UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 15, 2021

Lyell Immunopharma, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40502**	**83-3006753**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

201 Haskins Way
South San Francisco, California **94080**
(Address of Principal Executive Offices) **(Zip Code)**

Registrant's Telephone Number, Including Area Code: 650 695-0677

(Former Name or Former Address, if Changed Since Last Report)
Not Applicable

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**LYEL**	**NASDAQ Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.01 Entry into a Material Definitive Agreement.

On December 16, 2021, Lyell Immunopharma, Inc. ("Lyell" or the "Company") entered into a Second Amendment to Collaboration and License Agreement (the "Collaboration Amendment") with GlaxoSmithKline Intellectual Property (No.5) Limited and Glaxo Group Limited (together "GSK"). The Collaboration Amendment amends the terms of that certain Collaboration and License Agreement by and between the Company and GSK, dated as of May 23, 2019 (as amended, the "GSK Agreement"). Pursuant to the Collaboration Amendment, among other things, Lyell will manufacture the NY-ESO-1 + Epi-R TCR cell therapy product candidate for an initial planned Phase 1 clinical trial ("Epi-R Trial") at Lyell's manufacturing facility in Bothell, Washington. GSK will conduct the Epi-R Trial under its First Time in Humans Master Protocol for NY-ESO-1 ("FTIH Protocol") pursuant to a clinical plan agreed to by Lyell and GSK. Lyell is responsible for submitting the initial new drug application ("IND") for this product candidate with the U.S. Food and Drug Administration ("FDA"), and GSK is responsible for filing its updated FTIH Protocol and for regulatory interactions with FDA related to that protocol. Each party bears its own costs associated with its responsibilities under the GSK Agreement. The Collaboration Amendment further specifies that Lyell is eligible (i) to receive milestone payments for any use of an Anti-Exhaustion Component in connection with a collaboration target, whether or not there was a specific research program and (ii) for one set of milestone and royalty payments with respect to a collaboration target, even if the approved product uses more than one Anti-Exhaustion Component. The Collaboration Amendment also modifies the scope of license grants in the GSK Agreement to conform to the modified responsibilities under the Collaboration Amendment and specifies that Lyell owns improvements to the Epi-R and Gen-R technologies. Glaxo Group Limited remains a significant stockholder of the Company.

The foregoing description of the Collaboration Amendment does not purport to be complete and is subject to, and qualified in its entirety by, the full text of the Collaboration Amendment, a redacted copy of which will be filed as an exhibit to the Company's Annual Report on Form 10-K for the fiscal year ending December 31, 2021.

Item 8.01 Other Events.

On December 15, 2021, Lyell issued a press release announcing cGMP qualification of its LyFE manufacturing facility located in Bothell, Washington. A copy of this press release is attached to this Current Report on Form 8-K as Exhibit 99.1 and is incorporated herein by reference.

On December 16, 2021, Lyell issued a press release announcing clearance by the U.S. Food and Drug Administration of its Investigational New Drug application for LYL797, which is a novel, ROR1-targeted CAR T-cell product that incorporates genetic and epigenetic reprogramming technologies, Gen-R and Epi-R, to potentially overcome barriers of CAR T-cell therapies in solid tumors. The Phase 1 clinical trial is designed to evaluate the safety and anti-tumor activity of LYL797 in patients with ROR1+ triple negative breast cancer or non-small cell lung cancer. A copy of this press release is attached to this Current Report on Form 8-K as Exhibit 99.2 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release dated December 15, 2021
99.2	Press release dated December 16, 2021
104	Cover page interactive data file (embedded within the Inline XBRL document)

Forward Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements expressed or implied in this Current Report on Form 8-K include, but are not limited to, statements regarding: anticipated activities by Lyell and GSK under the

Collaboration Amendment; the potential receipt of milestone and royalty payments by the Company under the Collaboration Amendment; the planned submission of an IND to the FDA and other regulatory activity contemplated by the Collaboration Amendment; anticipated manufacturing and clinical trial activity under the Collaboration Amendment, including with respect to the planned Epi-R Trial; 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; the initiation of the planned Epi-R Trial and enrollment of patients in that trial; Lyell's ability to manufacture and supply product candidate for planned Epi-R Trial; 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 maintain the GSK Agreement with GSK, including the risks that GSK may fail to meet its obligations under the GSK Agreement or may fail to apply sufficient efforts at developing and commercializing products under the GSK Agreement; 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 in Lyell's future reports to be filed with the SEC. Forward-looking statements contained in this Current Report on Form 8-K are made as of this date, and Lyell undertakes no duty to update such information except as required under applicable law.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Lyell Immunopharma, Inc.

