Lyell Immunopharma Reports Business Highlights and Financial Results for the Fourth Quarter and Full Year 2023

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- On track to report initial clinical and translational data from lead CAR T-cell and TIL product candidates in 2024
- Received Orphan Drug Designation for LYL845 for the treatment of melanoma
- Expect to submit IND for second generation ROR1-targeted CAR T-cell product in the first half of 2024
- Presented nonclinical data demonstrating the ability of Lyell's novel genetic and epigenetic reprogramming technologies to generate potent T-cell product candidates with durable cytotoxic function at multiple scientific conferences
- Advanced manufacturing innovations to reduce cost and build scale for both CAR T-cell and TIL product candidates
- Cash, cash equivalents and marketable securities of $562.7 million as of December 31, 2023 supports advancing pipeline into 2027 through multiple clinical milestones

SOUTH SAN FRANCISCO, Calif., Feb. 28, 2024 (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 today reported financial results and business highlights for the fourth quarter and year ended December 31, 2023.

"We are focused on generating clinical data in our two Phase 1 clinical trials and advancing new reprogramming technologies designed to generate T cells with the ability to resist exhaustion and maintain the stem-like qualities needed to drive durable cytotoxic functionality in solid tumors. This year, we plan to share clinical and translational data from our lead CAR T-cell and TIL product candidates that we expect will provide the first of several opportunities to understand the potential of our T-cell preprogramming technologies to deliver meaningful advances in cell therapy for patients with solid tumors," said Lynn Seely, M.D., Lyell's President and CEO. "With our strong cash position that is expected to fund operations into 2027, we can advance our lead programs through multiple clinical milestones while continuing to invest in innovative technology platforms and earlier stage product candidates."

Fourth Quarter Updates and Recent Business Highlights

Lyell is advancing four wholly-owned product candidates. Two product candidates, LYL797 and LYL845 are in Phase 1 clinical development. Two additional product candidates, LYL119 and a second-generation tumor infiltrating lymphocyte (TIL) product candidate, are in preclinical development and our T-cell rejuvenation technology is in research.

LYL797 – A ROR1-targeted Chimeric Antigen Receptor (CAR) T-cell product candidate genetically reprogrammed to overexpress c-Jun and epigenetically reprogrammed using Lyell's proprietary Epi-R™ manufacturing protocol, designed for differentiated potency and durability

- Enrollment in the Phase 1 clinical trial of LYL797 is ongoing. The study includes patients with relapsed or refractory triple-negative breast cancer (TNBC) or non-small cell lung cancer (NSCLC).
- Initial clinical and translational data from at least 20 patients in the Phase 1 trial of LYL797 are expected in the first half of 2024.
- Initiated a CAR T-cell manufacturing proof-of-concept collaboration with Cellares as part of an overall manufacturing strategy to build scale and reduce cost. Under the collaboration, the companies have agreed on a proof-of-concept technology transfer process for the manufacture of Lyell's LYL797 CAR T-cell therapy, using Cellares' Cell Shuttle™.
- Announced initial results from Lyell's ROR1 screening program indicating that expression of ROR1 in TNBC and NSCLC, 53% (N=77) and 33% (N=18), respectively, is consistent with what has been reported in the literature. The screening program is designed to support Lyell's current and future clinical trials.
- Presented a LYL797 Trial in Progress poster at the 38th Annual Meeting of the Society for Immunotherapy of Cancer (SITC).

LYL845 – A novel epigenetically reprogrammed TIL product candidate using Lyell's proprietary Epi-R™ manufacturing protocol, designed for differentiated potency and durability

- Enrollment in the Phase 1 clinical trial for LYL845 is ongoing. The study includes patients with relapsed and/or refractory metastatic or locally advanced melanoma, NSCLC and colorectal cancer.

- Initial clinical and translational data from the Phase 1 trial of LYL845 are expected in the second half of 2024.
- Received FDA Orphan Drug Designation for LYL845 for the treatment of stage IIB-IV melanoma.
- Presented nonclinical data at SITC highlighting the Epi-R P2 manufacturing process, which is designed to shorten TIL manufacturing time to less than three weeks without impacting cell number and phenotype. Epi-R P2 is expected to be incorporated into the Phase 1 trial of LYL845 in 2024.
- Presented a LYL845 Trial in Progress poster at SITC.

