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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number 001-40502

Lyell Immunopharma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**83-1300510**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
201 Haskins Way **South San Francisco, California**	**94080**
(Address of Principal Executive Offices)	(Zip Code)

(650) 695-0677

Registrant's telephone number, including area code

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	The Nasdaq Global Select Market

Securities registered pursuant to section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports); and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		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. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant on June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $1.1 billion based on the closing price reported for such date on the Nasdaq Global Select Market.

The registrant had outstanding 249,609,247 shares of common stock as of February 24, 2023.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for the 2023 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K to the extent stated herein. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2022.

Lyell Immunopharma, Inc.
2022 Annual Report on Form 10-K
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned nonclinical studies and clinical trials, results of nonclinical studies and clinical trials, research and development costs, planned regulatory submissions, regulatory approval, and the timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "believe," "estimate," "predict," "potential," or "continue," or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the sufficiency of our existing cash to fund our future operating expenses and capital expenditure requirements;
- the accuracy and timing of our estimates regarding expenses, revenue opportunities, capital requirements and needs for additional financing;
- the scope, progress, results and costs of developing LYL797, LYL845, LYL119 or any other product candidates we may develop, and conducting nonclinical studies and clinical trials, including for LYL797, LYL845 and LYL119;
- the timing and costs involved in obtaining and maintaining regulatory approval of LYL797, LYL845, LYL119 or any other product candidates we may develop, and the timing or likelihood of regulatory filings and approvals, including any expectations regarding seeking special designations for our product candidates for various diseases;
- our plans relating to the commercialization of LYL797, LYL845, LYL119 or any other product candidates we may develop, if approved, including the geographic areas of focus and our ability to grow a sales force;
- the size of the market opportunity for LYL797, LYL845, LYL119 or any other product candidates we may develop in each of the diseases we may target;
- our reliance on third parties to conduct nonclinical research activities for LYL797, LYL845, LYL119 or any other product candidates we may develop;
- the characteristics, safety, efficacy and therapeutic effects of LYL797, LYL845, LYL119 or any other product candidates we may develop;
- our estimates of the number of patients in the United States who suffer from the diseases we target and the number of subjects that will enroll in our clinical trials;
- the progress and focus of our current and planned clinical trials of our product candidates, and the reporting of data from those trials, including the timing thereof;
- the ability of our clinical trials to demonstrate the safety and efficacy of LYL797, LYL845, LYL119 or any other product candidates we may develop, and other positive results;
- the success of competing therapies that are, or may become, available;
- developments relating to our competitors and our industry, including any existing or future competing product candidates and therapies;
- our plans relating to the further development and manufacturing of LYL797, LYL845, LYL119 or any other product candidates we may develop, including additional indications that we may pursue;
- existing regulations and regulatory developments in the United States and other jurisdictions;
- our potential and ability to successfully manufacture and supply LYL797, LYL845, LYL119 or any other product candidates we may develop for clinical trials and for commercial use, if approved;
- the rate and degree of market acceptance of LYL797, LYL845, LYL119 or any other product candidates we may develop, as well as the pricing and reimbursement of LYL797, LYL845, LYL119 or any other product candidates we may develop, if approved;

- our continued reliance on third parties to conduct additional clinical trials of LYL797, LYL845, LYL119 or any other product candidates we may develop, and for the manufacture of our product candidates;
- the scope of protection we are able to establish and maintain for intellectual property rights, including LYL797, LYL845, LYL119 or any other product candidates we may develop;
- our ability to retain the continued service of our key personnel and to identify, hire and then retain additional qualified personnel;
- our expectations regarding the impact of the COVID-19 pandemic on our business and operations, including clinical trials, manufacturing suppliers, collaborators, use of contract research organizations (CROs) and employees;
- our expectations regarding the impact of inflation, macroeconomic conditions and geopolitical conflicts on our business and operations, including on our manufacturing suppliers, collaborators, CROs and employees; and
- our anticipated use of our existing cash, cash equivalents and marketable securities.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described under "Risk Factors" in Part I, Item 1A, and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in these forward-looking statements. Except as required by applicable law, we undertake no obligation to update or supplement any forward-looking statements publicly, or to update or supplement the reasons that actual results could differ materially from those projected in these forward-looking statements, even if new information becomes available in the future.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

SUMMARY OF RISK FACTORS

Below is a summary of material factors that make an investment in our securities speculative or risky. Importantly, this summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, as well as other risks and uncertainties that we face, can be found under "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. This summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should carefully consider the risks and uncertainties described under "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K as part of your evaluation of an investment in our common stock.

- We are an early clinical stage biopharmaceutical company and have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing net losses for the foreseeable future.
- We operate in a rapidly evolving field and have a limited operating history, which may make it difficult to evaluate the success of our business to date and to assess our future viability.
- We currently have no products approved for sale and have never generated revenue from product sales. We may never generate revenue from product sales or achieve profitability.
- We will require substantial additional capital to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Our success payment obligations in our success payment agreements may result in dilution to our stockholders or may be a drain on our cash resources to satisfy the payment obligations.
- We are early in our research and development efforts and just beginning clinical development of our product candidates. If we are unable to successfully develop and commercialize product candidates or experience significant delays in doing so, our business may be harmed.
- Our product candidates and technology platforms are based on novel technologies that are unproven and may not result in approvable or marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval, and we may not be successful in our efforts to use and expand our technology platforms to build a pipeline of product candidates.
- We currently have no marketing, sales or distribution infrastructure, and we intend to either establish a sales and marketing infrastructure or outsource this function to a third party. Either of these commercialization strategies carries substantial risks to us.
- Our business could continue to be adversely affected by the effects of health epidemics, including the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.
- We intend to manufacture at least a portion of our product candidates ourselves. Delays in further qualifying or in receiving regulatory approvals for our manufacturing facility and product candidates could delay our development plans and thereby limit our ability to generate product revenues.
- The manufacturing of cellular therapies is very complex. We are subject to a multitude of manufacturing risks, including risks associated with supply chain complexity related to patient materials, any of which could substantially increase our costs, delay our programs or limit supply of our product candidates.
- If our sole clinical or commercial manufacturing facility or our contract manufacturing organization is damaged or destroyed or production at these facilities is otherwise interrupted, our business would be negatively affected.
- If we are unable to develop or scale our own manufacturing, we may have to rely on third parties to manufacture our product candidates, which subjects us to risks and could delay or prevent our development and/or commercialization, if approved, of our product candidates.
- Cell-based therapies rely on the availability of specialty raw materials, which may not be available to us on acceptable terms or at all.
- We intend to rely on third parties to conduct, supervise and monitor a significant portion of our research and nonclinical studies and clinical trials for our product candidates, and, if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements or otherwise perform satisfactorily, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.

- We have in the past, and we may in the future, form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.
- We depend on the enrollment and retention of patients in our current and planned clinical trials for our product candidates. If we experience delays or difficulties enrolling or retaining patients in our clinical trials, our research and development efforts and business, financial condition and results of operations could be materially adversely affected.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Our cellular therapy product candidates represent new therapeutic approaches that could result in heightened regulatory scrutiny, delays in clinical development or delays in or our inability to achieve regulatory approval, commercialization or payor coverage of our product candidates.
- The results of research, nonclinical studies or earlier clinical trials are not necessarily predictive of future results. Any product candidate we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval.
- Clinical development involves a lengthy and expensive process with an uncertain outcome.
- Interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as we make changes to our manufacturing processes and are subject to audit and verification procedures that could result in material changes in the final data.
- Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.
- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be adversely affected.
- We have in-licensed a significant portion of our intellectual property from our partners. If we breach any of our license agreements with these partners, we could potentially lose the ability to continue the development and potential commercialization of one or more of our product candidates.

PART I

Item 1. Business

Overview

We are a clinical-stage cell therapy company advancing a pipeline of product candidates for patients with solid tumors utilizing our proprietary *ex vivo* genetic and epigenetic T-cell reprogramming technologies. Our investigational therapies use the patient's own cells as the starting point to generate highly tumor-reactive, longer-lasting functional T cells with enhanced ability to defeat solid tumors. Our innovative reprogramming technologies address what we believe are the primary barriers that limit consistent and long-lasting responses to T-cell therapy in solid tumors: T-cell exhaustion and lack of durable stemness. Our technologies are designed to generate T cells with the ability to persist and self-renew while driving durable tumor cytotoxicity, even in the setting of an immunosuppressive tumor microenvironment. The goal is for our technologies to provide patients with T cells that are potent and long-lasting enough to achieve durable antitumor responses. Furthermore, our technologies can be applied in a target agnostic manner to multiple T-cell modalities, including chimeric antigen receptor (CAR), tumor-infiltrating lymphocytes (TIL) and T-cell receptor (TCR) therapies.

We apply our technologies with the aim to develop T-cell therapies with improved durable clinical outcomes. Our growing pipeline of promising cell product candidates targets solid tumor indications with large unmet needs that are collectively responsible for approximately 180,000 deaths in the US annually. Each of our programs provide opportunities to expand into additional indications beyond the patient populations we are initially targeting. Our product candidates are summarized in the Table 1 below:

Table 1: Lyell's Pipeline

Product Candidate/ Modality	Target	Genetic Reprogramming		Epigenetic Reprogramming		Target Indications	Preclinical	Phase 1	Phase 2 / Pivotal	Next Expected Milestone
		c-Jun	NR4A3	Epi-R™	Stim-R™					
LYL797 CAR T Cell	ROR1	√		√		TNBC NSCLC Other Solid Tumors				Initial data in 1H 2024
LYL119 CAR T Cell	ROR1	√	√	√	√	ROR1+ Solid Tumors				Submit IND in 1H 2024
LYL845 TIL	Multiple antigens			√		Melanoma CRC, NSCLC Other Solid Tumors				Initial data in 2024
2nd Generation TIL	Multiple antigens	**Genetic and Epigenetic Reprogramming**				Solid Tumors				

ROR1, receptor tyrosine kinase-like orphan receptor 1; IND, investigational new drug; CAR, chimeric antigen receptor; NSCLC, non-small cell lung cancer; TNBC, triple-negative breast cancer; TIL, tumor infiltrating lymphocytes; CRC, colorectal cancer

Our Strategy

Our goal is to develop innovative therapies for patients with solid tumors based on our proprietary T-cell reprogramming technologies, which generate tumor-reactive, long-lasting functional T cells that resist exhaustion and maintain the ability to self-renew and persist to drive durable tumor cytotoxicity.

Key components of our business strategy to achieve this goal include:

- ***Efficiently advance our diverse pipeline of product candidates*** — We believe our autologous T-cell therapies will deliver improved, durable clinical outcomes for patients with solid tumors. We have two wholly owned product candidates in two distinct T-cell modalities, CAR T cell and TIL, currently in Phase 1 development targeting indications with unmet medical needs in large commercial opportunities. We anticipate having initial clinical data for both programs in 2024 and filing a new Investigational New Drug (IND) application for our third wholly-owned product candidate in the first half of 2024.

- ***Leverage our proprietary, cell reprogramming technology platforms to create highly tumor-reactive, longer-lasting functional T cells with enhanced ability to defeat solid tumors*** — We seek to develop T-cell therapies to defeat solid tumors by addressing the major barriers to successful cell therapy in solid tumors, including overcoming exhaustion of T cells and creating populations of T cells with properties of durable stemness. Our pipeline of therapeutic candidates includes programs designed to outlast and eradicate solid tumors utilizing our proprietary, stackable genetic and epigenetic T-cell reprogramming technologies: c-Jun overexpression, NR4A3 knockout, Epi-R™ and Stim-R™.
- ***Continually innovate to develop and advance novel, breakthrough technologies for cell therapy*** — We are committed to continuing to discover, develop and advance disruptive technologies that have the potential to revolutionize cell therapy and its promise to improve the lives of patients with solid tumors. For example, our new NR4A3 gene knockout and Stim-R reprogramming technologies are designed to further improve the potency and durability of T cells. These novel technologies are being utilized in our new CAR T-cell product candidate, LYL119, in addition to c-Jun overexpression and Epi-R, with the goal of creating even greater benefit to patients with cancer.
- ***Maintain proprietary state-of-the-art infrastructure and capabilities to control all aspects of cell product manufacturing*** — We have and will continue to invest in manufacturing with the goal to reliably produce the highest quality cell therapy products for patients. This is achieved through implementing consistent processes and mitigating risks, including risks arising from the challenges of managing production, supply chain, patient specimen chain of custody and quality. We have built and operate a wholly-owned manufacturing facility, LyFE™, which is a multi-product manufacturing center that can produce plasmid, lentiviral vector and cell products. LyFE has been commissioned and qualified in compliance with U.S. Food and Drug Administration's Current Good Manufacturing Practices (cGMP) and is manufacturing cell product for our clinical trials. We expect maintaining our own manufacturing facility to not only enable us to implement consistent processes and manage risk, but also to protect proprietary aspects of our reprogramming technologies, support seamless collaboration across research, development and manufacturing, access more detailed and timely product characterization information and rapidly incorporate new innovations. Our technology infrastructure enables real-time monitoring of our manufacturing process and the ability to incorporate insights into our research, manufacturing and clinical development efforts.
- ***Generate, secure and defend intellectual property on our differentiated technology platforms and product candidates*** — We have developed and secured intellectual property, including know-how, through our internal research efforts, licensing agreements and collaborations. We rigorously analyze, file and protect our intellectual property in an ongoing manner.

Our Reprogramming Technologies

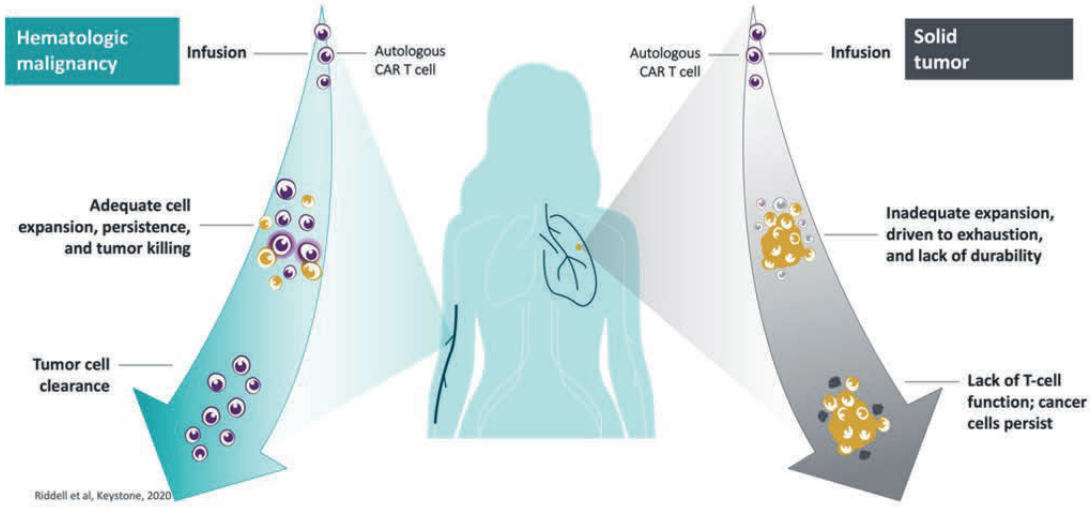
Cell therapy has demonstrated profound results in some patients suffering from hematologic malignancies, but solid tumors are more complex and have evolved multiple mechanisms to evade and ultimately resist clearance by the immune system. This has limited the use of cell therapy in solid tumors. Based on clinical data and other scientific evidence, we believe **T-cell exhaustion** and **lack of durable stemness**, which include the ability of T cells to persist and self-renew to drive durable tumor cytotoxicity, are two apical barriers limiting the efficacy of cell therapy in solid tumors.

We have developed proprietary, stackable genetic and epigenetic reprogramming technologies to address these two major barriers. Our reprogramming technologies are designed to generate potent T cells with durable cytotoxic function, irrespective of target and irrespective of whether they are delivered as CAR, TIL or TCR therapies. We have generated T cells that have demonstrated in nonclinical studies the ability to sustain cancer cell killing in murine models of solid tumors and an increased ability to maintain stemness to drive more durable tumor cytotoxicity.

T-cell exhaustion describes a dysfunctional cellular state characterized by increased expression of cell surface markers such as PD-1, TIM-3, and LAG-3, and importantly the functional inability to respond to antigen and elimination of target cells. A clinical study previously conducted by one of our founders, Stanley Riddell, M.D., Professor in Immunology, Burke O'Reilly Family Endowed Chair in Immunotherapy, Fred Hutchinson Cancer Center, illustrated the different fates of CAR T cells in solid tumors versus hematologic malignancies and identified T-cell exhaustion as a key barrier to successful cell therapy in the solid tumor microenvironment. In this study, conceptually depicted in Figure 1, autologous ROR1-targeted CAR T cells infused into patients with chronic lymphocytic leukemia underwent rapid expansion and retained T-cell effector functions, leading to tumor cell clearance and clinical responses. However, when CAR T cells generated with the same method are infused into patients with solid tumor such as triple-negative breast cancer (TNBC) or non-small cell lung cancer (NSCLC), these T cells often failed to expand adequately, rapidly developed

cell surface markers of T-cell exhaustion and adopted a dysfunctional state. The outcome of these studies clearly demonstrated that T-cell exhaustion is a major barrier to successful cell therapy in solid tumors.

Figure 1: Solid tumors drive T cells down a path to exhaustion.



Durable stemness describes the quality of a population of T cells to persist through self-renewal, as well as generate differentiated effector cell progenies to provide durable tumor cytotoxicity. Emerging research has shown that effective immunotherapy requires T-cell populations with stem-like characteristics to produce clinical responses, where the presence of stem-like T cells correlates with solid tumor responses to cancer immunotherapy in the setting of solid tumors, including TIL and immune checkpoint blockade therapy (Sade-Feldman et al., *Cell*, Nov. 2018; Krishna et al., *Science*, Dec. 2020)

Genetic reprogramming technologies*:* Our two proprietary *ex vivo* genetic reprogramming technologies are c-Jun overexpression and NR4A3 gene knockout. c-Jun and NR4A3 are involved in the regulation of the activator protein 1 (AP-1) transcription factor pathway, which plays a key role in T-cell effector function. These complementary reprogramming technologies function within this critical biological pathway to endow resistance to T-cell exhaustion.

Overexpression of c-Jun is based on the work of Lyell co-founder, Crystal Mackall, M.D., the Ernest and Amelia Gallo Family Professor of Pediatrics and Medicine at Stanford University and Founding Director of the Stanford Center for Cancer Cell Therapy. Dr. Mackall discovered that exhausted T cells have an imbalance in the AP-1 family of transcription factors, and that correcting for this imbalance by overexpression of c-Jun enables T cells to resist exhaustion, infiltrate solid tumors and maintain their functionality and potency. This work was fully described in a *Nature* publication in 2019 (Lynn et al., *Nature*, Dec. 2019).

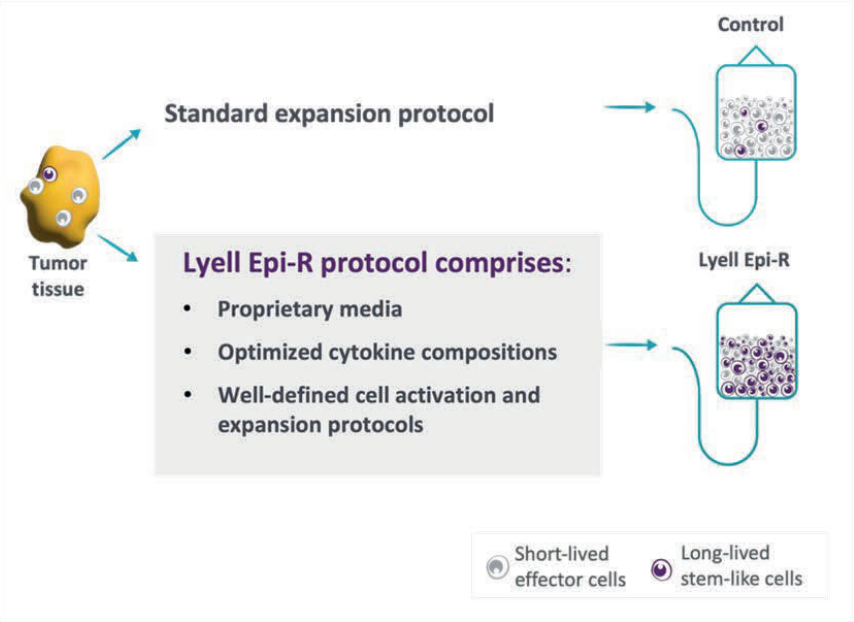
Our second genetic reprogramming technology, NR4A3 gene knockout, builds on the approach of reprogramming of the AP-1 transcription factor pathway to delay exhaustion and improve antitumor function. We and others have previously observed that the NR4A family of transcription factors is upregulated in exhausted T cells and may contribute to T-cell exhaustion in part by restricting the activity of AP-1. We hypothesize that disruption of NR4A3 expression, along with c-Jun overexpression, can further unleash the potential for maximal c-Jun activity and endow greater functional resistance to exhaustion. Our nonclinical data suggest the combination of these two technologies, NR4A3 gene knockout and c-Jun overexpression, can act in a complementary fashion and have the potential to further improve the potency and durability of our CAR therapy.

Epigenetic reprogramming technologies: Our two proprietary *ex vivo* epigenetic reprogramming technologies are Epi-R and Stim-R. These novel manufacturing technologies generate product candidates with more stem-like cells and with greater potency during *ex vivo* T-cell expansion.

Epi-R is our proprietary *ex vivo* epigenetic reprogramming technology that intentionally and reproducibly generates a population of T cells with durable stemness. T cells with properties of durable stemness have an increased ability to self-renew and persist to drive durable tumor cytotoxicity. This technology is built upon the groundbreaking science conducted at the National Cancer Institute (NCI), where it was demonstrated that products with more stem-like and functional T cells can be achieved by altering the metabolic state of the cells during expansion

(Vodnala et al., *Science*, Mar. 2019). Key NCI scientists conducting this research subsequently joined Lyell where they advanced this research substantially to create the Epi-R manufacturing protocol, which intentionally produces T-cell populations with desirable stem-like properties that can be measured both phenotypically and functionally. This novel Epi-R protocol includes proprietary media, well-defined cell activation and expansion processes, as well as customized cytokine combinations. Lyell's Epi-R protocol enables manufacturing of T-cell therapy product candidates that are highly potent against cancer cells but also retain characteristics of stemness, which have been clinically associated with effective antitumor immunotherapies (Figure 2). Furthermore, relating specifically to TIL, the application of Epi-R has generated T-cell populations that exhibit a high degree of polyclonality, i.e., the retention of a broad repertoire of TCR clonotypes that may react to a broader set of tumor antigens, thus improving the potential of our TIL therapy to counteract the heterogeneous nature of solid tumors. Additionally, we are able to reliably and reproducibly manufacture our TIL products from a variety of solid tumors, including those that have been traditionally hard to manufacture such as from checkpoint refractory malignant melanoma, NSCLC and colorectal cancer (CRC).

Figure 2: Lyell's proprietary Epi-R protocol produces T-cell populations with long-lived stem-like characteristics. This protocol is used in both our LYL797 CAR T cell product candidate and in our LYL845 TIL product candidate as shown below.