Date: December 17, 2021

By: /s/ Heather Turner
Heather Turner
Chief General Counsel

Lyell Immunopharma Announces cGMP Qualification of LyFE™ Manufacturing Center in Advance of Initiating Clinical Programs

- Lyell's cGMP-compliant manufacturing facility, is designed to produce cell products at scale for upcoming clinical trials across its CAR, TIL and TCR programs
- LyFE Manufacturing Center integrates digital data analytics into processes for real-time production monitoring and optimization

SOUTH SAN FRANCISCO, Calif., Dec. 15, 2021 — Lyell Immunopharma, Inc. (Lyell), (Nasdaq: LYEL), a T-cell reprogramming company dedicated to the mastery of T cells to cure patients with solid tumors, announced today that its LyFE Manufacturing Center in Bothell, Washington has been commissioned and qualified in compliance with the U.S. Food and Drug Administration's (FDA's) Current Good Manufacturing Practices (cGMP).

The cGMP qualification confirms Lyell has the proper design, monitoring and control of its manufacturing facility. Since becoming operational in April 2021, the LyFE Center has completed successful engineering runs at scale in support of the Company's planned upcoming clinical trials.

"We are advantageously positioned with qualified manufacturing infrastructure that we own and control to support consistent and reliable manufacture of cell products for our upcoming clinical trials," said Liz Homans, Chief Executive Officer of Lyell. "We believe that combining cGMP manufacturing with our deep understanding of T-cell biology will help us achieve our vision of curing patients with solid tumors."

With 70,000 square feet of space, the LyFE Manufacturing Center provides several key capabilities for cell therapy manufacturing. The facility utilizes electronic systems with advanced data and analytics for real-time feedback, batch monitoring and process optimization. To support its digital manufacturing capabilities, Lyell collaborates with Amazon Web Services (AWS). The LyFE Manufacturing Center is one of the first cell therapy manufacturing facilities to benefit from AWS's extensive experience with cloud computing, Internet of Things (IoT) and advanced analytics.

"Lyell is dedicated to developing safe and effective cell therapies for patients by investing in innovative operations and technology, including our LyFE Manufacturing Center that is designed to support a broad pipeline and is now qualified to support cGMP manufacturing standards," said Stephen Hill, Chief Operating Officer of Lyell. "Integrating digital systems into our manufacturing operations means quicker access to data, leading to faster recognition and implementation of process improvements."

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, ability to self-renew and ability to 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: Lyell's ability to produce cell products at scale for upcoming clinical trials across the Company's

CAR, TIL and TCR programs; the integration of digital systems into our manufacturing operations and whether such integration will result in quicker access to data and faster recognition and implementation of process improvements; Lyell's ownership and control of manufacturing infrastructure to support consistent and reliable manufacture of cell products for upcoming clinical trials; 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.

Contact:

Ellen Rose
Vice President, Communications and Investor Relations
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Lyell Immunopharma Announces FDA Clearance of its IND for LYL797, a CAR T-Cell Therapy Incorporating Novel Reprogramming Technologies for Solid Tumors

- Expects to begin screening patients for the Phase 1 clinical trial by the end of the first quarter; initial data presentation expected in 2023
- ROR1-targeted CAR T-cell therapy designed to overcome T-cell exhaustion and promote durable stemness incorporates Lyell's novel genetic and epigenetic reprogramming technologies, Gen-R™ and Epi-R™
- LYL797 targets ROR1, a highly expressed cell surface antigen present on many aggressive solid tumors

SOUTH SAN FRANCISCO, Calif., Dec. 16, 2021 — Lyell Immunopharma, Inc. (Lyell), (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 its Investigational New Drug (IND) application to initiate a Phase 1 clinical trial for LYL797, Lyell's first therapeutic candidate incorporating T-cell reprogramming technologies for the treatment of solid tumors. LYL797 is an investigational chimeric antigen receptor (CAR) T-cell therapy for patients with receptor tyrosine kinase-like orphan receptor 1-positive ($ROR1^{+}$) solid tumors. LYL797 incorporates two Lyell technologies designed to address major barriers to successful Adoptive Cell Therapy (ACT): Gen-R, a genetic reprogramming technology that endows T cells with the ability to resist exhaustion, and Epi-R, an epigenetic reprogramming technology that creates populations of T cells with the properties of durable stemness. Durable stemness is the quality that enables T cells to self-renew, proliferate and persist, and create daughter cells with anti-tumor functionality. Lyell expects to begin screening patients with relapsed/refractory triple-negative breast cancer (TNBC) who have failed at least two lines of therapy by the end of the first quarter for the Phase 1 dose escalation phase of the trial and plans to expand the trial to include patients with non-small cell lung cancer (NSCLC) when a recommended dose is determined.