LYL119 – A ROR1-targeted CAR T-cell product candidate incorporating Lyell's four stackable and complementary reprogramming technologies for enhanced cytotoxicity

- LYL119 is a ROR1-targeted CAR T-cell product enhanced with Lyell's four novel genetic and epigenetic reprogramming technologies: c-Jun overexpression, NR4A3 knockout, Epi-R manufacturing protocol and Stim-R^{TM} T-cell activation technology.
- An investigational new drug (IND) application for LYL119 is expected to be submitted in the first half of 2024.
- Presented posters highlighting preclinical development of LYL119 at the American Society for Gene and Cell Therapy (ASGCT) and at SITC. In preclinical studies, 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 and prolonged survival in a mouse xenograft tumor model at very low cell doses.

Rejuvenation – Novel partial reprogramming technology designed to maintain T-cell identity while reducing cells' epigenetic age

- Presented nonclinical data at the International Society for Stem Cell Research (ISSCR) 2023 Annual Meeting demonstrating that Lyell's T-cell Rejuvenation technology generates cells with improved expansion capacity and increased expression of biomarkers associated with T-cell stemness, that also exhibit improved antitumor properties compared with non-rejuvenated T-cell controls in sequential cell-killing assays.
- Presented nonclinical data at SITC demonstrating that TIL generated with Lyell's Rejuvenation technology retain a broad TCR repertoire and demonstrate improved T-cell function and antitumor properties.

Corporate Updates

- Appointed Matt Lang, J.D., Chief Business Officer. Mr. Lang, who also serves as Lyell's Chief Legal Officer and Corporate Secretary, is an experienced company builder who has successfully led growth in complex organizations.

Fourth Quarter and Full Year 2023 Financial Results

Lyell reported a net loss of $52.9 million and $234.6 million for the fourth quarter and year ended December 31, 2023, respectively, compared to a net loss of $8.4 million and $183.1 million for the same periods in 2022. Non-GAAP net loss, which excludes non-cash stock-based compensation, non-cash expenses related to the change in the estimated fair value of success payment liabilities and certain non-cash investment gains and charges, was $43.9 million and $177.4 million for the fourth quarter and year ended December 31, 2023, respectively, compared to $0.3 million and $104.2 million for the same periods in 2022.

Revenue

- Revenue was approximately zero and $0.1 million for the fourth quarter and year ended December 31, 2023, respectively, compared to $48.4 million and $84.7 million for the same periods in 2022. No research and development pursuant to our collaboration and license agreement with GlaxoSmithKline (GSK Agreement) was performed in 2023 due to the termination of the GSK Agreement in December 2022, which drove the decrease in revenue.

GAAP and Non-GAAP Operating Expenses

- Research and development (R&D) expenses were $47.0 million and $182.9 million for the fourth quarter and year ended December 31, 2023, respectively, compared to $38.0 million and $159.2 million for the same periods in 2022. The increase in fourth quarter 2023 R&D expenses of $9.0 million was primarily driven by non-cash expenses related to the change in the estimated fair value of success payment liabilities. The increase in annual 2023 R&D expenses of $23.8 million was primarily driven by a $11.2 million increase in personnel-related expenses, including $4.6 million for one-time severance payments and other employee-related costs in connection with the reduction in workforce, and an increase of $8.8 million in research activities, collaborations and outside services costs primarily due to research and laboratory costs associated with clinical trials. Non-GAAP R&D expenses, which exclude non-cash stock-based compensation and non-cash expenses related to the change in the estimated fair value of success payment liabilities for the fourth quarter and year ended December 31, 2023, were $42.9 million and $165.7 million, respectively, compared to $41.0 million and $147.6 million for the same periods in 2022. The increase in fourth quarter 2023 non-GAAP R&D expenses was driven by an increase in

research and laboratory costs primarily associated with clinical trials.