Our second epigenetic reprogramming technology, Stim-R, is a proprietary synthetic cell mimetic that mediates more precise and natural T-cell activation in the manufacturing process. Current manufacturing platforms typically utilize antibody-conjugated beads that were developed decades ago for expanding T cells. This standard approach does not provide precise control over the strength or duration of the signaling that drives T-cell expansion *ex vivo*. Our Stim-R platform optimizes signaling parameters during T-cell activation using degradable lipid-coated silica rods that can be functionalized to regulate cell activation more closely mimicking natural T-cell stimulation. This technology allows for greater control over the duration, intensity and type of signals delivered during cell expansion and manufacturing, resulting in the generation of more potent T-cell products.

T-cell rejuvenation technologies: We and others have documented the impact of aging on T-cell function, which begins to decline after puberty, and at an increasingly accelerated rate after age 65. Morbidity and mortality from cancer also increase with age. Thus, we are working to advance another novel reprogramming technology that focuses on rejuvenation of antitumor T cells. We are developing a method to maintain T-cell identity while reducing the epigenetic age of the cells. This technology is currently in the research stage. We have generated data illustrating the ability to "turn back" the epigenetic clock in a process called cellular rejuvenation, without changing the T-cell's identity as would occur in the setting of induced pluripotent stem cell-derived T cells.

Our Clinical Programs

We are advancing a diverse pipeline of CAR T cell and TIL product candidates that incorporate our stackable reprogramming technologies designed to generate potent T cells with durable cytotoxic function, irrespective of target and irrespective of whether they are delivered as CAR T, TIL or TCR T therapies. Each of our programs currently target

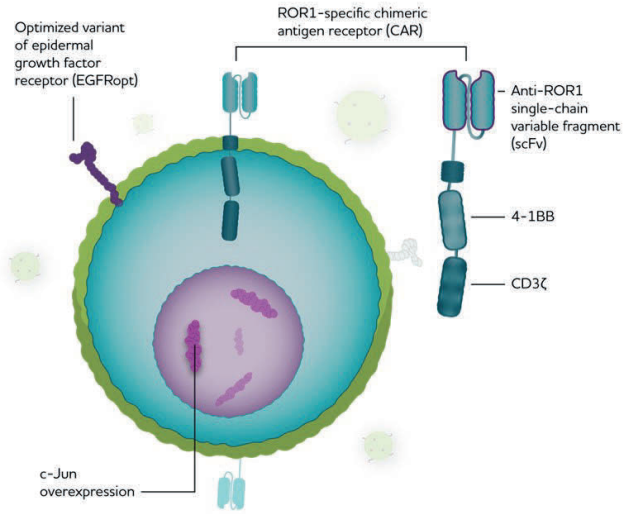
cancers with large unmet need and provide opportunity to expand into additional indications. We have deployed our technologies in our pipeline in the following manner to provide rapid clinical proof-of-concept (Table 1):

- LYL797 incorporates our c-Jun and Epi-R technologies and is undergoing evaluation in a Phase 1 clinical trial enrolling patients with relapsed/refractory TNBC or NSCLC.
- LYL119 incorporates our c-Jun, NR4A3, Epi-R and Stim-R technologies and is currently in preclinical development.
- LYL845 incorporates our Epi-R technology and is undergoing evaluation in a Phase 1 clinical trial including patients with advanced melanoma, relapsed/refractory NSCLC or CRC.

LYL797: A genetically and epigenetically reprogrammed ROR1 CAR T-cell product candidate designed for differentiated potency and durability targeting multiple solid tumor indications.

We are applying our c-Jun and Epi-R technologies to our lead CAR T-cell product candidate, LYL797, which is expected to be an intravenously-administered CAR T-cell product targeting the receptor tyrosine kinase-like orphan receptor 1 (ROR1) protein. ROR1 is a fetal protein expressed during embryogenesis and is believed to be important in cell migration, polarity and survival. It is expressed in several cancer types, including TNBC, NSCLC, ovarian cancer and chronic lymphocytic leukemia, and is generally associated with a poor prognosis. LYL797 (Figure 3) contains a CAR with a 4-1BB/CD3ζ intracellular domain, a transmembrane domain, an optimized spacer domain and a single-chain variable fragment (scFv) derived from an R12 rabbit monoclonal antibody that recognizes and binds with high specificity to human ROR1. LYL797 also incorporates c-Jun and a proprietary optimized truncated version of human EGFR ($EGFR_{opt}$) used for tracking the CAR T cells in the peripheral blood post treatment and can also be used as a safety measure with the administration of cetuximab, if needed. LYL797 is manufactured utilizing our proprietary Epi-R technology.

Figure 3: LYL797 construct.



Phase 1 Clinical Trial

Our Phase 1 clinical trial (NCT05274451) is designed to evaluate the safety and antitumor activity of LYL797 in patients with ROR1-positive TNBC or NSCLC.

The trial is designed as an open label, dose escalation and expansion trial in patients with relapsed/refractory TNBC who have failed at least two lines of therapy and patients with relapsed/refractory NSCLC who have failed at least one line of therapy. Per protocol, dose expansion at the recommended dose identified during dose escalation is expected to occur in at least 15 patients with TNBC and 15 patients with NSCLC. The primary outcome measure assesses the safety and tolerability of LYL797. Patients will be monitored for cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome, as well as tissue-specific toxicities in ROR1-expressing organs. Secondary outcome measures 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.

We plan to share initial data from the trial when we have a meaningful number of patients and an indication of clinical effect, which we expect to occur in the first half of 2024.

Target Indications

We are initially developing LYL797 for the treatment of ROR1-positive TNBC and NSCLC. Significant subsets of patients with common cancers express ROR1, including TNBC (~60%) and NSCLC (~40%), two of the highest ROR1-expressing solid tumor indications. If successful, we may expand into other ROR1-positive cancers with a lower incidence of ROR1 expression, including potentially hormone-receptor positive breast cancer, ovarian and other solid tumors.

Breast cancer is the second most common cancer in American women. Currently, the average risk for a woman in the United States to develop breast cancer is approximately 13%. Breast cancers that demonstrate the absence of estrogen receptor and progesterone receptor and no overexpression of HER2 are referred to as TNBC. Approximately 10-15% of patients with breast cancer have TNBC and triple negative status tends to be more common in women younger than age 40, who are African American or who have a BRCA1 mutation. TNBCs have a high tendency to metastasize, and patients are at a higher risk to relapse compared to other molecular types. TNBCs differ from other types of invasive breast cancer in that TNBC tumors grow and spread faster, have limited treatment options and have a worse prognosis. In the United States, there are approximately 40,000 new cases of TNBC annually and approximately 22% of breast cancer deaths are from TNBC. Once TNBC has spread to distant parts of the body, the 5-year survival rate is only 11.5% despite currently available treatment options. Available treatments include surgery, neoadjuvant and adjuvant chemotherapy such as capecitabine or gemcitabine, taxanes, anthracyclines and eribulin, check-point inhibitors such as pembrolizumab, and poly ADP ribose polymerase or PARP inhibitors such as olaparib and talazoparib. At recurrence, the antibody-drug conjugate sacituzumab govitecan-hziy may be prescribed.

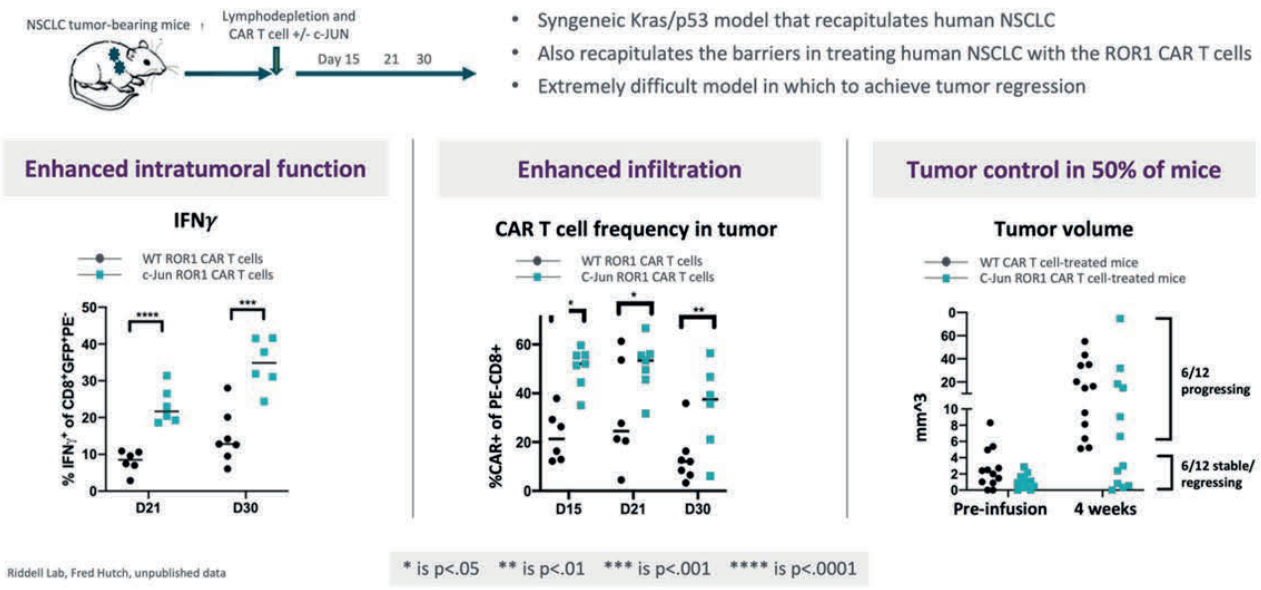
Lung cancer is the second most common cancer and is the leading cause of cancer mortality worldwide. NSCLC, defined as any type of epithelial lung cancer other than small-cell lung carcinoma, accounts for about 84% of all lung cancers. In 2016, the incidence of NSCLC varied widely, ranging from 3 to 57 per 100,000 in Africa and North America respectively, with ~2 million cases diagnosed globally. It is estimated that 110,000 deaths from this disease occurred in the United States in 2022. For people with localized NSCLC, the overall 5-year survival rate is ~61%. For regional NSCLC, the 5-year survival rate is ~35%. Based on current data, when cancer metastasizes, the 5-year survival rate is 6% despite surgery, radiation and treatment with multiple currently-approved therapies, including chemotherapy, immunotherapy and targeted drug therapy.

Nonclinical Data

We have conducted extensive nonclinical *in vitro* and *in vivo* studies supporting development of LYL797. Nonclinical studies of ROR1 CAR T cells that overexpress c-Jun have demonstrated tumor reduction, enhanced cytokine production and tumor infiltration in an aggressive NSCLC syngeneic animal model (Figure 4). CAR T cells generated with our Epi-R manufacturing protocol exhibit enhanced durability and cytotoxicity (Figure 5). Additionally, in a nonclinical xenograft tumor model, LYL797, combining c-Jun overexpression and Epi-R, demonstrated prolonged survival in a xenograft NSCLC animal model (Figure 6). During the past year, we have presented these and other nonclinical findings at scientific and medical conferences, including in April, at the American Association of Cancer Research Annual Meeting.

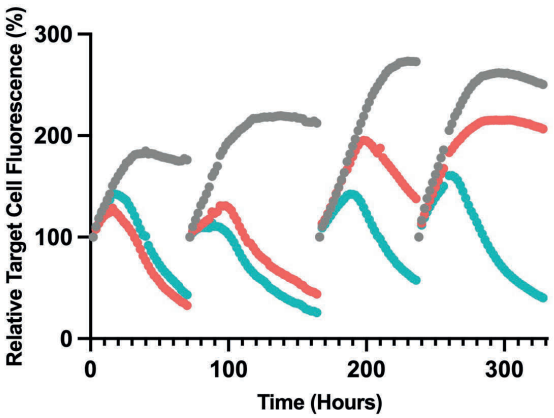
Our scientific co-founder, Stanley Riddell, M.D., first tested the hypothesis that overexpression of c-Jun could improve T-cell function in a rigorous solid tumor model of NSCLC (Figure 4). Riddell and colleagues utilized a transgenic mouse model with inducible oncogenic driver mutations KRASG12D and p53 deletion. Once triggered, these mice developed tumors *de novo* that recapitulate an immunosuppressive tumor microenvironment, akin to human NSCLC. Previous studies have shown that this aggressive tumor model does not respond to chemotherapy or PD-L1 immunotherapy. In our study, we observed that this aggressive tumor model is also resistant to treatment with ROR1 CAR T cells, just as was observed in treating human NSCLC with ROR1 CAR T cells. In contrast, tumor-bearing mice treated with ROR1 CAR T cells that overexpressed c-Jun demonstrated greater infiltration by the T cells into the tumor, enhanced function of those T cells and tumor regression or stabilization in 50% of the mice versus the 100% tumor progression observed in mice treated with ROR1 CAR without overexpression of c-Jun.

Figure 4: Nonclinical efficacy demonstrated with c-Jun overexpressing ROR1 CAR T cells in aggressive NSCLC model.



We have also demonstrated that CAR T cells generated with Epi-R are able to kill tumor cells over time in an experiment where the CAR T cells are repeatedly challenged to kill tumor cells over multiple rounds (Figure 5). In this experiment, CAR T cells are co-cultured with ROR1-positive tumor cells, and tumor cell killing can be assessed and quantified by measurement of decreasing fluorescence. CAR T cells were repeatedly challenged with tumor cells over multiple rounds to assess the durability of tumor cell killing. Cells generated through standard expansion protocols gradually lose their functionality by the third round and are significantly less effective in killing tumor cells by the fourth round of tumor cell killing. In contrast, cells generated with the Epi-R protocol continue to kill tumor cells. Importantly, the Epi-R cells are no longer in the Epi-R protocol, suggesting that the stem-like attribute derived from the epigenetic reprogramming is sustained after the manufacturing protocol and for the duration of the experiment.

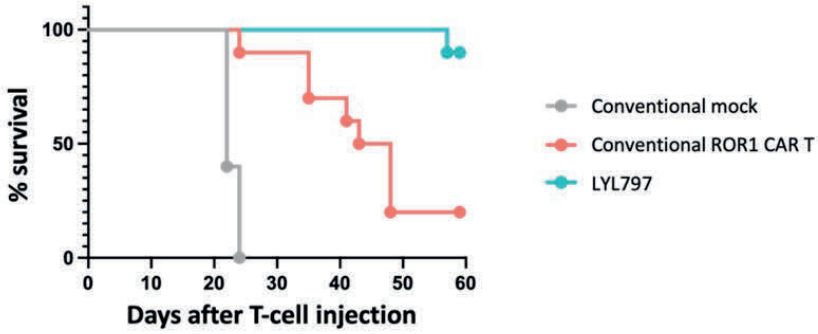
Figure 5: The Epi-R protocol produces populations of T cells with durable cytotoxicity.



In May, at the American Society of Gene and Cell Therapy Annual Meeting, we presented a study that assessed *in vivo* functional activity of LYL797 (ROR1 CAR T cells with c-Jun and Epi-R) compared to conventional ROR1 CAR T cells in an established human ROR1-positive H1975 mouse xenograft model. In this study, LYL797 demonstrated improved expansion in the peripheral blood of tumor-bearing animals and control of tumor growth, which led to prolonged survival (Figure 6).

Taken together, these nonclinical data characterize LYL797 and demonstrate that ROR1-targeted CAR T cells reprogrammed with c-Jun and Epi-R can overcome barriers of T-cell exhaustion and lack of durable stemness.

Figure 6: LYL797 prolongs survival in NSCLC (H1975) xenograft model.



LYL845: A novel epigenetically reprogrammed TIL product candidate designed for differentiated potency and durability targeting multiple solid tumor indications.

We are applying our epigenetic reprogramming technology, Epi-R, to develop LYL845, which is expected to be an intravenously-administered autologous TIL therapy for multiple solid tumors. Our Epi-R protocol comprises proprietary media, optimized cytokine compositions and well-defined cell activation and expansion protocols used during our manufacturing process.

TIL have previously shown clinical benefit in patients with advanced melanoma and other solid tumors with high mutational burden. Published data from third-party TIL trials show that treating metastatic melanoma patients with TIL can result in complete and durable responses. Response rates to TIL therapy in patients with other advanced solid tumors such as lung, colorectal and breast are much lower than that observed in advanced melanoma. Broad TIL efficacy has been limited by poor enrichment of tumor-reactive T cells and the poor quality and limited growth potential of expanded T cells. Failure to maintain polyclonality of TIL during production may also limit their ability to eradicate cancer cells given the inherent heterogeneous nature of solid tumors. LYL845 incorporates our Epi-R technology that has shown promising improvements in enhancing T-cell potency, antitumor activity and increased polyclonality of TIL in nonclinical experiments.

Phase 1 Clinical Trial

Our Phase 1 clinical trial (NCT05573035) is designed to evaluate the safety and antitumor activity of LYL845 in patients with advanced melanoma, NSCLC and CRC. If successful, we expect to expand into additional indications.

The trial is designed as an open label, dose escalation and expansion trial in patients with relapsed and/or refractory metastatic or locally advanced solid tumors. Per protocol, dose expansion at the recommended dose identified during dose escalation is expected to occur in at least 15 patients with advanced melanoma, 15 patients with NSCLC and 15 patients with CRC. The primary outcome measure assesses the safety and tolerability of LYL845. Secondary outcome measures include clinical activity based on the evaluation of antitumor activity as evaluated by RECIST criteria and characterization of the pharmacokinetic profile of LYL845. Evaluation of T-cell expansion, phenotype, clonal diversity and persistence will also be assessed. Patients will be monitored for CRS and auto-immunity.

We plan to share initial data from the trial when we have a meaningful number of patients and an indication of clinical effect, which we expect to occur in 2024.

Target Indications

We are initially developing LYL845 for advanced melanoma, NSCLC and CRC. Based on our success with those, we plan to include patients with other solid tumors, potentially including head and neck, cervical, breast and pancreatic cancer. Although patients with these cancers may benefit initially from radiation therapy, chemotherapy, surgery, and more advanced alternatives such as checkpoint therapies, immunotherapies or targeted therapies, most patients with these types of cancers eventually relapse. After becoming resistant to initial lines of therapy, patients are limited to palliative care, experimental therapies in clinical trials or chemotherapy regimens that are often highly toxic and largely ineffective. Overall, despite recent advances in therapeutic development, for most patients diagnosed with advanced solid tumors, long-term survival rates remain low.

Melanoma of the skin is among the most common cancers in the United States behind breast, prostate, lung and CRC. It is one of the most common cancers in young adults and especially in young women. It is estimated there are over 100,000 new cases of melanoma diagnosed in the United States per year. Melanoma arises due to genetic mutations in melanocytes, the pigment producing cells, which can be found in the skin, eye, inner ear and leptomeninges, and represents

the most aggressive and the deadliest form of skin cancer. Although melanoma accounts for only ~1% of all dermatologic cancers, it is responsible for ~80% of deaths from skin cancer. Only ~14% of patients with advanced melanoma survive for five years. Available treatment options include surgery, radiation therapy, immunotherapy (PD-1 inhibitors), chemotherapy and targeted therapies (MEK and BRAF inhibitors).

A description of NSCLC can be found above in the section describing the Phase 1 clinical trial for LYL797.

Colorectal cancer is the third leading cause of cancer-related deaths in both men and women in the United States. Most colorectal cancers are a type of tumor called adenocarcinoma, which is cancer of the cells that line the inside tissue of the colon and rectum. In 2022, it was estimated that there were approximately 150,000 new cases of CRC in the United States with an estimated cause of approximately 53,000 deaths each year. For patients diagnosed with metastatic disease, the 5-year survival rate is 14%. Approximately 25% of patients have metastatic disease at diagnosis, and about 50% of patients with colorectal cancer will eventually develop metastases. Over 35% of the patients with a new diagnosis of CRC will die within five years. Currently available treatments include surgery, radiation therapy, chemotherapy, immunotherapy and targeted therapy (vascular endothelial growth factor, epidermal growth factor receptor, BRAF, NTRK, HER2 and kinase inhibitors).

Nonclinical Data

We have conducted nonclinical studies supporting the development of LYL845. These studies have demonstrated that TIL generated with our Epi-R technology have phenotypes (stemness markers and cytotoxic T cells) associated with clinical responses in published literature and preserved polyclonal tumor reactive cells. In addition, using Epi-R allows us to expand TIL in not only immunologically hot tumors such as melanoma, but also immunologically colder tumors such as NSCLC and CRC. During the past year, we have presented these findings at scientific and medical conferences. These presentations are summarized below:

In November, at the 2022 Annual Meeting of the Society for Immunotherapy of Cancer (SITC), we presented data that demonstrated the ability of our Epi-R technology to successfully and reliably expand TIL across three tumor types as compared to the standard (control) process. In this study, expanding TIL with Epi-R technology resulted in a 100% success rate (at least 10B cells) vs. 58% with control, including across twelve more difficult-to-expand tumor samples collected from checkpoint inhibitor refractory melanoma, NSCLC and CRC patients (Figure 7). Further, in this study Epi-R technology yielded a product (LYL845) with qualities that have been linked with antitumor functionality and improved outcomes in previous TIL clinical trials, including a greater proportion of CD8+ cytotoxic T cells and enrichment of T cells with stem-like profiles (Figure 8), and better metabolic fitness compared to control TIL.

Figure 7: Our Epi-R protocol more consistently successfully expands TIL from immunologically cold solid tumors vs. standard expansion processes.

