



Lyell Immunopharma Presentations at SITC Highlight New Nonclinical Data on Product Candidates and Innovative Technology to Shorten TIL Manufacturing

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- *Six presentations highlight innovations designed to shorten TIL manufacturing, new nonclinical data on LYL119, new technologies and clinical trials in progress*

SOUTH SAN FRANCISCO, Calif., Oct. 31, 2023 (GLOBE NEWSWIRE) -- Lyell Immunopharma, Inc. (Nasdaq: LYEL), a clinical-stage T-cell reprogramming company advancing a diverse pipeline of cell therapies for patients with solid tumors, is presenting new nonclinical data at the 38th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) on innovations designed to shorten tumor infiltrating lymphocyte (TIL) manufacturing, LYL119, its second generation ROR1-targeted CAR T cell product candidate, as well as data on new technologies and the design of its two clinical trials in progress.

"We remain confident that generating T cells with the ability to resist exhaustion and qualities of durable stemness will unlock the potential of effective cell therapy for solid tumors, and our SITC presentations highlight the progress we are making across our robust pipeline of product candidates and platform technologies designed to achieve this," said Gary Lee, Ph.D., chief scientific officer at Lyell. "We also highlight new data on our Epi-R P2 manufacturing process, a manufacturing innovation designed to enable faster delivery of TIL product to patients without sacrificing the desired yield, stemness phenotype and retention of tumor reactive clones."

Details on the presentations are below.

New Nonclinical Data on LYL119, Innovation in Manufacturing and New Technologies

Four presentations highlight new nonclinical data from Lyell's product pipeline and research programs, including:

- Lyell's novel Epi-R™ P2 manufacturing protocol to shorten delivery time of TIL product to patients
- New nonclinical data on LYL119, Lyell's second-generation ROR1-targeted CAR T-cell therapy
- A new technology being advanced through a collaboration between Lyell and Outpace to enable tumor-restricted IL-12 activity to enhance solid tumor T cell therapies
- Lyell's rejuvenation technology which has shown the potential to "turn back" the epigenetic clock to generate more stem-like T cells with reduced epigenetic age and enhanced proliferation ability

A presentation titled "*Epi-R P2 protocol produces a scalable polyclonal TIL product with a greater expansion success rate across hot and cold tumors in shorter culture time*" highlights Lyell's Epi-R P2 manufacturing protocol that shortens manufacturing time for TIL while maintaining the desired yield, stemness phenotype and retention of tumor reactive clones. Current TIL production time is approximately four to six weeks. Literature suggests that a shorter culture time is associated with improved cell quality, functionality and positive clinical outcomes in metastatic melanoma patients. Lyell's Epi-R manufacturing protocols are designed to generate populations of TIL with stem-like properties to potentially improve antitumor activity. Epi-R P2 is an improved TIL manufacturing process that reduces the TIL culture duration to less than three weeks without impacting the quality of TIL.

- Presentation details: Abstract # 379, Friday, Nov. 3, 12–1:30 p.m. and 5:10–6:40 p.m.

New nonclinical data on LYL119, Lyell's second-generation ROR1-targeted CAR T-cell therapy, is highlighted in a presentation titled "*Preclinical development of LYL119, a ROR1-targeted CAR T-cell product incorporating four novel T-cell reprogramming technologies to overcome barriers to effective cell therapy for solid tumors*." LYL119 incorporates four of Lyell's complementary, stackable T-cell reprogramming technologies to create potent ROR1-targeted CAR T cells with durable function. In this study, LYL119 demonstrated superior cytotoxicity and sustained cytokine production upon repeated antigen stimulation compared to various controls lacking one or more of the reprogramming technologies and showed robust in vivo antitumor efficacy in a mouse xenograft tumor model at very low cell doses.

- Presentation details: Abstract #278, Saturday, Nov. 4, 2023, 11:55–1:25 p.m. and 7–8:30 p.m.