- General and administrative (G&A) expenses were $13.2 million and $67.0 million for the fourth quarter and year ended December 31, 2023, respectively, compared to $26.3 million and $117.3 million for the same periods in 2022. The decrease in both fourth quarter 2023 and annual 2023 G&A expenses were both primarily driven by decreases in non-cash stock-based compensation. Non-GAAP G&A expenses, which exclude non-cash stock-based compensation, for the fourth quarter and year ended December 31, 2023 were $8.5 million and $38.1 million, respectively, compared to $12.3 million and $52.1 million for the same periods in 2022. The decrease in 2023 non-GAAP G&A expenses was driven by a decrease in legal and corporate expenses.

A discussion of non-GAAP financial measures, including reconciliations of the most comparable GAAP measures to non-GAAP financial measures, is presented below under “Non-GAAP Financial Measures.”

Cash, cash equivalents and marketable securities

Cash, cash equivalents and marketable securities as of December 31, 2023 were $562.7 million compared to $710.3 million as of December 31, 2022. Lyell believes that its cash, cash equivalents and marketable securities balances will be sufficient to meet working capital and capital expenditure needs into 2027.

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 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 clinical trials; Lyell’s advancement of its pipeline and its research, development and clinical capabilities; the potential clinical benefits and therapeutic potential of Lyell’s product candidates; the advancement of Lyell’s technology platform; Lyell’s expectation that its financial position and cash runway will support advancement of its pipeline through multiple clinical milestones into 2027; Lyell’s plans to submit an IND for LYL119 and the timing thereof; expectations around enrollment and timing of initial clinical and translational data from Lyell’s Phase 1 trials for LYL797 and LYL845; the potential of Lyell’s technology transfer process with Cellares to build scale and reduce cost of manufacturing; 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 geopolitical instability; macroeconomic conditions, including actual or perceived changes in interest rates and economic inflation; Lyell’s ability to submit planned INDs or initiate or progress 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 nonclinical, 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; anticipated benefits and financial impact of Lyell’s workforce restructuring; 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, 2023, filed with the Securities and Exchange Commission (SEC) on November 7, 2023, and its Annual Report on Form 10-K for the year ended December 31, 2023, being filed with the SEC later today. 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.

Lyell Immunopharma, Inc.
Unaudited Selected Consolidated Financial Data
(in thousands)

Statement of Operations Data:

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
Revenue	$ 13	$ 48,386	$ 130	$ 84,683
Operating expenses:				
Research and development[(1)]	46,995	38,032	182,945	159,188
General and administrative	13,167	26,348	66,983	117,307
Other operating income, net	(641)	(1,210)	(2,790)	(4,754)

Total operating expenses	59,521	63,170	247,138	271,741
Loss from operations	(59,508)	(14,784)	(247,008)	(187,058)
Interest income, net	7,084	3,453	23,453	7,053
Other income (expense), net[1]	(506)	2,934	1,846	1,887
Impairment of other investments	—	—	(12,923)	(5,000)
Total other income (loss), net	6,578	6,387	12,376	3,940
Net loss	$ (52,930)	$ (8,397)	$ (234,632)	$ (183,118)

(1) As of December 31, 2022, the Company's success payment liability was recognized at fair value as Fred Hutch had provided the requisite service obligation to earn the potential success payment consideration under the continued collaboration. The change in the estimated fair value of Fred Hutch success payment liabilities beginning in Q1 2023 was recognized within other income (expense), net in the unaudited Condensed Consolidated Statements of Operations and Comprehensive Loss. The change in the estimated fair value of Fred Hutch success payment liabilities in 2022 was recognized within research and development expenses in the unaudited Condensed Consolidated Statements of Operations and Comprehensive Loss.