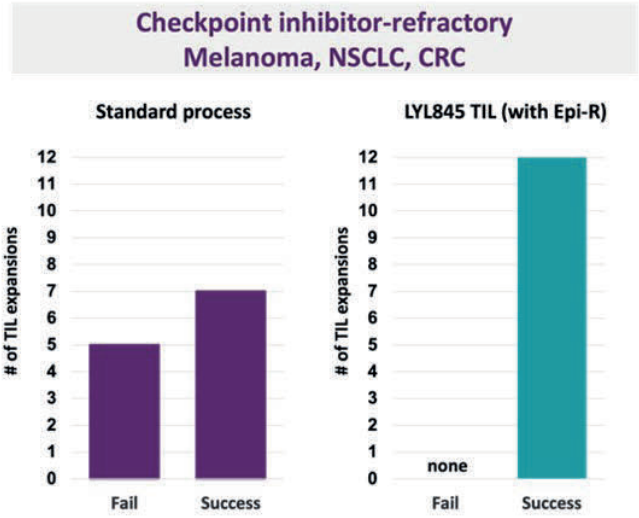
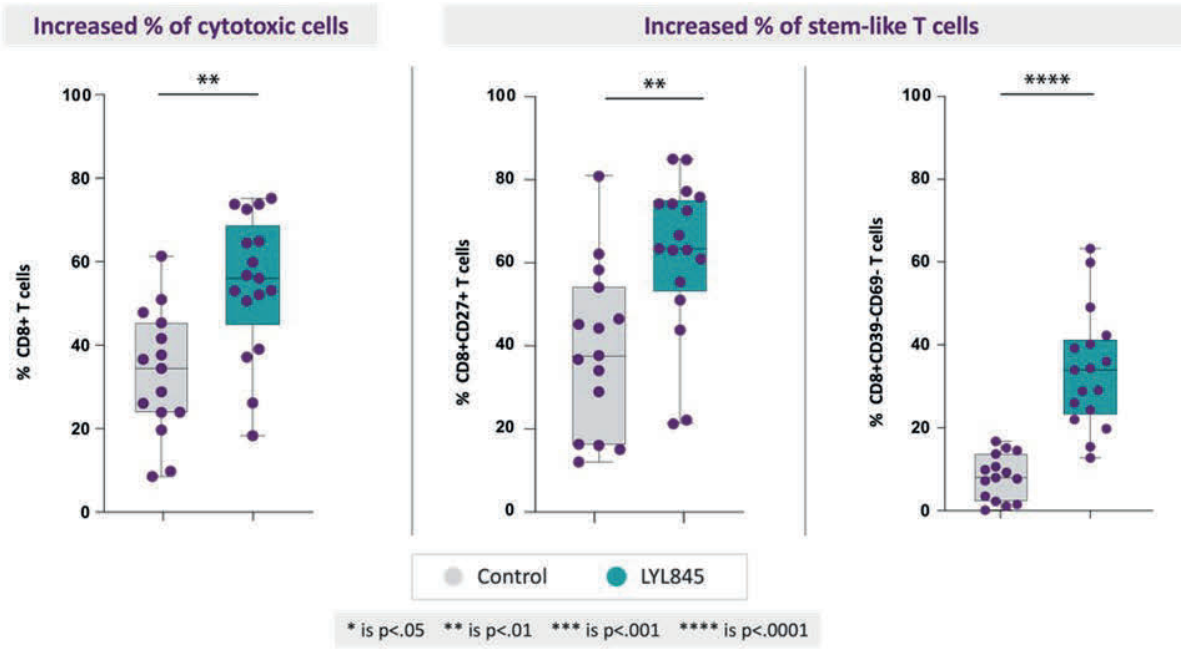
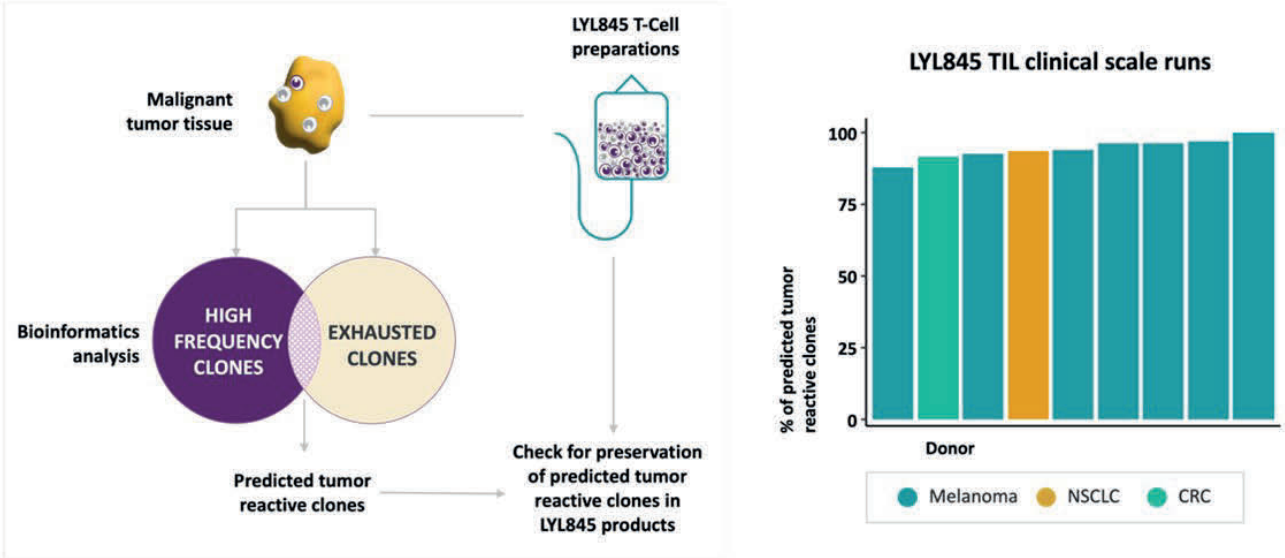


Figure 8: LYL845 is enriched for cells with characteristics associated with improved clinical outcomes (Krishna et al., *Science,* Dec. 2020).



We also presented at the 2022 meeting of SITC comprehensive analyses of transcriptomic profiles, polyclonality and prediction of tumor reactive T cell clones in our LYL845 product candidate. In particular, our bioinformatic analyses demonstrated that LYL845 products expanded using Epi-R technology at clinical scale were highly polyclonal and preserved approximately 94% of the predicted tumor reactive clones (Figure 9). Further, preserved putative tumor reactive clones in LYL845 products have increased stemness and reduced exhaustion-associated genes compared to TIL products derived from the standard process. Moreover, the tumor-specific reactivity of LYL845 was confirmed by demonstrating dose-dependent antitumor cytolytic activity and cytokine secretion in tumor cell specific co-culture assays.

Figure 9: LYL845 TIL preserve ~94% of predicted tumor reactive clones to enable targeting of heterogeneous solid tumors.



LYL119: An innovative ROR1 CAR T-cell product candidate designed for enhanced cytotoxicity.

A key pillar of our strategy is to continually innovate to develop and advance novel, breakthrough technologies that address key barriers to successful cell therapy for solid tumors. We have advanced a new genetic reprogramming

technology, NR4A3 knockout, and a new epigenetic reprogramming technology, Stim-R, that are being applied in our new CAR T-cell product candidate, LYL119. These technologies are stackable and complementary to c-Jun and Epi-R and are designed to further improve the antitumor potency and durability of T cells. LYL119 is being advanced with the goal of potentially creating even greater benefit for patients with ROR1-positive solid tumors. An IND application is expected to be submitted for LYL119 in the first half of 2024.

Nonclinical Data

In November at the 2022 meeting of SITC, we presented nonclinical data demonstrating that our NR4A3 knockout and Stim-R technologies further enhance survival *in vivo* in a murine H1975 xenograft tumor model at a reduced CAR T-cell dose. We presented data demonstrating that the combination of our two genetic reprogramming technologies, NR4A3 gene knockout and c-Jun overexpression, enhances the functional activity of ROR1 CAR T cells as shown 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* (Figure 10). In a separate abstract, we also presented nonclinical data demonstrating that Stim-R generates potent CAR T-cell products with increased cell proliferation and persistence *in vivo*, as well as improved tumor control (Figure 11).

Figure 10: Combining c-Jun overexpression with NR4A3 knockout enables T cells to further resist exhaustion and prolongs survival.

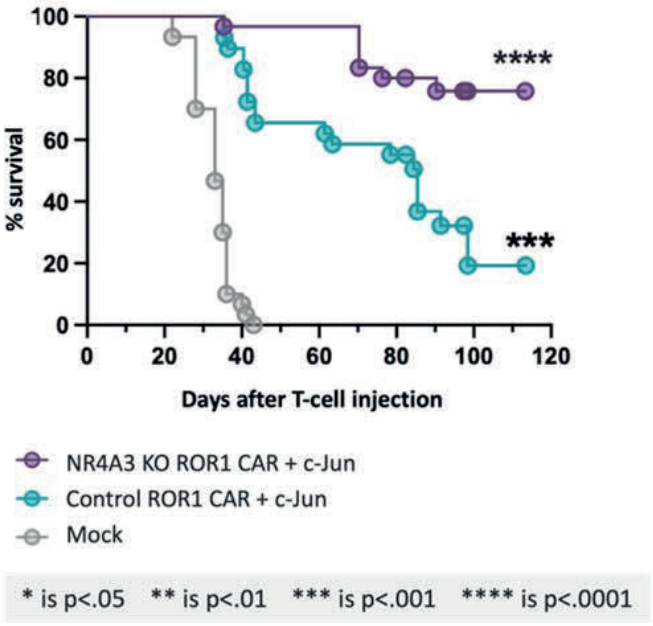
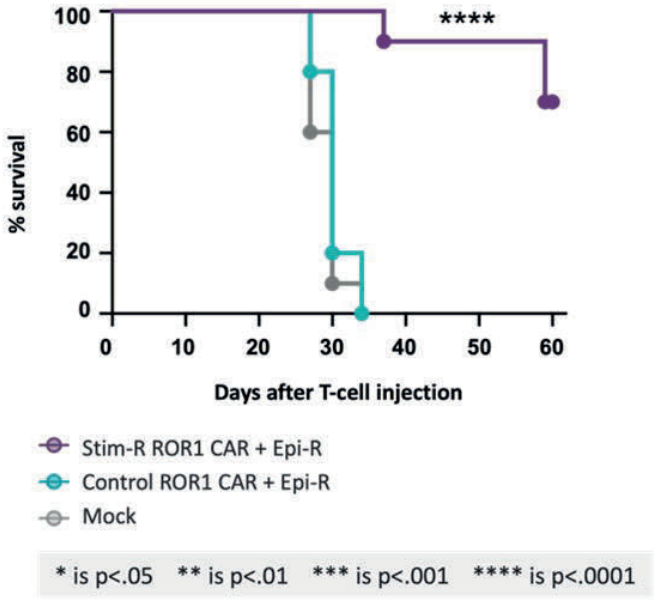


Figure 11: Stim-R ROR1 CAR T cells demonstrate improved potency and prolongs survival.



Our Manufacturing Capabilities

We believe it is critically important to own, control and continuously monitor all aspects of the cell therapy manufacturing process to mitigate risks, including challenges in managing production, supply chain, patient specimen chain of custody and quality control. We made a strategic decision to invest in building our own manufacturing facility to control our supply chain, maximize efficiencies in cell product production time, optimize cost and quality, and have the ability to rapidly incorporate disruptive advancements and new innovations. Controlling manufacturing also enables us to protect proprietary aspects of our reprogramming technologies. We view our manufacturing team and capabilities as a significant competitive advantage.

Our LyFE manufacturing center located in Bothell, Washington is approximately 73,000 square feet and is comprised of manufacturing suites, laboratories and offices. LyFE is commissioned and designed to be in compliance with U.S. and European Union cGMP standards and has a flexible and modular design enabling CAR T cell, TIL, TCR T cell and GMP viral vector production to control and de-risk the manufacturing sequence and timing of the major components of our supply chain. Owning our own facility encourages seamless collaboration across research, process development and manufacturing for high-quality reproducibility at manufacturing scale.

We are currently producing clinical supply for our Phase 1 trials at LyFE. At full staffing and capacity, we expect to be able to manufacture approximately 500 infusions per year depending on product candidate mix. At this time, we believe this capacity is sufficient to support our pipeline programs into pivotal trials and, if approved, early commercialization.

Competition

The pharmaceutical industry is highly competitive and dynamic, owing to rapidly advancing technologies. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing treatments and new treatments that may become available in the future. In addition, during development, our product candidates may compete against other experimental treatments, whether cell therapy or other modalities, for patients with certain histologies or patients with tumors expressing certain antigen targets of interest.

We are aware of a number of companies using *ex vivo* cell therapy approaches to treat solid tumors. Some of these companies may have substantially greater financial and other resources than we have, such as larger research and development staff and well-established marketing and sales forces, or may operate in jurisdictions where lower standards of evidence are required to bring products to market.

T-cell therapies for the treatment of solid tumors are being developed by a number of companies, including but not limited to Adaptimmune Therapeutics plc, ArsenalBio, AstraZeneca plc, Bristol Myers Squibb Co.,

Gilead Sciences Inc., Immunocore Holdings plc, Iovance Biotherapeutics Inc., the Janssen Pharmaceutical Companies of Johnson & Johnson, Nanjing Legend Biotech, Novartis AG, Nurix Therapeutics Inc., Precigen Inc. and Turnstone Biologics. We are also aware that other companies are developing therapies in modalities such as monoclonal antibodies and antibody drug conjugates for cancers that express ROR1, such as Merck & Co., Inc.

Among companies developing cell therapies for solid tumors, we believe we are substantially differentiated by our reprogramming technologies, knowledge, experience, scientific personnel and robust intellectual property portfolio. We believe the key competitive factors affecting the success of any of our product candidates will include efficacy, safety, accessibility, price and cost of manufacturing.

License, Collaboration and Success Payment Agreements

Fred Hutch License Agreement and Success Payment Agreement

In December 2018, we entered into a license agreement with Fred Hutchinson Cancer Center (Fred Hutch) (as amended in June 2019, September 2019, January 2020, and August 2020) that grants us a worldwide, sublicensable license under certain patent rights (exclusive) and certain technology (non-exclusive), to research, develop and commercialize products and processes for all fields of use utilizing CARs and/or TCRs. We paid Fred Hutch an upfront payment of $150,000. In connection with the license agreement, we entered into a letter agreement with Fred Hutch pursuant to which we issued to Fred Hutch 1,075,000 shares of our common stock.

The license agreement will expire, on a product-by-product and country-by-country basis, on the later of (a) the expiration of the last to expire valid claim of the patents rights covering such product in such country and (b) ten (10) years after the date of the first commercial sale of such product in such country. We may terminate the agreement at will in its entirety or with respect to any patent. Fred Hutch has the right to terminate the agreement in the event of our uncured breach.

We also entered into a letter agreement with Fred Hutch in December 2018 under which we agreed to make success payments to Fred Hutch, payable in cash or publicly tradable equity at our discretion. These success payments are based on increases in the per share fair market value of our common stock (as all our Series A convertible preferred stock were converted into an equivalent number of shares of our common stock upon the closing of our initial public offering) during the success payment period, which is a period of time that begins on the date of our letter agreement with Fred Hutch and ends on the earlier of: (a) the ninth anniversary of that date and (b) the earlier of (i) the date on which we sell, lease, transfer or exclusively license all or substantially all of our assets to another company and (ii) the date on which we merge or consolidate with or into another entity (other than a merger in which our pre-merger stockholders own a majority of the shares of the surviving entity). Success payments will be owed (if applicable) after measurement of the value of our common stock in connection with the following valuation dates during the success payment period: (1) the date of the first anniversary of our initial public offering; (2) the second anniversary of such date; (3) each two year anniversary thereafter (i.e., the four year anniversary, six year anniversary, etc. of such date); (4) the date on which we sell, lease, transfer or exclusively license all or substantially all of our assets to another company; (5) the date on which we merge or consolidate with or into another entity (other than a merger in which our pre-merger stockholders own a majority of the shares of the surviving entity); and (6) the last day of the nine-year period. Any success payment will generally be made within 45 days after the applicable valuation date, except that in the case of a merger or sale of all of our company's assets, the success payment will be made on the earlier of the 90th day following the transaction or the first date that transaction proceeds are paid to any of our stockholders. In the case of (1), (2) and (3), the value of our common stock will be determined by the average trading price of a share of our common stock over the consecutive 90-day period preceding the date the success payment is made; the value will otherwise be determined either, in the case of a merger or stock sale, by the consideration paid in the transaction for each share of our stock or the stock of the acquiring entity (or their parent or affiliate). The amount of a success payment is determined based on whether the value of our common stock meets or exceeds certain specified threshold values ascending from $18.29 per share to $91.44 per share, in each case subject to adjustment for any stock dividend, stock split, combination of shares or other similar events. Each threshold is associated with a success payment, ascending from $10.0 million at $18.29 per share to a cumulative total of $200.0 million at $91.44 per share, payable if such threshold is reached. Any previous success payments made to Fred Hutch are credited against the success payment owed as of any valuation date, so that Fred Hutch does not receive multiple success payments in connection with the same threshold. The success payments paid to Fred Hutch will not exceed, in aggregate, $200.0 million, which would be owed only when the value of the common stock reaches $91.44 per share. To date, no success payments have been incurred as the per share fair value of our common stock was below the price required for payment.

Stanford License Agreement and Success Payment Agreement

In January 2019, we entered into a license agreement with The Board of Trustees of the Leland Stanford Junior University (Stanford) that grants us a worldwide, sublicensable license under certain patent rights (exclusive), and certain other patent rights and technology (non-exclusive), to research, develop and commercialize products and processes for all fields of use utilizing CARs and/or TCRs. We also have the right to add certain Stanford patent applications covering certain inventions that are improvements to the existing patents and patent applications, as well as a right of first negotiation for other patent applications covering inventions made in the principal investigator's lab that relate to and are necessary or useful for utilizing CARs and/or TCRs.

We paid Stanford an upfront payment of $400,000. In connection with the license agreement, we entered into a letter agreement in January 2019 with Stanford pursuant to which we issued to Stanford 910,000 shares of our common stock. We are required to pay Stanford an annual maintenance fee in the mid tens of thousands of dollars on the second anniversary of entering into this agreement, and each anniversary thereafter until the date of the first commercial sale of a licensed product. We are obligated to pay Stanford up to a maximum of $3.7 million per target upon achievement of certain specified clinical and regulatory milestones. We are also obligated to pay Stanford $2.5 million collectively for all licensed products upon our achievement of a certain commercial milestone. In addition, the license agreement provides that we are required to pay Stanford low single-digit tiered royalties based on annual net sales of the licensed products by us and by our sublicensees. If we seek to challenge the validity of any of the licensed patents, during the pendency of such action our royalty rate will increase, and if the outcome of such challenge finds that patent is both valid and infringed our royalty rate will increase further. We are also required to pay Stanford (a) royalties in the mid-teens percentage of the payments that we receive from sublicensees of the rights solely licensed to us by Stanford, or (b) sublicensing fees if sublicensed with other intellectual property on a tiered basis up to $300,000.

The license agreement will expire, on a licensed product-by-licensed product and country-by-country basis, on the expiration of the last to expire valid claim of the licensed patents rights covering such licensed product in such country. We may terminate the agreement at will in its entirety or with respect to any licensed patent. Stanford has the right to terminate the agreement in the event of our uncured breach.

We also entered into a letter agreement with Stanford in October 2020, under which we agreed to make success payments to Stanford, payable in cash or publicly tradable equity at our discretion. These success payments are based on increases in the per share fair market value of our common stock (as all our Series A convertible preferred stock were converted into an equivalent number of shares of our common stock upon the closing of our initial public offering) during the success payment period, which is a period of time that begins on the date of our letter agreement with Stanford and ends on the earlier of: (a) the ninth anniversary of that date and (b) the earlier of (i) the date on which we sell, lease, transfer or exclusively license all or substantially all of our assets to another company and (ii) the date on which we merge or consolidate with or into another entity (other than a merger in which our pre-merger stockholders own a majority of the shares of the surviving entity). Success payments will be owed (if applicable) after measurement of the value of our common stock in connection with the following valuation dates during the success payment period: (1) the date of the first anniversary of our initial public offering; (2) the second anniversary of such date; (3) each two year anniversary thereafter (i.e., the four year anniversary, six year anniversary, etc. of such date); (4) the date on which we sell, lease, transfer or exclusively license all or substantially all of our assets to another company; (5) the date on which we merge or consolidate with or into another entity (other than a merger in which our pre-merger stockholders own a majority of the shares of the surviving entity); and (6) the last day of the nine-year period. Any success payment will generally be made within 45 days after the applicable valuation date, except that in the case of a merger or sale of all of our company's assets, the success payment will be made on the earlier of the 90th day following the transaction or the first date that transaction proceeds are paid to any of our stockholders. In the case of (1), (2) and (3), the value of our common stock will be determined by the average trading price of a share of our common stock over the consecutive 90-day period preceding the date the success payment is made; the value will otherwise be determined either, in the case of a merger or stock sale, by the consideration paid in the transaction for each share of our stock or the stock of the acquiring entity (or their parent or affiliate). The amount of a success payment is determined based on whether the value of our common stock meets or exceeds certain specified threshold values ascending from $18.29 per share to $91.44 per share, in each case subject to adjustment for any stock dividend, stock split, combination of shares or other similar events. Each threshold is associated with a success payment, ascending from $10.0 million at $18.29 per share to a cumulative total of $200.0 million at $91.44 per share, payable if such threshold is reached. Any previous success payments made to Stanford are credited against the success payment owed as of any valuation date, so that Stanford does not receive multiple success payments in connection with the same threshold. The success payments paid to Stanford will not exceed, in aggregate, $200.0 million, which would be owed only when the value of the common stock reaches $91.44 per share. To date, no success payments have been incurred as the per share fair value of our common stock was below the price required for payment.

GSK Collaboration and License Agreement

In 2019, we entered into a collaboration and license agreement with GlaxoSmithKline (GSK) that became effective on July 7, 2019 and was amended in June 2020 and December 2021 (GSK Agreement) for potential T-cell therapies that apply our platform technologies and cell therapy innovations with T-cell receptors (TCRs) or chimeric antigen receptors (CARs) under distinct collaboration programs. The GSK Agreement defined two initial collaboration targets, CD19 and NY-ESO-1, and allowed GSK to nominate seven additional targets through July 2024. After agreeing on the programs for those targets, we were expected to perform research and development services for each agreed program up until a defined point (GSK Option Point), at which time GSK would decide whether or not to exercise an option to obtain a license from us (License Option) and take over the future development and commercialization. For the LYL331 program (NY-ESO-1 TCR with c-Jun), GSK exercised the License Option in April 2021 and assumed sole responsibility for future development and commercialization of the program at its own cost and expense. No IND for LYL331 was submitted to the U.S. Food and Drug Administration (FDA). For the LYL132 program (NY-ESO-1 TCR with Epi-R), we filed an IND application, which cleared in January 2022, though no patients were treated. The program targeting CD19 was a research effort. No additional targets were nominated over the term of the GSK Agreement. GSK terminated the GSK Agreement effective December 24, 2022 and Lyell has discontinued any further work on these programs.

We received a non-refundable upfront payment of $45.0 million under the GSK Agreement. In connection with the GSK Agreement, in May 2019, we also entered into a stock purchase agreement with GSK (GSK Stock Purchase Agreement), pursuant to which we agreed to sell 30,253,189 shares of Series AA convertible preferred stock at a price of $6.78 per share, which was above the issuance date estimated fair value of $4.84 per share. The difference between the per share values resulted in $58.6 million additional deemed consideration, bringing the total upfront payment of the GSK Agreement to $103.6 million.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from our collaborators or other third parties. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. We also rely on trade secrets and know-how relating to our proprietary technology and product candidates, continuing innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of cell and gene therapy. We additionally plan to rely on data exclusivity, market exclusivity and patent term extensions when available, and if appropriate, may seek and rely on regulatory protection afforded through orphan drug designations. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned by third parties; to defend and enforce our proprietary rights, including our patents; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

We have in-licensed and procured, and filed for numerous patent applications, which include claims directed to compositions, methods of use, processes, dosing and formulations, and possess substantial know-how and trade secrets relating to the development and commercialization of our cell engineering technology platforms and related product candidates, including related manufacturing processes and protocols. Our intellectual property strategy is designed to provide multi-layered protection covering our T-cell reprogramming technologies, including but not limited to c-Jun, NR4A3, Epi-R and Stim-R, as well as various aspects of our product candidates. For all patent applications, we determine claiming strategy on a case-by-case basis. We may file patent applications containing claims for protection of all useful applications of our proprietary technology platforms and any products, as well as new applications and/or uses we discover for existing technology platforms and products. We continuously reassess the number and type of patent applications, as well as the pending and issued patent claims, to ensure that maximum coverage and value are obtained for our processes and compositions. Further, claims may be modified during patent prosecution to meet our intellectual property and business needs. Notwithstanding these efforts, we cannot be sure that any patents will be granted with respect to any patent application we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or patents that may be licensed or granted to us in the future will not be challenged, invalidated or circumvented or that such patents will be commercially useful in protecting our technologies.

