candidate, LYL119, currently in preclinical development.

An abstract titled "Engineering potent CAR T-cell therapies by controlling T-cell activation signaling parameters using the Stim-R™ technology, a programmable synthetic cell-signaling platform" being presented on Friday, Nov. 11 describes Stim-R, Lyell's new epigenetic reprogramming technology. Stim-R is a synthetic cell mimic that mediates precise signal molecule presentation to generate arrays of diverse ROR1-targeted CAR T-cell products (Abstract No. 252). This research demonstrates that Stim-R generates potent CAR T-cell products with increased polyfunctionality, persistence, anti-tumor activity, and reduced exhaustion following repeated antigen stimulation *in vitro*. These cells also showed greater CAR T-cell proliferation and persistence *in vivo*, as well as improved tumor control. Lyell also plans to incorporate this technology in LYL119.

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 anticipated progress, business plans, business strategy, planned research and clinical trials and plans to present at SITC; the growing pipeline of T-cell reprogramming technologies and product candidates and the potential clinical benefits and therapeutic potential of such product candidates; Lyell's plans to apply its research to grow its pipeline and its mission to develop adoptive T-cell therapies that deliver consistent, reliable and durable responses in solid tumors; the potential of Lyell's reprogramming technologies to overcome primary barriers to successful adoptive cell therapy in solid tumors, including the ability for Lyell's genetic reprogramming technologies to limit T cell exhaustion and improve anti-tumor function and for its new epigenetic reprogramming technology, Stim-R, to generate a more potent T-cell product, and Lyell's plans for such reprogramming technologies; 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; macroeconomic conditions; Lyell's ability to submit planned INDs or initiate or progress clinical trials on the anticipated timelines, if at all; Lyell's lack of experience as a company in enrolling, conducting or completing clinical trials; 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; 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 quarterly report on Form 10-Q and subsequent filings 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.

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