Balance Sheet Data:

	As of December 31,	
	2023	2022
Cash, cash equivalents and marketable securities	$ 562,729	$ 710,269
Property and equipment, net	$ 102,654	$ 123,023
Total assets	$ 750,029	$ 937,561
Total stockholders' equity	$ 654,952	$ 833,252

Non-GAAP Financial Measures

To supplement our financial results and guidance presented in accordance with U.S. generally accepted accounting principles (GAAP), we present non-GAAP net loss, non-GAAP R&D expenses and non-GAAP G&A expenses. Non-GAAP net loss and non-GAAP R&D expenses exclude non-cash stock-based compensation expense and non-cash expenses related to the change in the estimated fair value of success payment liabilities from GAAP net loss and GAAP R&D expenses. Non-GAAP net loss further adjusts non-cash investment gains and charges, as applicable. Non-GAAP G&A expenses exclude non-cash stock-based compensation expense from GAAP G&A expenses. We believe that these non-GAAP financial measures, when considered together with our financial information prepared in accordance with GAAP, can enhance investors' and analysts' ability to meaningfully compare our results from period to period, and to identify operating trends in our business. We have excluded stock-based compensation expense, changes in the estimated fair value of success payment liabilities and non-cash investment gains and charges from our non-GAAP financial measures because they are non-cash gains and charges that may vary significantly from period to period as a result of changes not directly or immediately related to the operational performance for the periods presented. We also regularly use these non-GAAP financial measures internally to understand, manage and evaluate our business and to make operating decisions. These non-GAAP financial measures are in addition to, and not a substitute for or superior to, measures of financial performance prepared in accordance with GAAP. In addition, these non-GAAP financial measures have no standardized meaning prescribed by GAAP and are not prepared under any comprehensive set of accounting rules or principles and, therefore, have limits in their usefulness to investors. We encourage investors to carefully consider our results under GAAP, as well as our supplemental non-GAAP financial information, to more fully understand our business.

Lyell Immunopharma, Inc.
Unaudited Reconciliation of GAAP to Non-GAAP Net Loss
(in thousands)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
Net loss - GAAP	$ (52,930)	$ (8,397)	$ (234,632)	$ (183,118)
Adjustments:				
Stock-based compensation expense	8,463	18,363	47,084	81,924
Change in the estimated fair value of success payment liabilities	529	(7,307)	(2,780)	(5,130)
Impairment of other investments	—	—	12,923	5,000
Gain on other investments	—	(2,923)	—	(2,923)
Net loss - Non-GAAP[1]	$ (43,938)	$ (264)	$ (177,405)	$ (104,247)

(1) There was no income tax effect related to the adjustments made to calculate non-GAAP net loss because of the full valuation allowance on our net U.S. deferred tax assets for all periods presented.

Lyell Immunopharma, Inc.
Unaudited Reconciliation of GAAP to Non-GAAP Research and Development Expenses
(in thousands)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
Research and development - GAAP	$ 46,995	$ 38,032	$ 182,945	$ 159,188
Adjustments:				
Stock-based compensation expense	(3,768)	(4,320)	(18,207)	(16,721)
Change in the estimated fair value of success payment liabilities[(1)]	(319)	7,307	930	5,130
Research and development - Non-GAAP	$ 42,908	$ 41,019	$ 165,668	$ 147,597

(1) As of December 31, 2022, the Company's success payment liability was recognized at fair value as Fred Hutch had provided the requisite service obligation to earn the potential success payment consideration under the continued collaboration. The change in the estimated fair value of Fred Hutch success payment liabilities beginning in Q1 2023 was recognized within other income (expense), net in the unaudited Condensed Consolidated Statements of Operations and Comprehensive Loss. The change in the estimated fair value of Fred Hutch success payment liabilities in 2022 was recognized within research and development expenses in the unaudited Condensed Consolidated Statements of Operations and Comprehensive Loss.

Lyell Immunopharma, Inc.
Unaudited Reconciliation of GAAP to Non-GAAP General and Administrative Expenses
(in thousands)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	2022	2023	2022
General and administrative - GAAP	$ 13,167	$ 26,348	$ 66,983	$ 117,307
Adjustments:				
Stock-based compensation expense	(4,695)	(14,043)	(28,877)	(65,203)
General and administrative - Non-GAAP	$ 8,472	$ 12,305	$ 38,106	$ 52,104

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