As of February 1, 2023, our in-licensed and owned patent portfolio consists of over 40 issued patents and over 135 pending patent applications that we have licensed and over 100 pending patent applications that we own. Our portfolio

covers various aspects of our T-cell reprogramming technologies, c-Jun, NR4A3, Epi-R and Stim-R, as well as our product candidates. The patents and patent applications in our portfolio are held primarily in the United States, Europe, Canada, Japan and Australia. For information related to our in-licensed intellectual property, see the subsection titled under "— License, Collaboration and Success Payment Agreements."

Individual patents extend for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States are effective for 20 years from the earliest nonprovisional filing date. In the United States, a patent's term may be lengthened by patent term adjustment (PTA), which compensates a patentee for administrative delays by the USPTO in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. In addition, in certain instances, the patent term of a U.S. patent that covers an FDA-approved drug may also be eligible for extension to recapture a portion of the term effectively lost as a result of clinical trials and the FDA regulatory review period, such extension is referred to as patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. However, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. The duration of patents outside of the United States varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest nonprovisional filing date. The actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

As of February 1, 2023, our registered trademark portfolio currently contains over 165 registered trademarks and pending trademark applications, consisting of approximately 9 pending trademark applications in the United States, over 80 foreign pending trademark applications in Argentina, Brazil, Canada, China, Hong Kong, India, Israel, Mexico, Oman, South Korea, Russia, Singapore, South Africa, the United Arab Emirates and Venezuela; and over 75 trademark registrations in the following countries through national filings: Australia, Brazil, China, Colombia, Costa Rica, European Union, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Oman, Russia, South Korea, Switzerland, the United Arab Emirates, the United Kingdom and Venezuela.

We may also rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets are difficult to protect. We seek to protect our technology and product candidates, in part, by entering into confidentiality agreements with those who have access to our confidential information, including our employees, contractors, consultants, collaborators and advisors. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or may be independently discovered by competitors. To the extent that our employees, contractors, consultants, collaborators and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For this and more comprehensive risks related to our proprietary technology, inventions, improvements and product candidates, see the subsection titled "Risk Factors — Risks Relating to Our Intellectual Property."

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We intend to either build a commercial infrastructure to support sales of any approved products or outsource this function to third parties. We intend to evaluate opportunities to work with partners that enhance our capabilities with respect to the development and commercialization of LYL797, LYL845, LYL119 and any other product candidates we may develop. In addition, we intend to commercialize our product candidates, if approved, in key markets either alone or with partners to maximize the worldwide commercial potential of our programs.

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along

with third-party contractors, will be required to navigate the various nonclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct trials or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Biologics Regulation

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal, state, local and foreign statutes and regulations. The process required by the FDA before biologics may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practice requirements (GLP);
- submission to the FDA of an IND application, which must become effective before clinical trials may begin;
- approval by an Institutional Review Board (IRB) or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations (commonly referred to as GCP), regulations and any additional requirements for the protection of human research subjects and their health information to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a Biologics License Application (BLA), after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency and, if applicable, to assess compliance with the FDA's current Good Tissue Practices (cGTPs) requirements for the use of human cellular and tissue products, and of selected clinical investigation sites to assess compliance with GCPs;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Before testing any biological product candidate in humans, the product candidate enters the nonclinical testing stage. Nonclinical tests, also referred to as preclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLPs.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical trials. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight of an Institutional Biosafety Committee (IBC) as set forth in the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules (the NIH Guidelines). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees

research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These trials are designed to test the safety, dosage tolerance, absorption, metabolism and excretion of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product in the intended therapeutic indication, particularly for long-term safety follow-up. These so-called Phase 4 trials may also be made a condition to approval of the BLA.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review by the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from nonclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including trials initiated by independent investigators. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within 10 months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may also convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. For a product candidate that is also a human cellular or tissue product, the FDA also will not approve the application if the manufacturer is not in compliance with cGTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues and cellular and tissue-based products (HCT/Ps), which are human cells or tissue intended for implantation, transplant, infusion or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities, or data collected from clinical trial sites are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a REMS, to ensure the benefits of the product outweigh its risks, or otherwise limit the scope of any approval. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-marketing trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the fast track program is intended to expedite or facilitate the process for reviewing new products that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Specifically, new biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a

fast track product at any time during the clinical development of the product. The sponsor of a fast track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug or biologic submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product candidate is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological product designated for priority review in an effort to facilitate the review. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to 10 months under standard review).

Additionally, product candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In 2017, the FDA established a new regenerative medicine advanced therapy (RMAT) designation, which is intended to facilitate an efficient development program for, and expedite review of, any drug or biologic that meets the following criteria: (i) the drug or biologic qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (ii) the drug or biologic is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug or biologic has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides all the benefits of breakthrough therapy designation, including more frequent meetings with the FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of clinical trial sites, including through expansion of trials to additional sites. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through submission of clinical evidence, clinical trials, patient registries or other sources of real-world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of such therapy. Fast track designation, breakthrough therapy designation, priority review, accelerated approval and RMAT designation do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for a particular drug or biologic for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Biologics are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Biologic manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain GMP compliance. Changes to the manufacturing process or facility are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or untitled letters;
- clinical holds on clinical trials;

- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits or civil or criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe, in their independent medical judgment, that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), includes a subtitle called the Biologics Price Competition and Innovation Act (BPCIA), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve (12) years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study. The BPCIA is complex and continues to be interpreted

and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and impact of the BPCIA is subject to significant uncertainty.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials.

In the European Union, for example, a clinical trial application (CTA) must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and the IRB, respectively. Once the CTA is approved in accordance with the applicable requirements, clinical trial development may proceed. The requirements and process governing the conduct of clinical trials are to a significant extent harmonized at the European Union-level but could vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. The way clinical trials are conducted in the European Union underwent a major change when the Clinical Trial Regulation (Regulation (EU) 536/2014) came into application in January 2022. The Regulation harmonizes the assessment and supervision processes for clinical trials throughout the European Union via a Clinical Trials Information System, which will contain a centralized European Union portal and database.

To obtain regulatory approval of an investigational biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements. Innovative products that target an unmet medical need may be eligible for a number of expedited development and review programs in the European Union, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the United States. Such products are generally eligible for accelerated assessment and may also benefit from different types of fast track approvals, such as a conditional marketing authorization or a marketing authorization under exceptional circumstances granted on the basis of less comprehensive clinical data than normally required (respectively in the likelihood that the sponsor will provide such data within an agreed timeframe or when comprehensive data cannot be obtained even after authorization).

The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric trials. No extension to any supplementary protection certificate can be granted on the basis of pediatric trials for orphan indications.

The criteria for designating an "orphan medicinal product" in the European Union are similar in principle to those in the United States. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the European Union when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the European Union to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the European Union, or if such a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing

authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan drug designation must be submitted before the application for marketing authorization. The applicant will receive a fee reduction for the marketing authorization application if the orphan drug designation has been granted, but not if the designation is still pending at the time the marketing authorization is submitted. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- The second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- The applicant consents to a second orphan medicinal product application; or
- The applicant cannot supply enough orphan medicinal product.

The medicinal products we are developing, which are based on genes, cells or tissues, may be considered advanced therapy medicinal products (ATMPs) in the European Union if they meet the scientific criteria for defining an ATMP. The principles of the aforementioned medicines legislation apply to ATMPs. All ATMPs must obtain a marketing authorization from the EMA and are regulated through the centralized authorization procedure. Regulation (EC) No 1394/2007 (the ATMP Regulation) provides specific incentives to accelerate the development of such products, including fee reductions for scientific advice, an ATMP classification procedure (for all developers) and a certification procedure for quality and nonclinical data (for SMEs only).

If tissues and cells are being used as starting materials in a medicinal product we may also need to comply with the requirements of Directive 2004/23/EC (the European Tissues and Cells Directive) covering standards for donation, procurement and testing, processing, preservation, storage and distribution of human tissues and cells, as well as its technical implementing directives; and Directive 2015/566, as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells.

In the European Union, early access mechanisms for innovative medicines (such as compassionate use programs and named patient supplies), pricing and reimbursement and promotion and advertising are subject to national regulations and oversight by national competent authorities and therefore significantly vary from country to country.

Sanctions for non-compliance with the aforementioned requirements, which may include administrative and criminal penalties, are generally determined and enforced at national level. However, under the European Union financial penalties regime, the EMA can investigate and report on alleged breaches of the European Union pharmaceutical rules by holders of a marketing authorization for centrally authorized medicinal products and the European Commission could adopt decisions imposing significant financial penalties on infringing marketing authorization holders.

The United Kingdom left the European Union on January 31, 2020 (Brexit). Following the Transition Period which ended on December 31, 2020, Brexit could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom in the coming years.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Other Healthcare Laws

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business and may

constrain the financial arrangements and relationships through which we research, sell, market and distribute any products for which we obtain marketing approval. Such laws include, without limitation, federal and state anti-kickback, fraud and abuse, false claims, data privacy and security, price reporting and physician and other health care provider transparency laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and imprisonment.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor but the exceptions and safe harbors are drawn narrowly and require strict compliance in order to offer protection. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

Additionally, the intent standard under the Anti-Kickback Statute and the criminal healthcare fraud statutes under the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) was amended by the ACA to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (FCA) (discussed below).

The FCA prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses.

HIPAA also created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the federal Physician Payments Sunshine Act within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners) and teaching hospitals and certain ownership and investment interests held by these physicians and their immediate family members.

We may also be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and its implementing regulations, impose requirements on covered entities, including certain healthcare providers, health plans, healthcare clearinghouses and their respective business associates that create, receive,

maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations

Coverage and Reimbursement

Sales of any product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a product is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational. A third-party payor could also require that certain lines of therapy be completed or failed prior to reimbursing our therapy. The principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services (HHS). CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Third-party payors determine which products and procedures they will cover and establish reimbursement levels. Even if a third-party payor covers a particular product or procedure, the resulting reimbursement payment rates may not be adequate. These third-party payors are increasingly reducing coverage and reimbursement for medical products, drugs and services. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Healthcare Reform

In the United States, in March 2010, the ACA was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement adjustments and changes to fraud and abuse laws. For example, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- required manufacturers to participate in a coverage gap discount program, under which they must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs;
- expanded the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, the Tax Act was enacted, which includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such additional challenges and healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have also been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which began in 2013 and will remain in effect through 2031. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several Congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented, but it is likely to have a significant impact on the pharmaceutical industry.

Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We anticipate that these new laws will result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products (if approved). In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition and results of operations. For example, it is possible that additional governmental action is taken in response to address the COVID-19 pandemic.

Other Privacy and Security Laws

We may become subject to privacy laws in the jurisdictions in which we are established or in which we sell or market our products or run clinical trials. For example, in Europe we may be subject to Regulation (EU) 2016/679, the General Data Protection Regulation (GDPR) in relation to our collection, control, processing and other use of personal data (i.e., data relating to an identifiable living individual). The GDPR is directly applicable in each European Union Member State, however, it provides that European Union Member States may introduce further conditions, including limitations that could limit our ability to collect, use and share personal data (including health and medical information), or could cause our compliance costs to increase, ultimately having an adverse impact on our business.

The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and implement policies as part of its mandated privacy governance framework. It also requires data controllers to be transparent and disclose to data subjects (in a concise, intelligible and easily accessible form) how their personal information is to be used, imposes limitations on retention of personal data; defines pseudonymized (i.e., key-coded) data; introduces mandatory data breach notification requirements; and sets higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. We are subject to the supervision of local data protection authorities in those European Union jurisdictions where we are established or otherwise subject to the GDPR. Fines for certain breaches of the GDPR are significant: up to the greater of €20 million or 4% of total global annual turnover. Further, following the withdrawal of the United Kingdom from the European Union on January 31, 2020, pursuant to the transitional arrangements agreed between the United Kingdom and the European Union, we will have to comply with the GDPR and separately the GDPR as implemented in the United Kingdom, each regime having the ability to fine up to the greater of €20 million/ £17 million or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, including how data transfers between European Union member states and the United Kingdom will be treated. These changes may lead to additional compliance costs and could increase our overall risk. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, orders to cease/change our use of data, enforcement notices, or potential civil claims including class action type litigation.

In addition, the GDPR includes restrictions on cross-border data transfers. Certain aspects of cross-border data transfers under the GDPR are uncertain as the result of legal proceedings in the European Union, including a recent decision by the Court of Justice for the European Union that invalidated the EU-U.S. Privacy Shield and, to some extent, called into question the efficacy and legality of using standard contract clauses. This may increase the complexity of transferring personal data across borders. The GDPR will increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. We are also subject to European Union rules with respect to cross-border transfers of personal data out of the European Union and European Economic Area (EEA). Recent legal developments in the European Union have created complexity and uncertainty regarding transfers of personal data from the EEA to the United States. On July 16, 2020, the Court of Justice of the European Union (CJEU) invalidated the EU-US Privacy Shield Framework (Privacy Shield) under which personal data could be transferred from the EEA to US entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy, subject to certain conditions, of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism), future regulatory guidance could result in changes to the use of standard contractual clauses. As supervisory authorities issue further guidance on personal

data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, the vote in the United Kingdom in favor of exiting the European Union, referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. Specifically, while the Data Protection Act of 2018, which "implements" and complements the GDPR achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, aspects of data protection in the United Kingdom, such as the transfer of data from the EEA to the United Kingdom, remain uncertain. During the period of "transition" (i.e., until December 31, 2020), European Union law will continue to apply in the United Kingdom, including the GDPR, after which the GDPR will be converted into United Kingdom law. Beginning in 2021, the United Kingdom will be a "third country" under the GDPR.

In addition, California enacted the California Consumer Privacy Act (CCPA), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal information. This private right of action may increase the likelihood of, and risks associated with, data breach litigation. The CCPA became effective on January 1, 2020, and (i) allows enforcement by the California Attorney General, with fines set at $2,500 per violation (i.e., per person) or $7,500 per intentional violation and (ii) authorizes private lawsuits to recover statutory damages for certain data breaches. In addition, laws in all 50 U.S. states require businesses to provide notice to consumers whose personal information has been disclosed as a result of a data breach. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we would become subject if it is enacted. The CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information. Further, the California Privacy Rights Act (the CPRA) recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required.

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977 (FCPA), prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Employees and Human Capital Management

Our Mission

We are a clinical stage T-cell reprogramming company dedicated to developing novel cell therapies to improve the lives of people with solid tumor cancers. We strive to create an environment where everyone can do the best work of their lives, be themselves and thrive personally and professionally. Our culture is grounded by innovative science and demands excellence. Patients are waiting for better therapies, and it is this need that drives our sense of urgency to achieve our important mission.

Our Values

We believe success comes when we and our employees align our core values with our mission to translate our ground-breaking science into medicines with the potential to transform patients' lives. Our core values are:

- *Science*: We focus and execute on the critical efforts that matter most.

- *Courage*: We are bold and willing to think and act differently.
- *Respect*: We seek to understand and communicate directly, transparently and honestly.
- *Collaboration*: We work across teams to solve our most challenging problems to continually improve and learn.

Our Employees

We view our employees as valuable assets in serving our mission. We compete in the highly competitive biotechnology industry, and attracting, retaining and developing a diverse group of talented employees is crucial to our strategy and our ability to compete effectively. We need to grow the size of our organization in order to support our current research, product development and manufacturing efforts and our future plans for commercializing our product candidates, if approved. This growth is critical to our success. There currently is a shortage of skilled individuals with substantial experience discovering, developing and manufacturing cell therapy medicines, which is likely to continue. We also operate in areas such as data capture and analytics, machine learning and artificial intelligence. As a result, competition for talent is intense and the turnover rate can be high. We face substantial competition among numerous biopharmaceutical companies and academic institutions as well as technology companies for individuals with these skills.

As of December 31, 2022, we had 274 employees, over 75% of whom were engaged in research and development activities, technical operations and process sciences. Our employees are highly skilled, and many hold advanced degrees. Many of our employees have experience with the development of cell therapies. Substantially all of our employees are located in California and Washington. None of our employees are subject to a collective bargaining agreement nor represented by labor unions. We consider our relationship with our employees to be good.

Developing our employees is important, and we focus on providing training and opportunities for development and advancement. Learning and development, training and career advancement are an integral part of retaining our employees. We hold talent discussions regularly, which include promotion cycles across functions and role levels. In 2022, we created a comprehensive talent management framework, which includes role leveling, competencies, training by role level and competencies and development planning.

Since inception, our employee turnover has remained consistently below average for the U.S. life sciences industry generally, as well as for life sciences companies located in Northern California and the Pacific Northwest. Given our expanding operations and need to further grow our headcount to support our business, we continually assess employee turnover, recruitment initiatives, compensation and benefits programs, safety in performing critical laboratory work, diversity and other matters relevant to human capital management, and we review results with our board of directors on a periodic basis.

Our Compensation and Benefits

Given the highly competitive nature of our industry and the importance of recruitment and retention to our success, we strive to provide our employees with what we believe is a competitive and comprehensive total rewards package of compensation, benefits and services. This package includes competitive market pay, healthcare benefits for employees and family members, a flexible spending account, paid time off benefits, family leave, flexible work schedules, flexible work locations, 401(k) matching, an employee assistance program and a new wellness program. In addition, we offer employees the benefit of equity ownership in the company through stock option grants and restricted stock units. Our employees are also eligible to participate in an employee stock purchase plan, which offers the opportunity to purchase our common stock at a discount of 15%.

Our Commitment to Diversity, Belonging, Inclusion and Equity

We strongly believe in a diverse workplace where all employees can thrive in an inclusive environment free from discrimination, harassment, bias and prejudice. We aim to treat all individuals with respect and dignity and to provide all employees with equal opportunity and fair treatment. By embracing diversity and inclusion, we seek to create an organization committed to working together to develop innovative solutions consistent with our values and in support of accomplishing our mission. Not only is a diverse, equitable and inclusive mindset and culture critical to an engaged and committed workplace, but it is also imperative to understanding and meeting the needs of the patients we seek to help with our medicines.

With the support of our executive leadership team, we convened a Diversity, Belonging, Inclusion and Equity (DBIE) working group in 2020 comprised of a diverse group of employees tasked with designing and implementing specific initiatives to promote greater diversity, belonging, inclusion and equity at Lyell. We also engaged an experienced DBIE consultant to advise us on the design and planning of new DBIE initiatives based on expertise and external benchmarking. The DBIE working group formalized a DBIE statement, a framework, a tactical plan and advanced a commitment to the importance of DBIE. In 2022, we offered several DBIE speaker events, rolled out Inclusivity@Lyell

training sessions, utilized Textio to reduce gender bias in role descriptions and postings, and tried several new recruiting sources to further diversify candidate pools. Although we are proud of our progress to date, we have and will continue to conduct relevant training and provide guidance with respect to best practices of similarly situated companies.

As of December 31, 2022, our employees were self-reportedly approximately 49.3% percent women and 47.4% of our employees were self-reportedly ethnically or racially diverse with 33.6% Asian, 4.0% Black or African American, 6.2% Hispanic or Latino and 3.6% of other minority groups or two or more races.

We believe in equitable pay practices and our compensation practices and philosophies are reviewed regularly. We establish components and ranges of compensation based on market and benchmark data. Within this context, we strive to pay all employees equitably within a reasonable range, taking into consideration factors such as role, market data, internal equity, job location, relevant experience, and individual and company performance. We review and analyze our compensation decisions for individual employees and our workforce as a whole on at least an annual basis. In 2022, we engaged an independent external firm to conduct a pay equity analysis, the results of which we believe demonstrated that our compensation practices and structure are equitable. If we identify employees with unjustified pay gaps that do not align with our pay philosophy, we review and take appropriate action to ensure fidelity between our stated philosophy and actions.

Employee Safety and COVID-19

Employee safety and well-being is of paramount importance to us in any year and has been of particular focus since 2020 in light of the evolving and continuing effects of the COVID-19 pandemic. In response to the pandemic, we have supported our employees and government efforts to curb the COVID-19 pandemic through safety and communication efforts and investments.

One of our top priorities is the protection of the health and well-being of our employees, partners and communities. While our employees have returned to work in our offices on a flexible-basis, all employees and substantially all other third parties that come onsite are required to be fully vaccinated. We continue to maintain rigorous procedures to address actual and suspected COVID-19 cases and potential exposure, including increased cleaning of high touch areas, provision of hand sanitizing stations and limited on-site contract tracing as needed, and we expect to continue such measures for the near foreseeable future.

We continue to closely monitor the COVID-19 pandemic and have strived to follow recommended containment and mitigation measures, including the guidance from the Centers for Disease Control and Prevention (CDC), Occupational Safety and Health Administration (OSHA), the states of California and Washington (including their state OSHA programs) and applicable counties.

Available Information

Our website address is www.lyell.com. We file annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. The SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information that we file with the SEC electronically. Copies of our reports on Form 10-K, Forms 10-Q, Forms 8-K, and amendments to those reports may also be obtained, free of charge, electronically on the investor relations page on our website located at ir.lyell.com as soon as reasonably practical after we file such material with, or furnish it to, the SEC.

We also use the investor relations page on our website as a channel of distribution for important company information. Important information, including press releases, analyst presentations and financial information regarding us, as well as corporate governance information, is routinely posted and accessible on the investor relations page on our website. Information on or that can be accessed through our website is not part of this Annual Report on Form 10-K, and the inclusion of our website address is an inactive textual reference only.

Item 1A. Risk Factors

Our business involves significant risks, some of which are described below. You should carefully consider the risks described below, as well as the other information contained in this Annual Report on Form 10-K, including our audited consolidated financial statements and unaudited condensed consolidated financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risks Related to Our Financial Condition, Limited Operating History and Need for Additional Capital

We are an early clinical stage biopharmaceutical company and have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing net losses for the foreseeable future.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to prove effective, gain regulatory approval or become commercially viable. We are an early clinical stage biopharmaceutical company, and we do not have any products approved by regulatory authorities and have incurred significant research, development and other expenses related to our ongoing operations and expect to continue to incur such expenses. Since our inception, we have not generated any revenue from product sales and have incurred significant net losses. Substantially all of our net losses since inception have resulted from our research and development programs and general and administrative costs associated with our operations. As of December 31, 2022, we had an accumulated deficit of $767.5 million.