"Lyell is applying our understanding of T-cell biology to address what we believe are the primary barriers to consistently effective cell therapies for difficult to treat solid tumors," said Liz Homans, Chief Executive Officer of Lyell. "Submission and clearance of our first IND is an important milestone for Lyell, and we remain on track to generate data for LYL797 in 2022 and plan to share initial data when we have a meaningful number of patients and an indication of clinical effect, which we expect to occur in 2023. We also remain on track to submit three additional INDs for our TIL and partnered TCR programs by the end of 2022."

"This is the first time the FDA has cleared an IND that includes a specific genetic modification to address T-cell exhaustion, a phenomenon that is recognized as being a major barrier to the eradication of tumors by T cells," stated Rick Klausner, MD, Chair of Lyell's Board of Directors. "We look forward to testing this first-generation technology platform in the clinic, thus specifically addressing the question of exhaustion as a barrier to successful cell therapy in solid tumors."

"While CAR T-cell therapies have proven effective in hematologic malignancies, patients with solid tumors have seen limited benefit from these approaches due to a tumor microenvironment that leads to T-cell exhaustion and a loss of durable stemness," said Tina Albertson, MD, PhD, Chief Medical Officer and Head of Development of Lyell. "LYL797 is the first program to clinically evaluate our two T cell reprogramming technologies which are designed to overcome these barriers, with the goal of developing more effective therapies for patients with solid tumor cancers."

Phase 1 Trial Design

The Phase 1 clinical trial is designed to evaluate the safety and anti-tumor activity of LYL797 in patients with ROR1$^+$ TNBC or NSCLC.

The trial is an open label, dose escalation and expansion trial in patients with relapsed/refractory TNBC or NSCLC who have failed at least two lines of therapy. Once a dose is identified during dose escalation in TNBC, up to 15 patients with TNBC and 15 patients with NSCLC are expected to be enrolled at the recommended dose. The primary endpoint of this Phase 1 trial is safety and tolerability of LYL797. Secondary endpoints include clinical activity based on the evaluation of antitumor activity as evaluated by Response Evaluation Criteria in Solid Tumors (RECIST) criteria and characterization of the pharmacokinetic profile of LYL797. Exploratory biomarkers of T-cell function – exhaustion and stemness – will also be assessed.

About TNBC and NSCLC

Breast cancer is the second most common cancer in American women. Approximately 10-15% of patients with breast cancer have TNBC and triple negative status tends to be more common in women who are younger than age 40, who are African American, or who have a BRCA1 mutation. In the United States, approximately 135,000 women suffered from TNBC in 2017. TNBCs present a high tendency to metastasize, and patients are at a higher risk to relapse compared to other types of breast cancers. TNBCs differ from other types of invasive breast cancer in that they grow and spread faster, have limited treatment options, and a worse prognosis. Once TNBC has spread to other parts of the body, the 5-year survival rate is only 11.5%. ROR1 is overexpressed in approximately 60% of patients with TNBC and ROR1 expression is correlated with poorer outcomes.

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. ROR1 is overexpressed in approximately 40% of the patients with NSCLC. For people with 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%.

About LYL797

LYL797 is a novel, ROR1-targeted CAR T-cell product that incorporates genetic and epigenetic reprogramming technologies, Gen-R and Epi-R, to overcome barriers of CAR T-cell therapies in solid tumors. Gen-R is an *ex vivo* genetic reprogramming technology that engineers CAR T cells to overexpress c-Jun. Dysregulation of activator protein 1 (AP-1) has been implicated in CAR T-cell exhaustion, and studies have demonstrated that overexpression of c-Jun renders CAR T cells less susceptible to exhaustion through the AP-1 pathway, enhancing both anti-tumor efficacy and persistence in preclinical models of hematologic and solid tumors. Epi-R is a proprietary technology that is designed to produce populations of T cells which have the properties of durable stemness – the quality that enables T cells to self-renew, proliferate and persist, and create daughter cells with anti-tumor functionality.

Preclinical *in vitro* and *in vivo* experiments of LYL797 against ROR1$^+$ solid tumors have demonstrated that LYL797 maintains stem-like phenotypes and can resist exhaustion while inhibiting tumor growth in models of tumor cells expressing ROR1.

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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 and the timing thereof and to present initial data and the timing thereof; LYL797 and its ability to overcome T-cell exhaustion and promote durable stemness; Lyell's plans to screen patients with relapsed/refractory triple-negative breast cancer (TNBC) who have failed at least two lines of therapy by the end of the first quarter for the Phase 1 dose escalation phase of the trial and to expand the trial to include patients with non-small cell lung cancer (NSCLC) when a recommended dose is determined; Lyell's plans to submit three additional INDs for our TIL and partnered TCR programs and the timing thereof; 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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