A presentation titled "*Protein design and inducible expression allow context-dependent, localized IL-12 activity to enhance solid*

tumor T cell therapies' highlights an innovative tumor-restricted IL-12 (trIL-12) technology that delivers potent IL-12 stimulation at the tumor site while avoiding systemic exposure. IL-12 is an immune-stimulatory cytokine that can induce potent anti-tumor activity, but systemic delivery of IL-12 has been shown to cause severe toxicity in patients. trIL-12 was designed leveraging Outpace's OutSmart™ technology to rapidly auto-inactivate IL-12 after inducible secretion from engineered T cells with the aim of achieving safe, local delivery of IL-12 activity. trIL-12 is being advanced under a collaboration between Lyell and Outpace with the goal of improving efficacy for T-cell therapies while maintaining a favorable safety profile.

- Presentation details: Abstract #1047, Friday, Nov. 3, 12–1:30 p.m. and 5:10–6:40 p.m.

A presentation titled "*Rejuvenation of tumor-infiltrating lymphocytes (TIL) through Partial Reprogramming*" describes Lyell's rejuvenation technology which has shown the potential to "turn back" the epigenetic clock to generate more stem-like T cells with reduced epigenetic age and enhanced proliferation ability. Previously published studies have demonstrated the decline in T-cell function as a person ages. These new nonclinical data show TIL rejuvenated with Lyell's technology retain a broad TCR repertoire and demonstrate improved T-cell function and antitumor properties.

- Presentation details: Abstract #393, Friday, Nov. 3, 2023, 12–1:30 p.m. and 5:10–6:40 p.m.

Clinical Trials in Progress

Two additional presentations highlight the design of Lyell's two ongoing Phase 1 clinical trials in progress.

A presentation titled "*Phase 1 trial of LYL797, a ROR1-targeted CAR T-cell therapy enhanced with genetic and epigenetic reprogramming, in advanced triple-negative breast cancer (TNBC) and non-small cell lung cancer (NSCLC)*" describes the design of this dose-escalation, dose-expansion Phase 1 trial in patients with ROR1-positive relapsed refractory TNBC and NSCLC.

- Presentation details: Abstract #754, Saturday, Nov. 4, 2023, 11:55–1:25 p.m. and 7–8:30 p.m.

A presentation titled "*Phase 1 trial of LYL845, an autologous tumor-infiltrating lymphocyte (TIL) therapy enhanced with epigenetic reprogramming, for the treatment of advanced solid tumors*" describes the design of this dose-escalation, dose-expansion Phase 1 trial in advanced solid tumors, including advanced melanoma, NSCLC and colorectal cancer

- Presentation details: Abstract #747, Friday, Nov. 3, 2023, 12–1:30 p.m. and 5:10–6:40 p.m.

About Lyell Immunopharma, Inc.

Lyell is a clinical-stage T-cell reprogramming company advancing a diverse pipeline of cell therapies for patients with solid tumors. Lyell is currently enrolling a Phase 1 clinical trial evaluating a ROR1-targeted CAR T-cell therapy in patients with relapsed refractory triple-negative breast cancer (TNBC) and non-small cell lung cancer (NSCLC) and a second Phase 1 clinical trial evaluating reprogrammed tumor infiltrating lymphocytes (TIL) in patients with advanced melanoma, NSCLC and colorectal cancer. The technologies powering its product candidates are designed to address barriers that limit consistent and long-lasting responses to cell therapy for solid tumors: T-cell exhaustion and lack of durable stemness, which includes the ability to persist and self-renew to drive durable tumor cytotoxicity. 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 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 and planned clinical trials; the growing pipeline and potential clinical benefits and therapeutic potential of Lyell's product candidates; the features of and potential for the Epi-R P2 manufacturing process to shorten manufacturing time for TIL while maintaining the desired yield, stemness phenotype and retention of tumor reactive clones; Lyell's collaboration with Outpace Bio and the potential to enable context-dependent, localized IL-12 activity to enhance solid tumor T cell therapies and improve efficacy for T-cell therapies while maintaining a favorable safety profile; the potential for Lyell's stackable T-cell reprogramming technologies to create potent ROR1-targeted CAR T cells with durable function; the potential for Lyell's rejuvenation technology to "turn back" the epigenetic clock to generate more stem-like T cells with reduced epigenetic age and enhanced proliferation availability of; 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: macroeconomic conditions and the lingering 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 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 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; 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, 2022, filed with the Securities and Exchange Commission (SEC) on February 28, 2023, and the Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, filed with the SEC on August 8, 2023. 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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