We do not expect to generate revenue from product sales for the foreseeable future, if at all. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate these losses to increase as we continue to research, develop and seek regulatory approvals for our product candidates, expand our manufacturing capabilities, in-license or acquire additional technologies and potentially begin to commercialize product candidates that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period to period comparison of our results of operations may not be a good indication of our future performance. If any of our product candidates fails in research and development or clinical trials or does not gain regulatory approval, or, if approved, fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We anticipate that our expenses and operating losses will increase substantially over the foreseeable future. The expected increase in expenses will be driven in large part by our ongoing activities, if and as we:

- continue nonclinical development of our current and future product candidates and initiate additional nonclinical studies;
- commence and continue clinical trials of our current and future product candidates;
- advance our genetic and epigenetic reprogramming technologies as well as other research and development efforts;
- attract, hire and retain qualified personnel;
- seek regulatory approval of our current and future product candidates;
- expand our manufacturing and process development capabilities;
- expand our operational, financial and management systems;
- acquire and license technology or technology platforms;
- continue to develop, protect and defend our intellectual property portfolio; and
- incur additional legal, accounting or other expenses in operating our business, including the additional costs associated with operating as a public company.

We operate in a rapidly evolving field and have a limited operating history, which may make it difficult to evaluate the success of our business to date and to assess our future viability.

We operate in a rapidly evolving field and, having commenced operations in June 2018, have a limited operating history, which makes it difficult to evaluate our business and prospects. Our primary activities to date have included developing T-cell therapies, performing research and development, acquiring technology, entering into strategic collaboration and license agreements, enabling and executing manufacturing activities in support of our product candidate development efforts, organizing and staffing the company, business planning, establishing our intellectual property portfolio, regulatory submissions and other preparations to initiate clinical trials, raising capital and providing general and administrative support for these activities. Any predictions about our future success, performance or viability, may not be as accurate as they could be if we had a longer operating history or approved products on the market.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. We expect our

financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, any of our quarterly or annual periods' results are not indicative of future operating performance.

We currently have no products approved for sale and have never generated revenue from product sales. We may never generate revenue from product sales or achieve profitability.

To date, we have not generated any revenues from product sales. Our ability to generate revenues from product sales and achieve profitability will depend on our ability to successfully develop and subsequently obtain regulatory approval for and commercialize, our product candidates. Our ability to generate revenues and achieve profitability also depends on a number of additional factors, including our ability to:

- successfully complete our research activities to identify the technologies and product candidates to further investigate in clinical trials;
- successfully complete development activities, including the necessary clinical trials;
- complete and submit regulatory submissions to the FDA, the European Medicines Agency (EMA) or other agencies and obtain regulatory approval for indications for which there is a commercial market;
- obtain coverage and adequate reimbursement from third parties, including government and private payors;
- set commercially viable prices for our products, if any;
- develop manufacturing and distribution processes for our product candidates;
- produce commercial quantities of our products at acceptable cost levels;
- maintain adequate supply of our product candidates, including the starting materials and reagents needed;
- maintain the supply of our product candidates in a manner that is compliant with global legal requirements or to the extent necessary;
- establish and maintain manufacturing relationships with reliable third parties;
- achieve market acceptance of our products, if any;
- attract, hire and retain qualified personnel;
- protect our rights in our intellectual property portfolio;
- develop a commercial organization capable of sales, marketing and distribution for any products we intend to sell ourselves in the markets in which we choose to commercialize on our own; and
- find suitable distribution partners to help us market, sell and distribute our approved products in other markets.

Our revenues for any product for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price and whether we own the commercial rights for that territory. In addition, we anticipate incurring significant costs associated with commercializing any approved product. As a result, even if we generate revenue from product sales, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and may be forced to reduce our operations.

We will require substantial additional capital to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

We expect to expend substantial resources for the foreseeable future to advance and expand our research pipeline, conduct nonclinical studies and pursue clinical development and manufacturing of our product candidates. We also expect to continue to expend resources for the development of our technology platforms. These expenditures will include costs associated with research and development, potentially acquiring or licensing new technologies, conducting nonclinical studies and clinical trials and potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. We will also need to make significant expenditures to develop a commercial organization capable of sales, marketing and distribution for any products, if any, that we intend to sell ourselves in the markets in which we choose to commercialize. In addition, we may be required to make substantial payments related to our success payment agreements and other contingent consideration payments under our license and collaboration agreements. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably

estimate the actual amounts necessary to successfully complete the discovery, development and commercialization of our potential product candidates, and other unanticipated costs may arise.

As of December 31, 2022, we had approximately $710.3 million in cash, cash equivalents and marketable securities. As a result of expense timing, as well as diligent expense management, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to meet our working capital and capital expenditure needs into 2026. However, our future capital requirements and the period for which our existing resources will support our operations may vary significantly from what we expect, and we will in any event require additional capital to complete clinical development of any of our current programs.

We do not have any committed external source of funds. Additional funds may not be available when we need them on terms that are acceptable to us, or at all, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions or conditions in the biotechnology sector of the market, including disruptions to or volatility in the credit and financial markets in the United States and worldwide resulting from the COVID-19 pandemic and its effects, actual or perceived changes in interest rates and economic inflation and the current or anticipated impact of geopolitical instability. If adequate funds are not available to us on a timely basis, including pursuant to the Equity Distribution Agreement, we may be required to delay, limit, reduce or terminate nonclinical studies, clinical trials or other development activities for our product candidates or delay, limit, reduce or terminate our establishment of sales, marketing and distribution capabilities or other activities that may be necessary to commercialize our product candidates.

Our success payment obligations in our success payment agreements may result in dilution to our stockholders or may be a drain on our cash resources to satisfy the payment obligations.

We agreed to make success payments payable in cash or publicly-tradeable shares of our common stock at our discretion pursuant to our success payment agreements with Fred Hutch and Stanford. On each contractually prescribed measurement date, we may be required to make success payments based on increases in the per share fair value of our common stock. The total amount of success payments that we may become obligated to make is currently $400.0 million and may increase in the future due to amendments of our existing success payment agreements. For information related to our success payment obligations, see Note 3, *License, Collaboration and Success Payment Agreements*, in the accompanying notes to the audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

In order to satisfy our obligations to make these success payments, if and when they are triggered, we may issue equity or convertible debt securities that may cause dilution to our stockholders, or we may use our existing cash to satisfy the success payment obligation in cash, which may adversely affect our financial position. In addition, these success payments may impede our ability to raise money in future public offerings of debt or equity securities or to obtain a third-party line of credit.

The success payment agreements may cause operating results to fluctuate significantly from quarter to quarter and year to year, which may reduce the usefulness of our consolidated financial statements.

Our success payment obligations are recorded as liabilities on our consolidated balance sheets. Under U.S. generally accepted accounting principles (GAAP), we are required to estimate the fair value of these liabilities as of each quarter end and changes in the estimated fair value are accreted to research and development expense over the service period of the collaboration agreement. Factors that may lead to increases or decreases in the estimated fair value of this liability include, among others, changes in the value of the common stock, changes in volatility and changes in the risk-free rate. As a result, our operating results and financial condition as reported by GAAP may fluctuate significantly from quarter to quarter and from year to year and may reduce the usefulness of our GAAP consolidated financial statements. See Note 3, *License, Collaboration and Success Payment Agreements*, in the accompanying notes to the audited consolidated financial statement included in Part II, Item 8 of this Annual Report on Form 10-K for additional information.

Risks Related to Our Business and Industry

We are early in our research and development efforts and just beginning clinical development of our product candidates. If we are unable to successfully develop and commercialize product candidates or experience significant delays in doing so, our business may be harmed.

We are early in our research and development efforts and are just beginning clinical development of our product candidates. Besides LYL797 and LYL845, which are in Phase 1 clinical development, our other proprietary product candidates are currently in nonclinical development. We have not yet demonstrated our ability to successfully complete any clinical trials (including any Phase 3 or other pivotal clinical trials), obtain regulatory approvals, manufacture a commercial

scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. We have invested substantial resources in developing our technology platforms and our product candidates, conducting nonclinical studies, commencing clinical trials and building our manufacturing facilities and capabilities, each of which will be required prior to any regulatory approval and commercialization. Our ability to generate revenue from product sales, which we do not expect will occur for several years, if ever, will depend heavily on the successful research and development and eventual commercialization of one or more product candidates. The success of our efforts to identify and develop product candidates will depend on many factors, including the following:

- timely and successful completion of our nonclinical studies and research activities to identify and develop product candidates to investigate in clinical trials;
- submission of INDs to the FDA to proceed with clinical trials, or comparable applications to foreign regulatory authorities that allow the commencement of our planned clinical trials for our product candidates;
- successful enrollment and completion of clinical trials in compliance with GCP requirements with positive results;
- the level of efficacy observed with our product candidates;
- the prevalence and severity of adverse events experienced with any of our product candidates;
- successfully developing, or making arrangements with third parties for, manufacturing and distribution processes for our product candidates and for commercial manufacturing and distribution for any of our product candidates that receive regulatory approval;
- receipt of timely regulatory approvals from applicable authorities for our product candidates for their intended uses;
- protecting our rights in our intellectual property portfolio, including by obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- establishing capabilities and infrastructure to obtain the tumor tissues needed to develop and, if successful, commercialize approved products;
- manufacturing our product candidates at an acceptable cost;
- launching commercial sales of our products, if approved by applicable regulatory authorities, whether alone or in collaboration with others;
- acceptance of our products, if approved by applicable regulatory authorities, by patients and the medical community;
- obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our products, if approved by applicable regulatory authorities;
- effectively competing with other marketed therapies;
- maintaining compliance with regulatory requirements, including the cGMP requirements;
- maintaining a continued acceptable benefit/risk profile of the products following approval; and
- maintaining and growing an organization of scientists and functional experts who can develop and commercialize our products and technology.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our product candidates, which could harm our business. If we do not receive marketing approvals for any product candidate we develop, we may not be able to continue our operations.

Our product candidates and technology platforms are based on novel technologies that are unproven and may not result in approvable or marketable products, which exposes us to unforeseen risks and makes it difficult for us to predict the time and cost of product development and potential for regulatory approval, and we may not be successful in our efforts to use and expand our technology platforms to build a pipeline of product candidates.

We are seeking to identify and develop a broad pipeline of product candidates using our proprietary technology platforms. The scientific research that forms the basis of our efforts to develop product candidates with our technology platforms is still ongoing. We are not aware of any FDA approved therapeutics utilizing similar technology. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on our technology platforms are both preliminary and limited. Additionally, although LYL797 and LYL845 are in Phase 1 clinical development, our current

clinical data are limited, and nonclinical data from murine tumor models and *in vitro* experiments with tumor cell lines may not translate into humans or may not accurately predict the safety and efficacy of our product candidates in humans. As a result, we are exposed to a number of unforeseen risks, and it is difficult to predict the types of challenges and risks that we may encounter during development of our product candidates.

Given the novelty of our technology platforms, we intend to work closely with the FDA and comparable foreign regulatory authorities to perform the requisite scientific analyses and evaluation of our methods to obtain regulatory approval for our product candidates; however, due to a lack of relevant experiences, the regulatory pathway with the FDA and comparable regulatory authorities may be more complex and time-consuming relative to other more well-known therapeutics. Even if we obtain human data to support our product candidates, the FDA or comparable foreign regulatory agencies may lack experience in evaluating the safety and efficacy of our product candidates developed using our technology platforms, which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our product candidates. The validation process takes time and resources, may require independent third-party analyses and may not be accepted or approved by the FDA and comparable foreign regulatory authorities. There can be no assurance as to the length of clinical development, the number of patients that the FDA may require to be enrolled in clinical trials to establish the safety, purity and potency of our product candidates or the acceptability to the FDA of data generated in these clinical trials to support marketing approvals. We cannot be certain that our approach will lead to the development of approvable or marketable products, alone or in combination with other therapies.

We are highly dependent on our key personnel and, if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, manufacturing, scientific and medical personnel. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors and our inability to find suitable replacements could result in delays in product development and harm our business. We conduct substantially all of our operations at our facilities in the San Francisco, Seattle and Bothell metropolitan areas. These regions are headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in these markets is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. For example, in 2022 our former Chief Executive Officer resigned for personal reasons and our former Chief General Counsel resigned to pursue opportunities elsewhere. We could experience additional resignations of other executives and employees in the future given the intensity of the competition for talent in the biotechnology industry, particularly in the San Francisco and Seattle metropolitan areas.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity that vests over time. The value to employees of equity incentives that vest over time may be significantly affected by factors beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

Any litigation or adversarial proceedings could be costly and time-consuming to defend.

We have been and may in the future become subject to legal proceedings and claims that arise in the ordinary course of business, such as claims brought by us or third parties in connection with commercial disputes or employment claims made by our current or former employees. Litigation or adversarial proceedings might result in substantial costs and may divert management's attention and resources, which might seriously harm our business, reputation, overall financial condition and operating results. For example, in February 2021, we filed a demand for arbitration seeking, among other things, rescission of each of the joint-development agreement (PACT Commitment Agreement) and stock purchase agreement (PACT SPA) we entered with PACT Pharma, Inc. (PACT) and recovery of the consideration paid thereunder. In October 2022, we entered into a settlement agreement with PACT to resolve the outstanding legal dispute. See Part I, Item 3, *Legal Proceedings*, of this Annual Report on Form 10-K for additional details regarding the outcome of our arbitration with PACT. Insurance might not cover such claims, might not provide sufficient payments to cover all the costs to resolve one or more such claims and might not continue to be available on terms acceptable to us. Any claim brought by us or against us that is uninsured or underinsured could result in unanticipated costs, thereby harming our business.

If we cannot maintain our company culture as we grow, our success and our business may be harmed.

We believe our culture has been a key contributor to our success to date. Any failure to preserve our culture could negatively affect our ability to retain and recruit personnel, which is critical to our growth, and to effectively focus on and pursue our objectives. As we grow and are required to implement more complex organizational management structures, we may find it increasingly difficult to maintain the beneficial aspects of our culture. If we fail to maintain our company culture, our business may be adversely affected.

We currently have no marketing, sales or distribution infrastructure, and we intend to either establish a sales and marketing infrastructure or outsource this function to a third party. Either of these commercialization strategies carries substantial risks to us.

We currently have no marketing, sales and distribution capabilities. To support commercial marketing and distribution of any of our product candidates that complete clinical development and are approved, we would either establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates in a legally compliant manner or outsource this function to a third party. There are risks involved if we decide to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services. To the extent that we enter into collaboration agreements with respect to marketing, sales or distribution, our product revenue may be lower than if we directly marketed or sold any approved products. Such collaborative arrangements with partners may place the commercialization of our products outside of our control and would make us subject to a number of risks, including that we may not be able to control the amount or timing of resources that our collaborative partner devotes to our products or that our collaborator's willingness or ability to complete its obligations, and our obligations under our arrangements may be adversely affected by business combinations or significant changes in our collaborator's business strategy.

If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize any approved products. If we are not successful in commercializing any approved products, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses, which would have a material adverse effect on our business, financial condition and results of operations.

Our business could continue to be adversely affected by the effects of health epidemics, including the COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations.

Our business could continue to be adversely affected by health epidemics, including the COVID-19 pandemic and its effects, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of potential clinical trial sites or other business operations. For example, the COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting employees, patients, communities and business operations, as well as the United States and international economy and financial markets. In this regard, the COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as significant reductions in business-related activities have occurred, supply chains have been disrupted and manufacturing and clinical development activities have been impacted.

Remote work policies, quarantines, shelter-in-place and similar government orders, shutdowns or other restrictions on the conduct of business operations related to the COVID-19 pandemic could materially and adversely affect our operations. Following guidance from federal, state and local authorities, we had previously implemented policies that restrict the number and nature of employees who can be on site, and such types of policies may be considered again in the future. We have also implemented preventative measures at our facilities, including requiring that each employee or contractor who enters a facility be vaccinated. In addition, we encourage all individuals on-site to follow recommendations for frequent hand washing and other precautions. In connection with these and potential future measures, we may be subject to claims based upon, arising out of or related to the COVID-19 pandemic and our actions and responses thereto, including any determinations that we have made and may make in the future with respect to our on-site operations. Further, current and future government restrictions as well as our remote work policies may materially and adversely impact productivity, disrupt our business and delay our nonclinical studies and clinical trial plans, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. We continue to evaluate the impact that the COVID-19 pandemic may have on our ability to effectively conduct our business operations as planned. However, there can be no assurance that we will be able to avoid materially adverse impacts from the evolving effects of the COVID-19 pandemic. The COVID-19 pandemic may continue to negatively impact healthcare and hospital resources, including both front-line and administrative staff, which may delay enrollment in our current and planned clinical trials. Some patients may not be able to comply with clinical trial protocols

due to potential quarantines, lack of healthcare support or potential interruptions of healthcare services, and we may be unable to obtain blood samples for testing.

The extent of the impact of the COVID-19 pandemic on our business, operations and development timelines and plans remains uncertain and will depend on future developments that cannot be predicted at this time. Such developments include the continued spread of the Omicron variants and subvariants in the U.S. and other countries and the potential emergence of other SARS-CoV-2 variants that may prove especially contagious or virulent, the ultimate duration of the pandemic and the resulting impact on our clinical trial plans, CROs, contract manufacturing organizations and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel, and the effectiveness of actions taken globally to contain and treat the disease, including the rate at which vaccinations or boosters are made available, the percentage of the population that becomes vaccinated or boosted and the effectiveness of the vaccines or boosters against Omicron, its subvariants or other SARS-CoV-2 variants. We do not yet know the full extent of potential delays or impacts on our business, our planned nonclinical studies or clinical trials, healthcare systems or the global economy, as a whole. The foregoing and other continued disruptions to our business, as a result of the evolving effects of the COVID-19 pandemic, could materially and adversely affect our business, results of operations, financial condition and cash flows. Furthermore, the effects of the COVID-19 pandemic could heighten the risks in certain of the other risk factors described herein.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

The global credit and financial markets have experienced extreme volatility and disruptions (including as a result of the COVID-19 pandemic and actual or perceived changes in interest rates and economic inflation), which has included severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, high inflation, uncertainty about economic stability and swings in unemployment rates. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military conflict, acts of terrorism or other geopolitical events. Sanctions imposed by the United States and other countries in response to such conflicts, including the one in Ukraine, may also continue to adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions, including disruption to enrollment within our ongoing trials and our ability to purchase necessary supplies on acceptable terms, if at all. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget.

Risks Related to Manufacturing

We intend to manufacture most of each product candidate ourselves. Delays in qualifying or in receiving regulatory approvals for our manufacturing facility and product candidates could delay our development plans and thereby limit our ability to generate product revenues.

We have built our own manufacturing facility in Bothell, Washington. The facility is designed to support the production of nonclinical and development product candidates and early commercialization of products, and ongoing facility and equipment qualification to support clinical production is required. If we are not able to qualify the facility or the appropriate regulatory approvals for the facility are delayed, we may be unable to manufacture sufficient quantities of our product candidates, if at all, which would limit our development activities and our opportunities for growth.

In addition, our manufacturing facility will be subject to ongoing, periodic inspection by the FDA, EMA or other applicable regulatory agencies to ensure compliance with cGMPs and cGTPs. Our failure to follow and document our adherence to these regulations or other regulatory requirements may lead to significant delays in the availability of products for clinical or, in the future, commercial use. This may result in the termination of or a hold on a clinical trial, or may delay or prevent filing or approval of commercial marketing applications for our product candidates. We also may encounter problems with the following:

- achieving adequate or clinical-grade materials that meet regulatory agency standards or specifications with consistent and acceptable production yield and costs;

- maintaining continuity among our key manufacturing-related electronic systems;
- shortages of qualified personnel, raw materials or key contractors; and
- ongoing compliance with cGMP regulations and other requirements of the FDA, EMA or other comparable regulatory agencies.

Failure to comply with applicable regulations could also result in sanctions being imposed on us, including fines, injunctions, civil penalties, a requirement to suspend or put on hold one or more of our clinical trials, failure of regulatory authorities to grant marketing approval of our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could harm our business.

Developing advanced manufacturing techniques and process controls is required to fully utilize our facility. Without further investment, advances in manufacturing techniques may render our facility and equipment inadequate or obsolete. We may also require further investment to build additional manufacturing facilities or expand the capacity of our existing ones.

The manufacturing of cellular therapies is very complex. We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs, delay our programs or limit supply of our product candidates.

Developing commercially viable manufacturing processes for cellular therapies is a difficult and uncertain task and requires significant expertise and capital investment. We are developing and implementing manufacturing processes for our product candidates. In particular, for autologous cell therapies, the starting material is the patient's own cells, which inherently adds complexity and variability to the manufacturing process. In addition, our ability to consistently and reliably manufacture our cellular therapy product candidates is essential to our success, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including cost overruns, potential problems with process scale-up, process reproducibility, stability issues, consistency and timely availability of reagents or raw materials. Furthermore, our manufacturing processes may have significant dependencies on third parties, which will pose additional risks to our manufacturing capabilities. Additionally, we do not yet have sufficient information to reliably estimate the cost of the commercial manufacturing and processing of our product candidates, and the actual cost to manufacture and process our product candidates could materially and adversely affect the commercial viability of our product candidates. As a result, we may never be able to develop a commercially viable product.

In addition to the factors mentioned above, the overall process of manufacturing cellular therapies is extremely susceptible to product loss due to low cell viability, contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing and distribution processes for any of our product candidates could result in reduced production yields, impact to key product quality attributes and other supply disruptions. Product defects can also occur unexpectedly. These deviations and disruptions could delay our programs. If we are not able to capably manage this complexity and variability, our ability to timely and successfully provide our products candidates to patients could be delayed. In addition, the complexities of utilizing a patient's own cells as the starting material requires that we have suitable cells capable of yielding a viable cellular therapy product, which may not be possible for severely immune-compromised or heavily pre-treated patients.

The process of successfully manufacturing products for clinical testing and commercialization may be particularly challenging, even if such products otherwise prove to be safe and effective. The manufacture of these product candidates involves complex processes. Some of these processes require specialized equipment and highly skilled and trained personnel. The process of manufacturing these product candidates will be susceptible to additional risks, given the need to maintain aseptic conditions throughout the manufacturing process. Contamination with microbes, viruses or other pathogens in either the donor material or materials utilized in the manufacturing process or ingress of microbiological material at any point in the process may result in contaminated, unusable product or necessitate the closing of a manufacturing facility for an extended period of time to allow us to investigate and remedy the contamination. These types of contaminations could result in delays in the manufacture of products, which could result in delays in the development of our product candidates. These contaminations could also increase the risk of adverse side effects.

Any adverse developments affecting manufacturing operations for our product candidates may result in lot failures, inventory shortages, shipment delays, product withdrawals or recalls or other interruptions in supply that could delay the development of our product candidates. If we are unable to obtain sufficient supply of our product candidates, whether due to production shortages or other supply interruptions resulting from the continuing effects of the COVID-19 pandemic or otherwise, our clinical trials or regulatory approval may be delayed. We may also have to write off inventory, incur other charges and expenses for supply of product that fails to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. In addition, parts of the supply chain may have long lead times or may come from a small number of suppliers. If we are not able to appropriately manage our supply chain, our ability to

successfully produce our product candidates could be delayed or harmed. Inability to meet the demand for our product candidates could damage our reputation and the reputation of our products among physicians, healthcare payors, patients or the medical community that supports our product development efforts, including hospitals and outpatient clinics.

Furthermore, the manufacturing facilities in which our product candidates will be made could be adversely affected by earthquakes and other natural disasters, equipment failures, labor shortages, power failures, health epidemics and numerous other factors. If any of these events were to occur and impact our manufacturing facilities, our business would be materially and adversely affected.

If our sole clinical or commercial manufacturing facility or our contract manufacturing organization is damaged or destroyed or production at these facilities is otherwise interrupted, our business would be negatively affected.

If any manufacturing facility in our manufacturing network, or the equipment in these facilities, is either damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity, if we are able to replace it at all. In the event of a temporary or protracted loss of a facility or its equipment, we may not be able to transfer manufacturing to a third party in the time required to maintain supply. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements or may require regulatory approval before selling any products manufactured at that facility. Such an event could substantially delay our clinical trials or commercialization of our product candidates.

Currently, we maintain insurance coverage against damage to our property and to cover business interruption and research and development restoration expenses. However, our insurance coverage may not reimburse us, or may not be sufficient to reimburse us, for any expenses or losses we may suffer. We may be unable to meet our requirements for our product candidates if there were a catastrophic event or failure of our current manufacturing facility or processes.

If we are unable to develop or scale our own manufacturing, we may have to rely on third parties to manufacture our product candidates, which subjects us to risks and could delay or prevent our development and/or commercialization, if approved, of our product candidates.

If we are unable to develop or scale our own manufacturing capabilities for our product candidates, we will be reliant on third parties to manufacture our product candidates. We may be unable to identify manufacturers for our product candidates or the materials required to develop the cellular therapy on acceptable terms or at all because the number of potential manufacturers is limited. Engaging a third-party manufacturer will require testing and regulatory interactions, and a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA questions, if any. Such potential third-party manufacturers may be unable to timely formulate and manufacture our product or produce the quantity and quality required to meet our clinical and commercial needs, if any.

Furthermore, the facilities used by manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state agencies to ensure strict compliance with government regulations and corresponding foreign standards, and we do not have control over third-party manufacturers' compliance with cGMPs for the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to obtain and/or maintain regulatory approval for our product candidates manufactured in these facilities. In addition, we have no control over the ability of our third-party manufacturers to maintain adequate control, quality assurance and qualified personnel required to meet our clinical and commercial needs, if any. If the FDA or a comparable foreign regulatory authority does not approve the manufacture of our product candidates at these facilities or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. In addition, any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates or that any approvals we have obtained could be revoked, which would adversely affect our business and reputation.

We may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our products. Also, our third- party manufacturers could breach or terminate their agreement with us because of their own financial difficulties or business priorities, at a time that is costly or otherwise inconvenient for us. If we were unable to find adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

Furthermore, our third-party manufacturers would also be subject to the same risks we face in developing our own manufacturing capabilities, as described above. Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenue.

Cell-based therapies rely on the availability of specialty raw materials, which may not be available to us on acceptable terms or at all.

Our product candidates require many specialty raw materials. As a result, we may be required to outsource aspects of our manufacturing supply chain. Many of the specialty raw materials may be manufactured by small companies with limited resources and experience to support a commercial product, and the suppliers may not be able to deliver raw materials to our specifications. In such case, identifying and engaging an alternative supplier or manufacturer could result in delay, and we may not be able to find other acceptable suppliers or manufacturers on acceptable terms, or at all. Switching suppliers or manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. If we change suppliers or manufacturers for commercial production, applicable regulatory agencies may require us to conduct additional studies or trials. If key suppliers or manufacturers are lost, or if the supply of the materials is diminished or discontinued, we may not be able to develop, manufacture and market our product candidates in a timely and competitive manner, or at all. An inability to continue to source product from any of these suppliers, which could be due to a number of issues, including regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands or quality issues, could adversely affect our ability to satisfy demand for our product candidates, which could adversely and materially affect our product sales and operating results or our ability to conduct clinical trials, either of which could significantly harm our business.

In addition, those suppliers may not have the capacity to support commercial products manufactured by biopharmaceutical firms. The suppliers may be ill-equipped to support our needs, especially in non-routine circumstances like an FDA inspection, or medical crises such as widespread contamination. We may not be able to contract with these companies on acceptable terms or at all. Accordingly, we may experience delays in receiving key raw materials to support clinical or commercial manufacturing. In addition, some raw materials are currently available from a single supplier, or a small number of suppliers. We cannot be sure that these suppliers will remain in business, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these materials for our intended purpose. These factors could cause the delay of studies or trials, regulatory submissions, required approvals or commercialization of product candidates that we develop, cause us to incur higher costs and prevent us from commercializing our product candidates successfully.

Risks Related to Our Dependence on Third Parties

We intend to rely on third parties to conduct, supervise and monitor a significant portion of our research and nonclinical studies and clinical trials for our product candidates, and, if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements or otherwise perform satisfactorily, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.

We intend to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GCP-compliant clinical trials on our product candidates properly and on time. For example, we are relying on a CRO to conduct a significant part of our LYL797 Phase 1 clinical trial. Negotiating budgets and contracts with CROs and study sites may result in delays to our development timelines and increased costs. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. Further, the performance of our CROs and other third parties conducting our trials may also be interrupted or subject to delay as a result of the continuing effects of the COVID-19 pandemic, including due to staff shortages at the CRO, clinical site or other vendor or reallocation of resources due to the pandemic.

In addition, any third parties conducting our clinical trials or nonclinical studies will not be our employees, and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials or nonclinical studies may be extended, delayed or terminated and we may not be able to obtain regulatory approval or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We rely on these parties for execution of our nonclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials are conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to add patients to or repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If any of our relationships with the third parties that we currently use or that we may use in the future terminates, we may not be able to enter into arrangements with alternative third parties to do so on commercially reasonable terms. As a result, delays occur, which can materially impact our ability to meet desired research and clinical development timelines.

We do and will continue to or intend to rely on outside scientists and clinical trial investigators and their third-party research institutions for research and development and early clinical testing of our product candidates. These scientists, investigators and institutions may have other commitments or conflicts of interest, which could limit our access to their expertise and harm our ability to leverage our technology platforms.

We rely on our third-party research institution collaborators for some research capabilities. However, the research we are funding constitutes only a small portion of the overall research of each research institution. Other research being conducted by these institutions may at times receive higher priority than research on the programs we are funding. We typically have less control of the research, clinical trial protocols and patient enrollment than we might with activity led by our employees.

The outside scientists and clinical trial investigators who conduct the research and development upon which portions of our product candidate pipeline depends are not our employees; rather, they serve as either independent contractors or the primary investigators under research collaboration agreements that we have with their sponsoring academic or research institution. Such scientists and collaborators may have other commitments that would limit their availability to us. Although our scientific advisors generally agree not to do competing work, if an actual or potential conflict of interest between their work for us and their work for another entity arises, we may lose their services. These factors could adversely affect the timing of the clinical trials, the timing of receipt and reporting of clinical data, the timing of our IND submissions and our ability to conduct our current and planned clinical trials. It is also possible that some of our valuable proprietary knowledge may become publicly known through these scientific advisors if they breach their confidentiality agreements with us, which would cause competitive harm to, and have an adverse effect on, our business.

We have in the past, and we may in the future, form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such alliances or licensing arrangements.

We have entered into research and development collaborations in the past, and may in the future, enter into additional license and collaboration arrangements. Any collaboration arrangement that we enter into is subject to numerous risks, which may include the following:

- the collaborator has significant discretion in determining the efforts and resources that they will apply to a program or product candidate under the collaboration;
- the collaborator may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- the collaborator may delay or halt clinical trials, provide insufficient funding for a clinical trial, preferentially enroll patients on a portion of a clinical trial not testing our product candidates, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;

- the collaborator could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- the collaborator may not commit sufficient resources to marketing and distribution of our products;
- the collaborator may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and the collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- the collaboration may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- the collaborator may own or co-own intellectual property covering our product candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

In particular, failure by any collaborator to meet its obligations under our collaboration agreements or to apply sufficient efforts at developing and commercializing collaboration products may adversely affect our business, financial condition and our results of operations.

For example, we were previously party to a research and development collaboration with GSK for our NY-ESO-1 program and other potential product opportunities and, effective December 2022, GSK terminated the agreement and discontinued its development of product candidates targeting NY-ESO-1, including the second generation product candidates that incorporated our genetic and epigenetic reprogramming technologies (LYL132 and LYL331).

We may form or seek further strategic alliances, create joint ventures or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates, our research and any future product candidates that we may pursue. Such alliances will be subject to many of the risks set forth above. Moreover, any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex.

As a result of these risks, we may not be able to realize the benefit of our existing collaboration or any future collaborations or licensing agreements we may enter into. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

We may not realize the benefits of potential future collaborations, licenses, product acquisitions or other strategic transactions.

We have entered into, and may desire to enter into in the future, collaborations, licenses or other strategic transactions for the acquisition of products or business opportunities, in each case where we believe such arrangement will complement or augment our existing business. These relationships or transactions, or those like them, may require us to incur nonrecurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, reduce the potential profitability of the products that are the subject of the relationship or disrupt our management and business. For example, we entered into a collaboration agreement and stock purchase agreement with PACT in June 2020 and, in February 2021, we filed a demand for arbitration seeking to, among other things, rescind the agreements with PACT and recover the consideration paid thereunder. In October 2022, we entered into a settlement agreement with PACT to resolve the outstanding legal dispute. See Part I, Item 3, *Legal Proceedings*, of this Annual Report on Form 10-K for additional information regarding the PACT arbitration and settlement agreement. In addition, we face significant competition in seeking appropriate strategic alliances and transactions and the negotiation process is time-consuming and complex, and there can be no assurance that we can enter into any of these transactions even if we desire to do so. Moreover, we may not be successful in our efforts to establish a strategic alliance or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates or programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our product candidates and programs as having the requisite potential to demonstrate a positive benefit/risk profile. Any delays in entering into new strategic alliance agreements related to our product candidates could

also delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

If we license products or acquire businesses, we may not be able to realize the benefit of these transactions if we are unable to successfully integrate them with our existing operations and company culture. There are other risks and uncertainties involved in these transactions, including unanticipated liabilities related to acquired intellectual property rights, products or companies and disruption in our relationship with collaborators or suppliers as a result of such a transaction. We cannot be certain that, following an acquisition or license, we will achieve the financial or strategic results that would justify the transaction.

We depend on the enrollment and retention of patients in our current and planned clinical trials for our product candidates. If we experience delays or difficulties enrolling or retaining patients in our clinical trials, our research and development efforts and business, financial condition, and results of operations could be materially adversely affected.

Successful and timely completion of clinical trials require that we enroll and retain a sufficient number of patient candidates. Any clinical trials we conduct may be subject to delays for a variety of reasons, including as a result of patient enrollment taking longer than anticipated, manufacturing failures resulting in patients being unable to be treated, patient withdrawal or adverse events. These types of developments could cause us to delay the trial or halt further development. For example, enrollment for the Phase 1 trial of LYL797 has been slower than anticipated, and we now anticipate the presentation of our initial LYL797 clinical data to occur in the first half of 2024.

Our clinical trials compete with other clinical trials that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Moreover, enrolling patients in clinical trials for diseases in which there is an approved standard of care is challenging, as patients will first receive the applicable standard of care. Many patients who respond positively to the standard of care do not enroll in clinical trials. This may limit the number of eligible patients able to enroll in our clinical trials who have the potential to benefit from our product candidates and could extend development timelines or increase costs for these programs. Patients who fail to respond positively to the standard of care treatment will be eligible for clinical trials of unapproved drug candidates. However, these prior treatment regimens may render our therapies less effective in clinical trials.

Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Patient enrollment depends on many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- eligibility criteria for the trial;
- the proximity of patients to clinical sites;
- the design of the clinical protocol;
- the ability to obtain and maintain patient consents;
- perceived risks and benefits of the product candidate under evaluation, including any perceived risks associated with genetically modified product candidates;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the risk that patients enrolled in clinical trials will drop out of the trials before the administration of our product candidates or trial completion;
- the availability of competing clinical trials;
- the availability of such patients during the COVID-19 pandemic;
- the availability of new drugs approved for the indication the clinical trial is investigating; and
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow

down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

We face competition from numerous pharmaceutical and biotechnology enterprises, as well as from academic institutions, government agencies and private and public research institutions. Our ability to enroll clinical trials or our commercial opportunities will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we may develop. Additionally, our commercial opportunities will be reduced or eliminated if novel upstream products or changes in treatment protocols reduce the overall incidence or prevalence of our current or future target diseases. Competition could result in reduced sales and pricing pressure on our product candidates, if approved by applicable regulatory authorities. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us and impair any ability to commercialize our product candidates.

Risks Related to Regulation and Legal Compliance

We are just beginning the clinical development of our product candidates, and our future success is dependent on the successful development and regulatory approval of our product candidates.

We currently have no products approved for commercial sale, and we are just beginning the clinical development of our product candidates. Besides LYL797 and LYL845, which are in Phase 1 clinical development, our other proprietary product candidates are currently in nonclinical development. The future success of our business is substantially dependent on our ability to obtain regulatory approval for our product candidates for the indications we seek, and, if approved, to successfully commercialize one or more product candidates in a timely manner. Each of our programs and product candidates will require clinical development, regulatory approval, obtaining manufacturing supply, capacity and expertise, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts before we generate any revenue from product sales. We do not have any products that are approved for commercial sale, and we may never be able to develop or commercialize marketable products.

We cannot commercialize product candidates in the United States without first obtaining regulatory approval for the product from the FDA; similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence from and to the satisfaction of the FDA and foreign regulatory authorities, that the product candidate is safe, pure and potent for use for that target indication and that the manufacturing facilities, processes and controls are adequate with respect to such product candidate to assure safety, purity and potency.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of nonclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any future product candidates will ever obtain regulatory approval. Furthermore, the regulatory approval process for novel product candidates, such as T-cell product candidates and next-generation T-cell programs, can be more complex and consequently more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates.

Even if a product candidate were to successfully obtain approval from the FDA and comparable foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for one of our product candidates in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding to continue the development of that product or generate revenues attributable to that product candidate. Also, any regulatory approval of our current or future product candidates, once obtained, may be withdrawn.

Our cellular therapy product candidates represent new therapeutic approaches that could result in heightened regulatory scrutiny, delays in clinical development or delays in or our inability to achieve regulatory approval, commercialization or payor coverage of our product candidates.

Our future success is dependent on the successful development of our cellular therapies in general and our development product candidates, in particular. Because these programs represent a new approach to the treatment of cancer, developing and, if approved, commercializing our product candidates subject us to a number of challenges. Moreover, we cannot be sure that the manufacturing processes used in connection with our cellular therapy product candidates will yield a sufficient supply of satisfactory products that are safe, pure and potent, scalable or profitable.

In addition to oversight by the FDA and by IRBs under guidelines promulgated by the NIH, gene therapy clinical trials are also subject to review and oversight by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Although the FDA decides whether trials of cell therapies that involve genetic engineering may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

Actual or perceived safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved by applicable regulatory authorities, of physicians to subscribe to the novel treatment mechanics. The FDA or other applicable regulatory authorities may ask for specific post-market requirements, and additional information informing benefits or risks of our products may emerge at any time prior to or after regulatory approval.

Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Physicians may not be willing to undergo training to adopt this novel therapy, may decide the therapy is too complex to adopt without appropriate training or not cost-efficient and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

The results of research, nonclinical studies or earlier clinical trials are not necessarily predictive of future results. Any product candidate we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval.

Success in research, nonclinical studies and early clinical trials does not ensure that later clinical trials will generate similar results and otherwise provide adequate data to demonstrate the efficacy and safety of an investigational product. Likewise, a number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in late-stage clinical trials, even after seeing promising results in earlier nonclinical studies or clinical trials. Thus, even if the results from our initial research and nonclinical activities appear positive, we do not know whether subsequent late-stage clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any product candidates.

Moreover, final study results may not be consistent with interim study results. If later-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for any of our product candidates may be adversely impacted. Even if we believe that we have adequate data to support an application for regulatory approval to market any of our product candidates, the FDA or other regulatory authorities may not agree and may require that we conduct additional clinical trials.

Clinical development involves a lengthy and expensive process with an uncertain outcome.

We are just beginning clinical development of our product candidates. Besides LYL797 and LYL845, which are in Phase 1 clinical development, our other proprietary product candidates are currently in nonclinical development. The risk of failure of our product candidates is high. The clinical trials and manufacturing of our product candidates are, and the manufacturing and marketing of our products, if approved, will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and market our product candidates. Before obtaining regulatory approvals for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive nonclinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication. In particular, because our product candidates are subject to regulation as biological products, we will need to demonstrate that they are safe, pure and potent for use in their target indications. Each product candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

The clinical testing that will be required for any product candidates we choose to advance is expensive and can take many years to complete, and its outcome is inherently uncertain. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time during the clinical trial process. Even if our current and planned clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our product candidates for their targeted indications or support continued clinical development of such product candidates. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through nonclinical and clinical trials.

In addition, even if such trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

To date, we have not fully enrolled or completed any clinical trials required for the approval of our product candidates. We may experience delays in initiating, enrolling or conducting our current and planned clinical trials, and we do not know whether clinical trials will begin or enroll subjects on time, will need to be redesigned, will achieve expected enrollment rates or will be completed on schedule, if at all. For example, enrollment for the Phase 1 trial of LYL797 has been slower than anticipated. In addition, obtaining sufficient and specific tumor tissues will be needed for our planned Phase 1 clinical trial of LYL845 in multiple solid tumor indications. Our inability to obtain the specific tumor tissues or sufficient amount of tumor tissues in a timely manner or at all could delay or preclude our ability to initiate the planned clinical trial. There can be no assurance that the FDA or comparable foreign regulatory authorities will not put clinical trials of any of our product candidates on clinical hold in the future. Clinical trials can be delayed, suspended or terminated for a variety of reasons, including in connection with:

- inability to generate sufficient nonclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials;
- delays in reaching agreement with the FDA or other regulatory authorities as to the design or implementation of our clinical trials;
- obtaining regulatory authorization to commence a clinical trial;
- reaching an agreement on acceptable terms with clinical trial sites or prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different clinical trial sites;
- obtaining IRB or ethics committee approval at each trial site;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- inspections of clinical trial sites or operations by applicable regulatory authorities, or the imposition of a clinical hold;
- clinical sites, CROs or other third parties deviating from trial protocol or dropping out of a trial;
- failure to perform in accordance with applicable regulatory requirements, including the FDA's GCP requirements, or applicable regulatory requirements in other countries;
- addressing patient safety concerns that arise during the course of a trial, including occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- adding a sufficient number of clinical trial sites;
- manufacturing sufficient quantities of product candidate for use in clinical trials; or
- suspensions or terminations by IRBs of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities due to a number of factors, including those described above.

Further, a clinical trial may be suspended or terminated by us, the institutional review boards for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial or the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

We cannot predict with any certainty whether or when we might complete a given clinical trial, if at all. If we experience delays or quality issues in the conduct, completion or termination of any clinical trial of our product candidates, the approval and commercial prospects of such product candidate will be harmed, and our ability to generate product revenues from such product candidate will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority. As a result of safety or toxicity issues that we may experience in our clinical trials, we may not continue the development of nor receive approval to market any product candidates, which could prevent us from ever generating product revenues or achieving profitability. For example, previous clinical trials utilizing a CAR T cell to treat hematologic tumors have shown an increased risk of cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome. Adverse events may also be associated with the lymphodepletion regimen utilized with cellular therapies. Additionally, ROR1 is expressed on a number of normal tissues. As a result, ROR1 could cause on-target, off-tumor toxicity. c-JUN is also potentially an oncogene and could cause healthy cells to transform into malignant cells. Results of our trials could reveal an unacceptably high severity and incidence of side effects, or side effects outweighing the benefits of our product candidates. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our product candidates for any or all targeted indications. The side effects experienced could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims.

In the event that any of our product candidates receives regulatory approval and we or others later identify undesirable or unacceptable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit approvals of such products and require us to take our approved product off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies, or issue other communications containing warnings or other safety information about the product;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a risk evaluation and mitigation strategy (REMS) plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the dose or the way the product is administered, conduct additional clinical trials or change the labeling of the product;
- we may be subject to limitations on how we may promote or manufacture the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or our potential future partners from achieving or maintaining market acceptance of the affected product or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of any products.

Interim, topline or preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available or as we make changes to our manufacturing processes and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim, topline or preliminary data from our nonclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Further, modifications or improvements to our manufacturing processes for a therapy may result in changes to the characteristics or behavior of the product candidate that could cause our product candidates to perform differently and affect the results of our ongoing clinical trials. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose preliminary or interim data from our nonclinical studies and clinical trials. Preliminary or interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Additionally, disclosure of preliminary or interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our company in general. If the interim, topline or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, any of our potential product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

The FDA regulatory approval process is lengthy, time-consuming and inherently unpredictable. If we are not able to obtain required regulatory approval of our product candidates, our business will be substantially harmed.

We expect the novel nature of our product candidates to create challenges in obtaining regulatory approval. For example, the FDA has limited experience with commercial development of T-cell therapies for cancer. Accordingly, the regulatory approval pathway for our product candidates may be uncertain, complex, expensive and lengthy, and approval may not be obtained.

Prior to obtaining approval to commercialize any drug product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe, pure and potent for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional nonclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of clinical trial results may result in our failing to obtain regulatory approval and marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

We could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, the institutional review boards for the institutions in which such trials are being conducted, the Data Monitoring Committee for such trial or the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing our current or future product candidates.

If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

Even if our product candidates obtain regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, testing, labeling, packaging, distribution, import, export, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. In addition, any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations, as well as, for the manufacture of certain of our product candidates, the FDA's cGTPs for the use of human cellular and tissue products to prevent the introduction, transmission or spread of communicable diseases. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMPs, cGTPs and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, quality control and distribution.

If there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or our manufacture of a product, or if we or one of our distributors, licensees or co-marketers fails to comply with

regulatory requirements, the regulators could take various actions. These include issuing warning letters or untitled letters, imposing fines on us, imposing restrictions on the product or its manufacture and requiring us to recall or remove the product from the market. The regulators could also suspend or withdraw our marketing authorizations, requiring us to conduct additional clinical trials, change our product labeling or submit additional applications for marketing authorization. If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could materially adversely affect our business, financial condition and results of operations.

In addition, if we have any product candidate approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. In the United States, the FDA and the Federal Trade Commission (FTC) strictly regulate the promotional claims that may be made about pharmaceutical products to ensure that any claims about such products are consistent with regulatory approvals, not misleading or false in any particular way and adequately substantiated by clinical data. The promotion of a drug product in a manner that is false, misleading, unsubstantiated or for unapproved (or off-label) uses may result in enforcement letters, inquiries and investigations and civil and criminal sanctions by the FDA, FTC and other regulatory authorities. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions and may result in false claims litigation under federal and state statutes, which can lead to consent decrees, civil monetary penalties, restitution, criminal fines and imprisonment, and exclusion from participation in Medicare, Medicaid and other federal and state healthcare programs. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The government has also required that companies enter into consent decrees and/or imposed permanent injunctions under which specified promotional conduct is changed or curtailed.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- issue, or require us to issue, safety-related communications, such as safety alerts, field alerts, "Dear Doctor" letters to healthcare professionals, or import alerts;
- impose civil or criminal penalties;
- suspend, limit, or withdraw regulatory approval;
- suspend any of our nonclinical studies and clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our and our contract manufacturers' facilities; or
- seize or detain products, refuse to permit the import or export of products, or require us to conduct a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products, if approved. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Moreover, the policies of the FDA and of comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, during the Trump administration several executive actions were taken, including the issuance of a number of Executive Orders, that imposed significant burdens on, or otherwise delayed, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. It is difficult to predict how

similar orders in the future would be implemented, and the extent to which they would impact the FDA's ability to exercise its regulatory authority. If executive actions are taken that impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

We may be subject to applicable fraud and abuse, including anti-kickback and false claims, transparency, health information privacy and security and other healthcare laws. Failure to comply with such laws, may result in substantial penalties.

We may be subject to broadly applicable healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct research, market, sell and distribute any product candidates for which we obtain marketing approval. The healthcare laws that may affect us include: the federal fraud and abuse laws, including the federal anti-kickback, and false claims and civil monetary penalties laws; federal data privacy and security laws, including the Health Insurance Portability and Accountability Act, as amended by the Health Information Technology for Economic and Clinical Health Act; and federal transparency laws related to ownership and investment interests and payments and/or other transfers of value made to or held by physicians (including doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. In addition, many states have similar laws and regulations that may differ from each other and federal law in significant ways, thus complicating compliance efforts. Moreover, several states require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. Additionally, some state and local laws require the registration of biopharmaceutical sales representatives in the jurisdiction.

Ensuring that our operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock options for consulting services provided, may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, disgorgement, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and/or oversight if a corporate integrity agreement or similar agreement is executed to resolve allegations of non-compliance with these laws and the curtailment or restructuring of operations. In addition, violations may also result in reputational harm, diminished profits and lower future earnings. For additional detail on healthcare laws that may affect our business, see "Other Healthcare Laws" in the business section of this Annual Report on Form 10-K for the year ended December 31, 2022.

Changes in healthcare policies, laws and regulations may impact our ability to obtain approval for, or commercialize our product candidates, if approved.

In the United States and some foreign jurisdictions there have been, and continue to be, several legislative and regulatory changes and proposed reforms of the healthcare system in an effort to contain costs, improve quality and expand access to care. In the United States, there have been and continue to be a number of healthcare-related legislative initiatives, as well as executive, judicial and Congressional challenges to existing healthcare laws that have significantly affected, and could continue to significantly affect, the healthcare industry. For example, there have been efforts to repeal, substantially modify or invalidate some or all of the provisions of the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), some of which have been successful. While the U.S. Supreme Court dismissed in June 2021 a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress, allowing the ACA to remain in effect in its current form, such efforts may continue.

In addition, there continues to be heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs and review the relationship between pricing and manufacturer patient programs. For example, President Biden issued an executive order in July 2021 supporting legislation to enact drug pricing reforms and, in response, the U.S. Department of Health and Human Services

(HHS) released a Comprehensive Plan for Addressing High Drug Prices in September 2021 with specific legislative and administrative policies that Congress could enact to help improve affordability of, and access to, prescription drugs. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law, which among other things: (i) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, and subject drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. Additionally, the IRA will also extend enhanced subsidies for individuals purchasing health insurance coverage in the ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be effectuated but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. For additional detail on healthcare reform that may affect our business, see "Healthcare Reform" in the business section of our Annual Report on Form 10-K for the year ended December 31, 2022.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, assuming FDA approval. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational. Assuming we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. We or our collaborators will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we may seek for our product candidates.

Similarly, a significant trend in the healthcare industry is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. As such, cost containment reform efforts may result in an adverse effect on our operations. Obtaining coverage and adequate reimbursement for our product candidates may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Similarly, because our product candidates will be physician-administered, separate reimbursement for the product itself may or may not be available. Instead, the administering physician may or may not be reimbursed for providing the treatment or procedure in which our product is used.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key

personnel and accept the payment of user fees and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new biologics or modifications to be cleared or approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. In February 2022, the FDA resumed on-site inspections of domestic manufacturing facilities, subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Additionally, in April 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. According to the guidance, the FDA intends to request such remote interactive evaluations in situations where an in-person inspection would not be prioritized or deemed mission-critical, or where direct inspection is otherwise limited by travel restrictions, but where the FDA determines that remote evaluation would still be appropriate. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Relating to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be adversely affected.

We rely upon a combination of patents, trademarks, trade secrets and confidentiality agreements to protect the intellectual property related to our technology and product candidates. We own or possess certain intellectual property, and other intellectual property are owned or possessed by our partners and are in-licensed to us. When we refer to "our" technologies, inventions, patents, patent applications or other intellectual property rights, we are referring to both the rights that we own or possess as well as those that we in-license, many of which are critical to our intellectual property protection and our business. If the intellectual property that we rely on is not adequately protected, competitors may be able to use our technologies and erode or negate any competitive advantage we may have.

The patentability of inventions and the validity, enforceability and scope of patents in the biotechnology field is uncertain because it involves complex legal, scientific and factual considerations, and it has in recent years been the subject of significant litigation. Moreover, the standards applied by the U.S. Patent and Trademark Office (USPTO) and non-U.S. patent offices in granting patents are not always applied uniformly or predictably. There is also no assurance that all potentially relevant prior art relating to our patents and patent applications is known to us or has been found in the instances where searching was done. We may be unaware of prior art that could be used to invalidate an issued patent or prevent a pending patent application from issuing as a patent. There also may be prior art of which we are aware, but which we do not believe affects the validity, enforceability or patentability of a claim of one of our patents or patent applications, which may, nonetheless, ultimately be found to affect the validity, enforceability or patentability of such claim. As a consequence of these and other factors, our patent applications may fail to result in issued patents with claims that cover our product candidates in the United States or in other countries.

Even if patents have issued or do successfully issue from patent applications, and even if these patents cover our product candidates, third parties may challenge the validity, enforceability or scope thereof, which may result in these patents being narrowed, invalidated or held to be unenforceable. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable. Even if unchallenged, our patents and patent applications or other intellectual property rights may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. The possibility exists that others will develop products on an independent basis which have the same effect as our product candidates and which do not infringe our patents or other intellectual property rights, or that others will design around the claims of patents that we have had issued that cover our product candidates. If the breadth or strength of protection provided by our patents and patent applications with respect to

our product candidates is threatened, it could jeopardize our ability to commercialize our product candidates and dissuade companies from collaborating with us.

We may also desire to seek licenses from third parties who own or have rights to intellectual property that may be useful for providing exclusivity for our product candidates, or for providing the ability to develop and commercialize a product candidate in an unrestricted manner. There is no guarantee that we will be able to obtain such licenses from third parties on commercially reasonable terms, or at all.

In addition, the USPTO and various foreign governmental or inter-governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during and after the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete, irreversible loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market, which could have a material adverse effect on our business.

United States patent applications containing or that at any time contained a claim not entitled to a priority date before March 16, 2013 are subject to the "first to file" system implemented by the America Invents Act (2011). The first to file system requires us to be cognizant going forward of the time from invention to filing of a patent application. Because patent applications in the U.S. and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our partners were the first to file any patent application related to a product candidate.

In addition, our registered or unregistered trademarks or trade names may be challenged, infringed or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we view as valuable to building name recognition among potential partners and customers in our markets of interest. At times, competitors or other third parties have adopted or may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion and/or litigation. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce, protect or defend our proprietary rights related to trademarks may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and prospects.

The lives of our patents may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first nonprovisional effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from biosimilar or generic medications. In addition, although upon issuance in the United States a patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. While the patent term of certain patents can also be extended with respect to a specific product to recapture time lost in clinical trials and regulatory review by the FDA, a patent's life also can be shortened by a terminal disclaimer over an earlier filed patent or patent application. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, enforcing and defending patents on all of our product candidates in all countries throughout the world would be prohibitively expensive. Our intellectual property rights in certain countries outside the United States may be less extensive than those in the United States. In addition, the laws of certain foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we and our partners may not be able to prevent third parties from practicing our inventions in countries outside the United States, or from selling or importing infringing products made using our inventions in other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection or where we do not have exclusive rights under the relevant patents to develop their own products and, further, may export otherwise-infringing products to territories where we and our partners have patent protection but where enforcement is not as strong as that in the U.S. These infringing products may compete with our product candidates in jurisdictions where we or our partners have no issued patents or where we do not have exclusive rights under the relevant patents, or our patent claims and other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us and our partners to stop the infringement of our patents or marketing of competing products in violation of our intellectual property rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us or our partners. We or our partners may not prevail in any lawsuits that we or our licensors initiate, and even if we or our licensors are successful, the damages or other remedies awarded, if any, may not be commercially meaningful.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, we or our partners may have limited remedies, which could materially diminish the value of such patent. If we or our partners are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

If we are sued for infringing or misappropriating the intellectual property rights of third parties, the resulting litigation could be costly and time-consuming and could prevent or delay our development and commercialization efforts.

Our commercial success depends, in part, on us and our partners not infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation and other adversarial proceedings, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interference or derivation proceedings, oppositions, and inter partes and post-grant review proceedings before the USPTO and non-U.S. patent offices. Numerous U.S. and non-U.S. issued patents and pending patent applications owned by third parties exist in the fields in which we are developing, and may develop, product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of third parties' patent rights, as it may not always be clear to industry participants, including us, which patents cover various types of products, methods of making or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable.

Third parties may assert infringement or misappropriation claims against us based on existing or future intellectual property rights, alleging that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacturing of our product candidates that we failed to identify. For example, patent applications covering our product candidates could have been filed by others without our knowledge, since these applications generally remain confidential for some period of time after their filing date. Even pending patent applications that have been published, including some of which we are aware, could be later amended in a manner that could cover our product candidates or their use or manufacture. In addition, we may have analyzed patents or patent applications of third parties that we believe are relevant to our activities and believe that we are free to operate in relation to any of our product candidates, but our competitors may obtain issued claims, including in patents we consider to be unrelated, which may block our efforts or potentially result in any of our product candidates or our activities infringing their claims.

If we or our partners are sued for patent infringement, we would need to demonstrate that our product candidates, products and methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving that a patent is invalid is difficult and even if we are successful in the relevant proceedings, we may incur substantial costs, and the time and attention of our management and scientific personnel could be diverted from other activities. If one or more claims of any issued third-party patents were held by a court of competent jurisdiction to cover aspects of our materials, formulations, methods of manufacture or methods for treatment, we could be forced, including by court order, to cease developing, manufacturing or commercializing the relevant product candidate until the relevant patent expired. Alternatively, we may desire or be required to obtain a license from such third party in order to use the infringing technology and to continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonably terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property licensed to us. If we are unable to obtain a necessary license on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

We may face claims that we misappropriated the confidential information or trade secrets of a third party. If we are found to have misappropriated a third-party's trade secrets, we may be prevented from further using these trade secrets, which could limit our ability to develop our product candidates.

Defending against intellectual property claims, regardless of their merit, could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle before a final judgment, any litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. During the course of any intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions and other interim proceedings in the litigation and these announcements may have negative impact on the perceived value of our product candidates, programs or intellectual property. In the event of a successful intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent, or to redesign our infringing product candidates, which may be impossible or require substantial time and monetary expenditure. In addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, and the parties making claims against us may obtain injunctive or other equitable relief, which could impose limitations on the conduct of our business. We may also elect to enter into license agreements in order to settle patent infringement claims prior to litigation, and any of these license agreements may require us to pay royalties and other fees that could be significant. As a result of all of the foregoing, any actual or threatened intellectual property claim could prevent us from developing or commercializing a product candidate or force us to cease some aspect of our business operations.

We have in-licensed a significant portion of our intellectual property from our partners. If we breach any of our license agreements with these partners, we could potentially lose the ability to continue the development and potential commercialization of one or more of our product candidates.

We hold rights under license agreements with our partners. Our discovery and development technology platforms are built, in part, around intellectual property rights in-licensed from our partners. Under our existing license agreements, we are subject to various obligations, which may include diligence obligations with respect to development and commercialization activities, payment obligations upon achievement of certain milestones and royalties on product sales. If there is any conflict, dispute, disagreement or issue of nonperformance between us and our counterparties regarding our rights or obligations under these license agreements, including any conflict, dispute or disagreement arising from our failure to satisfy diligence or payment obligations, we may be liable to pay damages and our counterparties may have a right to terminate the affected license. The termination of any license agreement with one of our partners could adversely affect our ability to utilize the intellectual property that is subject to that license agreement in our discovery and development efforts, our ability to enter into future collaboration, licensing and/or marketing agreements for one or more affected product candidates and our ability to commercialize the affected product candidates. Furthermore, disagreements under any of these license agreements may arise, including those related to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes may infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

These disagreements may harm our relationship with the partner, which could have negative impacts on other aspects of our business.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to the intellectual property, through licenses from third parties and under patent applications that we own or will own, to develop our product candidates. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations, manufacturing methods or technologies to work effectively and efficiently, and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms; such failure would harm our business. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the

same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

Intellectual property discovered through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

We have acquired or licensed, or may require in the future, intellectual property rights that have been generated through the use of U.S. government funding or grant. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have an adverse effect on the success of our business.

Third parties may infringe our patents or misappropriate or otherwise violate our intellectual property rights. Our patent applications cannot be enforced against third parties practicing the technology claimed in these applications unless and until a patent issues from the applications, and then only to the extent the issued claims cover the technology. In the future, we or our partners may elect to initiate legal proceedings to enforce or defend our or our partners' intellectual property rights, to protect our or our partners' trade secrets or to determine the validity or scope of our intellectual property rights. Any claims that we or our partners assert against perceived infringers could also provoke these parties to assert counterclaims against us or our partners alleging that we or our partners infringe their intellectual property rights or that our intellectual property rights are invalid. In patent litigation in the United States, defendant counterclaims alleging noninfringement, invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert noninfringement, invalidity or unenforceability of a patent. The outcome following legal assertions of noninfringement, unpatentability, invalidity and unenforceability is unpredictable. With respect to the validity of patent rights, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of unpatentability, invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Interference, derivation or opposition proceedings provoked by third parties, brought by us or our partners, or brought by the USPTO or any non-U.S. patent authority, may be necessary to determine the priority of inventions or matters of inventorship with respect to our patents or patent applications. We or our partners may also become involved in other proceedings, such as reexamination or opposition proceedings, inter partes review, post-grant review or other pre-issuance or post-grant proceedings in the USPTO or its foreign counterparts relating to our intellectual property or the intellectual property of others. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. An unfavorable outcome in any of these proceedings could require us or our partners to cease using the related technology and commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our

partners a license on commercially reasonable terms if any license is offered at all. Even if we or our licensors obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Any intellectual property proceedings can be expensive and time-consuming. Our or our partners' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our partners can. Accordingly, despite our or our partners' efforts, we or our partners may not be able to prevent third parties from infringing upon or misappropriating our intellectual property rights, particularly in countries where the laws may not protect our rights as fully as in the U.S. Even if we are successful in the relevant proceedings, we may incur substantial costs, and the time and attention of our management and scientific personnel could be diverted from other activities. In addition, in an infringement proceeding, a court may decide that one or more of our patents is invalid or unenforceable, in whole or in part, may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question and/or may require us to pay the other party attorneys' fees. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may in the future be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we are unable to protect the confidentiality of our trade secrets and other proprietary information, the value of our technology could be adversely affected and our business could be harmed.

In addition to seeking the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and other elements of our technology, discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, including by enabling them to develop and commercialize products substantially similar to or competitive with our product candidates, thus eroding our competitive position in the market.

Trade secrets can be difficult to protect. We seek to protect our proprietary, confidential technology and processes, in part, by entering into confidentiality agreements and invention assignment agreements with our employees, consultants and outside scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific advisors might intentionally or inadvertently disclose our trade secrets or confidential, proprietary information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, the laws of certain foreign countries do not protect proprietary rights such as trade secrets to the same extent or in the same manner as the laws of the U.S. Misappropriation or unauthorized disclosure of our trade secrets to third parties could impair our competitive advantage in the market and could adversely affect our business, results of operations and financial condition.

We may be subject to claims that our employees, consultants or independent contractors have breached non-compete or non-solicit obligations and/or wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise breached non-compete or non-solicit obligations with respect to such individuals' prior employers, or used or disclosed confidential information of these third parties or such individuals' former employers. Dealing with such claims and negotiating with potential claimants could result in substantial cost and be a distraction to our management and employees. In addition, litigation may be necessary to defend against these claims, and even if we are successful in defending against these claims, such litigation could result in further costs to us and distraction to our management and employees.

Risks Related to Ownership of Our Common Stock

Delaware law and provisions in our amended and restated certificate of incorporation and bylaws might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our amended and restated certificate of incorporation and bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our organizational documents:

- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered three-year terms;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- eliminate cumulative voting in the election of directors;
- authorize our board of directors to issue shares of preferred stock and determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval;
- permit stockholders to take actions only at a duly called annual or special meeting and not by unanimous written consent;
- prohibit stockholders from calling a special meeting of stockholders;
- require that stockholders give advance notice to nominate directors or submit proposals for consideration at stockholder meetings;
- authorize our board of directors, by a majority vote, to amend certain provisions of the bylaws; and
- require the affirmative vote of at least 66 2/3% or more of the outstanding shares of common stock to amend many of the provisions described above.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL) prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, which is generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees, or stockholders to us or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or our amended and restated certificate of incorporation and bylaws; and
- any action asserting a claim governed by the internal affairs doctrine.

Furthermore, to prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation also provides that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (Securities Act). However, these provisions would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Any person purchasing or otherwise acquiring or holding any interest in shares of our capital stock is deemed to have received notice of and consented to the foregoing provisions. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds more favorable for disputes with us or with our directors, officers, other employees or agents or our other stockholders, which may discourage such lawsuits against us and such other persons, or may result in additional expense to a stockholder seeking to bring a claim against us. Alternatively, if a court were to find this choice of forum provision inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business, results of operations and financial condition.

We have in the past identified a material weakness in our internal control over financial reporting. If we identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting, we may not be able to accurately or timely report our financial condition or results of operations, which may significantly harm our business and the value of our common stock.

As a public company, we are required to maintain internal control over financial reporting and to report any material weaknesses in such internal control. Section 404 of the Sarbanes-Oxley Act (Section 404) requires that we evaluate and determine the effectiveness of our internal control over financial reporting. This assessment needs to include the disclosure of any material weaknesses in such internal control. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our consolidated financial statements will not be prevented or detected on a timely basis.

In connection with the finalization of our consolidated financial statements as of and for the year ended December 31, 2019, we and our independent auditors concluded that a material weakness existed in our internal control over financial reporting relating to the review of the technical accounting for settlement of tranche liabilities. Specifically, in connection with our Series A preferred stock financing in 2019, we recorded a correcting adjustment to increase other non-operating expense for the change in fair value of the Series A preferred tranche liability after we initially recorded the amount as a deemed dividend. There were and have been no other tranche liabilities after the settlement of this liability in February 2019.

Although we believe that we have remediated this material weakness by hiring additional accounting and financial reporting personnel and have not identified any material weaknesses in connection with the finalization of our consolidated financial statements as of and for the year ended December 31, 2022, we cannot assure you that we will not identify other material weaknesses in the future.

Furthermore, we may not have identified all material weaknesses, and our current controls and any new controls that we develop may become inadequate because of changes in personnel or conditions in our business or otherwise. Accordingly, we cannot assure you that any future material weaknesses will not result in a material misstatement of our consolidated financial statements and/or our failure to meet our public reporting obligations. In addition, if we and/or our independent registered public accounting firm are unable to conclude that our internal control over financial reporting is

effective in the future, investor confidence in the accuracy and completeness of our consolidated financial statements would be adversely affected, which could significantly harm our business and the value of our common stock.

General Risk Factors

If we fail to maintain proper and effective internal controls over financial reporting, our ability to produce accurate and timely consolidated financial statements could be impaired.

Pursuant to Section 404, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with this filing of an Annual Report on Form 10-K with the SEC and our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we will need to implement additional financial and management controls, reporting systems and procedures, and hire additional accounting and finance staff.

We cannot assure you that there will not be future material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The Nasdaq Stock Market, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act, and we must maintain disclosure controls and procedures designed to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement, causing us to fail to make a required related party transaction disclosure or identify a potential conflict of interest. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

The market price of our common stock may be volatile, which could result in substantial losses for investors.

The market price of our common stock may be volatile and may fluctuate substantially as a result of a variety of factors, many of which are beyond our control. Some of the factors that may cause the market price of our common stock to fluctuate are listed below and other factors described in this "Risk Factors" section:

- the timing and results of nonclinical studies and clinical trials for our product candidates;
- failure or discontinuation of any of our product development and research programs;
- the success of existing or new competitive product candidates or technologies;
- results of clinical trials or regulatory approvals of our competitors;
- commencement or termination of collaborations for our product development and research programs;
- regulatory or legal developments in the United States and other countries;
- the recruitment or departure of key personnel;
- developments or disputes including those concerning patent applications, issued patents, or other proprietary rights;
- the impact of the COVID-19 pandemic on our business and on global economic conditions;

- labor discord or disruption, geopolitical events, social unrest, war, including repercussions of the recent military conflict between Russia and Ukraine, tensions in U.S.-China relations, terrorism, political instability, acts of public violence, boycotts, hostilities and social unrest and other health pandemics;
- the level of expenses related to any of our research programs or clinical development programs;
- actual or anticipated changes in our estimates as to our financial results or development timelines;
- whether our financial results, forecasts and development timelines meet the expectations of securities analysts or investors;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- market conditions in the healthcare sector;
- general economic, industry and market conditions beyond our control, such as inflationary pressures, other macroeconomic factors and associated economic downturn; and
- the other factors described in this "Risk Factors" section.

In recent years, stock markets in general, and the market for biotechnology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors have affected and may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

If securities or industry analysts do not publish research or reports about our business, or if they publish negative or neutral evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts covering our business initiate coverage with a neutral or sell rating or downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Sales of a substantial number of shares of our common stock by our existing stockholders could cause the price of our common stock to decline.

At any time, sales of a substantial number of shares of our common stock in the public market could occur, or there could be a perception in the market that the holders of a large number of shares of common stock intend to sell shares, and any such event could reduce the market price of our common stock. As of December 31, 2022, we have 249,567,343 shares of common stock outstanding, with no shares of restricted stock awards outstanding that are subject to vesting requirements. Substantially all of the shares of our common stock outstanding and shares issued upon the exercise of stock options outstanding under our equity incentive plans, subject to applicable securities law restrictions and excluding shares of restricted stock that will remain unvested, may be able to be sold in the public market.

Moreover, holders of shares of our common stock will have rights, subject to conditions, to require us to file registration statements with the SEC covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or our products.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing securities issued in any such transactions. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of any future offerings. In August 2022, we entered into an Equity Distribution Agreement pursuant to which we may offer and sell, from time to time, up to $200.0 million in shares of our common stock. To the

extent that we raise additional capital through the sale of equity or debt securities, including pursuant to the Equity Distribution Agreement, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships, alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or our products, or grant licenses on terms unfavorable to us. Certain of the foregoing transactions may require us to obtain stockholder approval, which we may not be able to obtain.

We are no longer an "emerging growth company", and the reduced reporting requirements applicable to "emerging growth companies" will no longer apply, which will increase our costs as a result of being a public company and demands on management.

Effective December 31, 2022, we are no longer classified as an "emerging growth company" as defined in the JOBS Act. As such, we will incur significant additional expenses that we did not previously incur in complying with the Sarbanes-Oxley Act and rules implemented by the SEC. For instance, the cost of compliance with Section 404 has required, and will continue to require, us to incur substantial accounting expense and expend significant management time on compliance-related issues as we implement additional corporate governance practices and comply with reporting requirements, which could divert management attention and adversely affect our business, operating results and financial condition. Moreover, if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

Furthermore, investor perceptions of our company may suffer if, in the future, material weaknesses are found, and this could cause a decline in the market price of our stock. Irrespective of compliance with Section 404, any failure of our internal control over financial reporting could have a material effect on our stated operating results. If we are unable to implement these changes effectively or efficiently, it could harm our operations, financial reporting or financial results and could result in an adverse opinion on internal control from our independent registered public accounting firm.

In addition, as a "large accelerated filer," we will be required to hold a say-on-pay vote and a say-on-frequency vote at our 2023 annual meeting of stockholders. As a result, we expect that we will require additional attention from management with respect to our disclosures and will incur increased costs, which could include higher legal fees, accounting fees, consultant fees and fees associated with investor relations activities, among others, and, as a result, our business, operating results and financial condition could be adversely affected.

Future acquisitions, strategic investments, partnerships or alliances could be difficult to identify and integrate, divert the attention of management, disrupt our business, dilute stockholder value and adversely affect our operating results and financial condition.

We may in the future seek to acquire or invest in businesses, products or technologies that we believe could complement or expand our technology platforms, enhance our technical capabilities, or otherwise offer growth opportunities. The pursuit of potential acquisitions or strategic investments may divert the attention of management and cause us to incur various expenses in identifying, investigating and pursuing suitable acquisitions or investments, whether or not such transactions are completed. In addition, we have only limited experience in acquiring or investing in other businesses, and we may not successfully identify desirable targets, or if we acquire additional businesses, we may not be able to integrate them effectively following the acquisition. Acquisitions could also result in dilutive issuances of equity securities or the incurrence of debt, as well as unfavorable accounting treatment and exposure to claims and disputes by third parties, including intellectual property claims. We also may not generate sufficient financial returns to offset the costs and expenses related to any acquisitions. In addition, if an acquired business fails to meet our expectations, our business, operating results and financial condition may suffer.

The requirements of being a public company require our management to devote substantial time to compliance initiatives and corporate governance practices and could divert management's attention and strain our resources.

As a public company, we incur and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. Section 404, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements and rules of The Nasdaq Stock Market LLC (Nasdaq Listing Rules) and other applicable U.S. rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We continue to need to hire additional accounting,

finance and other personnel in connection with our efforts to comply with the requirements of being a public company, and our management and other personnel will continue to need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements have and will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, the rules and regulations applicable to us as a public company have made it more expensive for us to obtain director and officer liability insurance. We cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under the Tax Cuts and Jobs Act of 2017 (the Tax Act), as modified by the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act), our net operating losses (NOLs) generated in tax years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the Tax Act or the CARES Act. In addition, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended (the Code), if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. We may have experienced ownership changes in the past, including as a result of our IPO, and may experience future ownership changes as a result of subsequent shifts in our stock ownership (some of which may be outside our control). As a result, our ability to use our pre-change NOLs and tax credits to offset post-change taxable income, if any, could be subject to limitations. Similar provisions of state tax law may also apply. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California recently imposed limits on the usability of California state NOLs and tax credits to offset California taxable income in tax years beginning after December 31, 2019 and before January 1, 2022. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and tax credits.

Our business and operations would suffer in the event of computer system failures or security breaches.

Our internal computer systems, and those of our partners, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We exercise little or no control over these third parties, which increases our vulnerability to problems with their systems. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or inappropriate disclosure of confidential or proprietary information, we could incur liability, the further development of our product candidates could be delayed and our business could be otherwise adversely affected.

While we have not experienced any material system failure, accident or security breach to date, we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs, and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Indemnity provisions in various agreements potentially expose us to substantial liability for intellectual property infringement, data protection and other losses.

Our agreements with third parties may include indemnification provisions under which we agree to indemnify them for losses suffered or incurred as a result of claims of intellectual property infringement or other liabilities relating to

or arising from our contractual obligations. Large indemnity payments could harm our business and financial condition. Although we normally contractually limit our liability with respect to such obligations, we may still incur substantial liability. Any dispute with a third party with respect to such obligations could have adverse effects on our relationship with that third party and relationships with other existing or new partners, harming our business.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

California

Our current corporate headquarters are located in South San Francisco, California, where we lease approximately 108,000 square feet of office and laboratory space, pursuant to a lease agreement that commenced in February 2020 and expires in March 2031.

Washington

We lease approximately 34,000 square feet of office and laboratory space in Seattle, Washington, pursuant to a lease agreement that commenced in January 2019 and expires in December 2028. We lease approximately 73,000 square feet of manufacturing, office and laboratory space in Bothell, Washington, pursuant to a lease agreement that commenced in February 2020 and expires in May 2030.

We believe that these existing facilities will be adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

From time to time, we have been or may become involved in material legal proceedings or be subject to claims arising in the ordinary course of our business. For example, although not material to our operations, in February 2021 we filed a demand for arbitration to, among other things, seek rescission of the agreements we entered into with PACT in June 2020 and recover the consideration paid to PACT thereunder. An arbitration hearing occurred in March 2022 and April 2022. In October 2022, we entered into a settlement agreement with PACT to resolve the outstanding legal dispute, in connection with which we also entered into a stock purchase agreement for the issuance of PACT's Series D convertible preferred stock in exchange for the tender of previously acquired PACT Series C-1 convertible preferred stock and resolution of the arbitration. The acquisition of PACT's Series D convertible preferred stock, which are non-voting, have limited conversion rights and carry no right to appoint directors, resulted in our ownership increasing to approximately 80% of PACT's fully diluted shares outstanding. The settlement agreement also included the termination of the PACT Commitment Agreement to jointly develop a next generation anti-cancer T-cell therapy against solid tumors.

We are currently not party to any legal proceedings material to our operations or of which any of our property is the subject, nor are we aware of any such proceedings that are contemplated by a government authority.

Regardless of outcome, any such proceedings or claims is subject to inherent uncertainties and can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock has traded on the Nasdaq Global Select Market under the symbol "LYEL" since June 17, 2021. Prior to that date, there was no public trading market for our common stock.

Holders

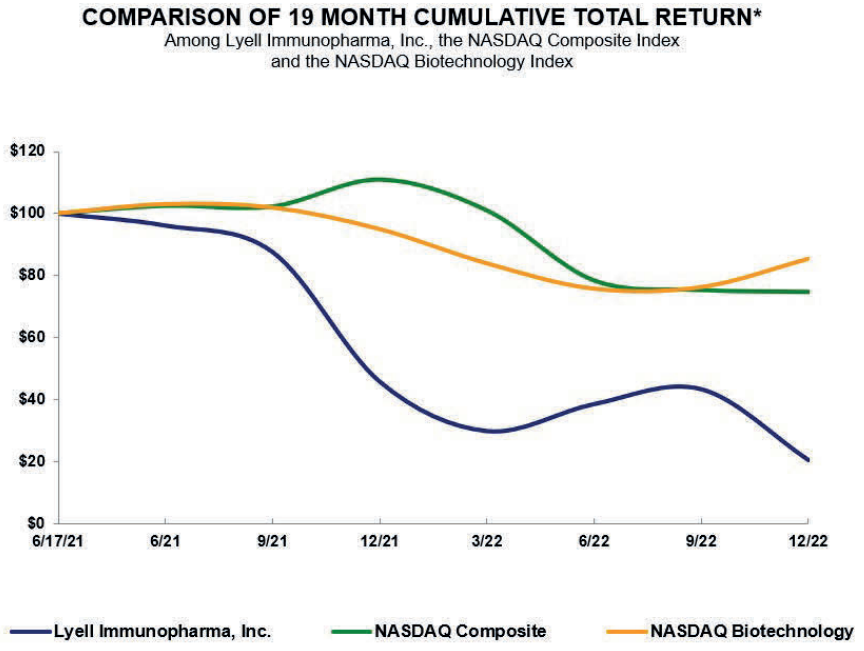
On February 24, 2023, there were 63 holders of record of our common stock. The number of record holders is based upon the actual number of holders registered on our books at such date and does not include holders of shares in "street names" or persons, partnerships, associations, corporations or other entities identified in security position listings maintained by depository trust companies.

Dividends

Since inception, we have not paid dividends on our common stock. We currently intend to retain all future earnings, if any, for use in our business and currently do not plan to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors.

Stock Performance Graph

The following stock performance graph compares the value of an investment in (i) our common stock, (ii) Nasdaq Composite Index and (iii) Nasdaq Biotechnology Index for the period from June 17, 2021 (the date our common stock commenced trading on the Nasdaq Global Select Market) through December 31, 2022. The figures represented below assume an investment of $100 in our common stock at the closing price on June 17, 2021 and in the Nasdaq Composite Index and Nasdaq Biotechnology Index on June 17, 2021 and the reinvestment of any dividends into shares of common stock. However, no dividends have been declared on our common stock to date. The comparisons in the table are required by the Securities and Exchange Commission and are not intended to forecast or be indicative of possible future performance of our common stock.



The above Stock Performance Graph and related information shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission nor shall such information be incorporated by reference into any

future filing under the Securities Act or the Exchange Act, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

Unregistered Sales of Equity Securities

None.

Repurchases of Equity Securities

None.

Use of Proceeds from our Initial Public Offering of Common Stock

In June 2021, we completed our initial public offering (IPO), pursuant to which we issued and sold 25,000,000 shares of our common stock at price to the public of $17.00 per share. The shares were registered pursuant to a registration statement on Form S-1 (File No. 333-256470) that was declared effective on June 16, 2021. As a result of our IPO, we raised a total of approximately $391.8 million in net proceeds after deducting underwriting discounts and commissions of $29.8 million and offering expenses of $3.4 million. Goldman Sachs & Co. LLC, BofA Securities, J.P. Morgan and Morgan Stanley acted as joint book-running managers for the IPO. Upon receipt, the net proceeds from our IPO were held in cash, cash equivalents and investments. No payments were made from our net proceeds directly or indirectly to our officers or directors, to persons owning 10% or more of any class of our equity securities or to any of our affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for services on our board. We are holding a significant portion of the balance of the net proceeds from the offering in money market funds and short-term investments.

The proceeds from the IPO have been used to fund ongoing operations, including the development of our product candidates and our clinical trials and research programs, and for working capital and general corporate purposes. There has been no material change in the planned use of proceeds from the IPO from that described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on June 21, 2021 (the Prospectus). We cannot predict with certainty all of the particular uses for the net proceeds from our IPO, or the amounts that we will actually spend on the uses set forth in the Prospectus and above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to access additional financing, the relative success and cost of our research, nonclinical and clinical development programs and whether we are able to enter into future collaboration and licensing arrangements. As a result, our management will continue to have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from our IPO.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. This discussion and analysis and other parts of this Annual Report on Form 10-K contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives and expectations for our business. Our actual results and the timing of selected events could differ materially from those described in or implied by these forward-looking statements as a result of several factors, including those set forth in the section titled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. See also the section titled "Special Note Regarding Forward-Looking Statements."

This section under Management's Discussion and Analysis of Financial Condition and Results of Operations generally discusses 2022 and 2021 items and year-to-year comparisons between 2022 and 2021. Discussions of 2020 items and year-to-year comparisons between 2021 and 2020 that are not included in this Annual Report on Form 10-K can be found in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021.

Overview

We are a clinical-stage cell therapy company advancing a pipeline of product candidates for patients with solid tumors utilizing our proprietary *ex vivo* genetic and epigenetic T-cell reprogramming technologies. Our investigational therapies use the patient's own cells as the starting point to generate highly tumor-reactive, longer-lasting functional T cells with enhanced ability to defeat solid tumors. Our innovative reprogramming technologies address what we believe are the primary barriers that limit consistent and long-lasting responses to T-cell therapy in solid tumors: T-cell exhaustion and lack of durable stemness. Our technologies are designed to generate T cells with the ability to persist and self-renew while driving durable tumor cytotoxicity, even in the setting of an immunosuppressive tumor microenvironment. The goal is for our technologies to provide patients with T cells that are potent and long-lasting enough to achieve durable antitumor responses. Furthermore, our technologies can be applied in a target agnostic manner to multiple T-cell modalities, including chimeric antigen receptor (CAR), tumor-infiltrating lymphocytes (TIL) and T-cell receptor (TCR) therapies.

We apply our technologies with the aim to develop T-cell therapies with improved durable clinical outcomes. Our growing pipeline of promising cell product candidates targets solid tumor indications with large unmet needs that are collectively responsible for approximately 180,000 deaths in the US annually. Each of our programs provide opportunities to expand into additional indications beyond the patient populations we are initially targeting.

For additional information regarding our business, see "Business" in Part I, Item 1 of this Annual Report on Form 10-K.

Pipeline Programs and Operational Updates

We are advancing four wholly-owned product candidates; two product candidates, LYL797 and LYL845, are in Phase 1 clinical development and two additional product candidates, LYL119 and a TIL product candidate incorporating novel genetic and epigenetic reprogramming technologies, are in preclinical development.

LYL797 – A ROR1 CAR T-cell product candidate genetically reprogrammed using c-Jun and epigenetically reprogrammed using our proprietary Epi-R manufacturing protocol, designed for differentiated potency and durability

- Enrollment in the Phase 1 clinical trial of LYL797 is ongoing. Initial clinical data from the Phase 1 trial of LYL797 are expected in the first half of 2024.
- Presented nonclinical data at the American Association of Cancer Research 2022 Annual Meeting characterizing LYL797 and demonstrating that our c-Jun overexpression and Epi-R reprogramming technologies can overcome barriers of T-cell exhaustion and lack of durable stemness in engineered T cells using a set of *in vitro* and *in vivo* models, including an aggressive syngeneic mouse tumor model and a xenograft lung cancer model.
- Presented nonclinical data demonstrating LYL797 showed improved expansion and anti-tumor activity and prolonged survival compared to conventional ROR1 CAR T cells in an established human ROR1-positive H1975 mouse xenograft model at the American Society of Gene and Cell Therapy Annual Meeting.

LYL119 – An innovative ROR1 CAR T-cell product designed for enhanced cytotoxicity

- LYL119 incorporates four of our stackable reprogramming technologies, including two novel technologies – a genetic knockout of NR4A3 and Stim-R. These technologies, which are complementary to c-Jun and Epi-R, are designed to further improve the anti-tumor potency and durability of T-cells.
- An IND for LYL119 is expected to be submitted in the first half of 2024.
- Presented nonclinical data demonstrating that the combination of two genetic reprogramming technologies, NR4A3 gene knockout and c-Jun overexpression, enhances the functional activity of ROR1 CAR T cells as shown 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* at The Society for Immunotherapy of Cancer 2022 Annual Meeting (SITC 2022).
- Presented nonclinical data at SITC 2022 demonstrating that our proprietary Stim-R epigenetic reprogramming technology, which enables precise control and optimized delivery of activation molecules during T-cell production, generates potent CAR T-cell product candidates with increased cell proliferation and persistence, as well as improved tumor control *in vivo*.

LYL845 – A novel epigenetically reprogrammed TIL product candidate designed for differentiated potency and durability

- Announced clearance of the IND for LYL845 in October 2022; enrollment in the Phase 1 clinical trial for LYL845 is ongoing. Initial clinical data from the Phase 1 trial of LYL845 are expected in 2024.
- Presented nonclinical data at SITC 2022 demonstrating the ability of Lyell's Epi-R technology to successfully expand TIL in both hot and cold tumors and to retain qualities linked with anti-tumor functionality and improved outcomes in previous TIL clinical trials. These qualities present in our Epi-R TIL include a greater proportion of CD8+ T cells, enrichment for T cells with stem-like profiles, better metabolic fitness and preserved polyclonality compared to control TIL preparations.
- Presented bioinformatic analyses, including comprehensive analyses of transcriptomic profiles, polyclonality and prediction of tumor-reactive T cell clones in our LYL845 product candidate, at SITC 2022. These analyses demonstrated that LYL845 expanded at clinical scale using Epi-R technology remained highly polyclonal and preserved approximately 94% of the predicted tumor reactive clones. Further, the preserved predicted tumor reactive clones in LYL845 have increased stemness and reduced exhaustion-associated genes compared to TIL products derived from the standard process.

Corporate and Operational Updates

- In December, Lynn Seely, M.D., a member of the company's board since May 2021 and former President and CEO of Myovant Sciences, was named President and CEO. Dr. Seely has extensive biopharmaceutical leadership experience with a track record of success building companies and developing new medicines in oncology and women's health.
- In September, Rahsaan W. Thompson was named Chief Legal Officer. Mr. Thompson is a biopharmaceutical industry veteran with more than 20 years of experience with development stage and commercial companies.
- In January, Gary Lee, Ph.D. was named Chief Scientific Officer. Dr. Lee is a veteran biotech leader with more than a decade of experience heading translational cell and gene therapy programs.

Macroeconomic Environment

Our business and operations may be affected by worldwide economic conditions, which may continue to be impacted by global macroeconomic challenges such as the effects of the ongoing geopolitical conflicts in Ukraine, tensions in U.S.-China relations, the COVID-19 pandemic, uncertainty in the markets and inflationary trends. Fiscal year 2022 was marked by significant market uncertainty, increasing inflationary pressures, supply constraints and ongoing effects from the COVID-19 pandemic. These market dynamics may continue into 2023 and these and similar adverse market conditions may negatively impact our business.

In particular, as the global COVID-19 pandemic and its effects continue to evolve, the extent of the impact of the COVID-19 pandemic on our business, operations and development timelines and plans remains uncertain and will continue to depend on certain developments, including the duration and spread of the outbreak, other next-level effects and the impact on our CROs, contract manufacturing organizations, clinical sites and other third parties with whom we do business, as well as the impact on regulatory authorities and our key scientific and management personnel.

There can be no assurance that we will be able to avoid materially adverse impacts from the effects of the COVID-19 pandemic. The effects of the COVID-19 pandemic may continue to negatively impact healthcare and hospital resources, including both front-line and administrative staff, which may delay enrollment in our current and planned clinical trials. Some patients may not be able to comply with clinical trial protocols due to potential quarantines, lack of healthcare support or potential interruptions of healthcare services, and we may be unable to obtain blood samples for testing. For example, limitations or modifications in surgery scheduling for oncology patients at collaborating institutions has limited and may continue to limit supply of patient tumor samples that we use in our research.

For a further discussion of trends, uncertainties and other factors that could impact our operating results, see the section entitled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

License, Collaboration and Success Payment Agreements

For a detailed description of our license, collaboration and success payment agreements, see the section titled "*Business—License, Collaboration and Success Payment Agreements*" in Part I, Item 1 of this Annual Report on Form 10-K and Notes 2 and 3 to our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Components of Results of Operations

Revenue

We have no products approved for sale and have never generated any revenue from product sales.

We have generated revenue primarily from the recognition of the upfront payment under the GSK Agreement, entered into in 2019 and amended in June 2020 and December 2021 with GSK. GSK terminated the GSK Agreement effective December 2022 and we do not expect further revenue from the collaboration. See Note 3, *License, Collaboration and Success Payment Agreements*, in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K for additional details regarding termination of the GSK Agreement.

In the future, we may generate additional revenue from other collaborations, strategic alliances, licensing agreements, product sales, or a combination of these.

Operating Expenses

Research and Development

To date, research and development expenses consist of costs incurred by us for the discovery and development of our technology platforms and product candidates, and include costs incurred in connection with strategic collaborations, costs to license technology, personnel-related costs, including stock-based compensation expense, facility and technology related costs, research and laboratory expenses, as well as other expenses, which include consulting fees and other costs. Upfront payments and milestones paid to third parties in connection with technology platforms that have not reached technological feasibility and do not have an alternative future use are expensed as incurred.

Research and development expenses also include non-cash expenses related to the change in the estimated fair value of the liabilities associated with our success payments granted to Fred Hutch and Stanford. See the subsection titled "Critical Accounting Policies and Estimates—*Success Payments*" below. Research and development expenses related to our success payment liabilities are unpredictable and may vary significantly from quarter-to-quarter and year-to-year due to changes in our assumptions used in the calculation.

We deploy our employee and infrastructure resources across multiple research and development programs for identifying and developing product candidates and establishing manufacturing capabilities. Due to the stage of development and number of ongoing programs and our ability to use resources across several programs, most of our research and development costs are not recorded on a program-specific basis. These include costs for personnel, laboratory and other indirect facility and operating costs.

Research and development activities account for a significant portion of our operating expenses. We anticipate that our research and development expenses will increase over the foreseeable future as we expand our research and development efforts including completing nonclinical studies, commencing planned clinical trials, conducting and completing current and planned clinical trials, seeking regulatory approval of our product candidates, identifying new product candidates and incurring costs to acquire and license technology platforms. A change in the outcome of any of these variables could mean a significant change in the costs and timing associated with the development of our product

candidates. Because we are early in our research and development efforts and beginning clinical development of our product candidates, and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the nonclinical development, clinical development and commercialization of product candidates or whether, or when, we may achieve profitability.

Our research and development expenses may vary significantly based on factors such as:

- the number and scope of nonclinical and IND-enabling studies;
- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates;
- the extent to which we establish additional collaboration or license agreements; and
- whether we choose to partner any of our product candidates and the terms of such partnership.

A change in the outcome of any of these variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates. We may obtain unexpected results from our nonclinical studies and clinical trials.

General and Administrative

General and administrative costs include personnel-related expenses, including stock-based compensation expense for personnel in executive, legal, finance and other administrative functions, legal costs, transaction costs related to collaboration and licensing agreements, as well as fees paid for accounting and tax services, consulting fees and facilities costs not otherwise included in research and development expenses. Legal costs include those related to corporate, dispute and patent matters.

We anticipate that our general and administrative expenses will increase over the foreseeable future to support our continued research and development activities, operations generally, future business development opportunities, consulting fees, as well as due to the increased costs of operating as a public company such as costs related to accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs and investor and public relations costs.

Other Operating Income, Net

Other operating income, net consists primarily of service and occupancy fees received associated with subleases as well as losses on the retirement of property and equipment.

Interest Income, Net

Interest income, net consists primarily of interest earned on our cash, cash equivalents and marketable securities balances.

Other Income (Expense), Net

Other income (expense), net consists primarily of a gain to record the PACT Series D convertible preferred shares, in addition to changes in the fair value of an equity warrant investment held.

Impairment of Other Investments

Impairment of other investments consists of a reduction in the value of certain other investments.

Deemed Dividends Upon Repurchase of Convertible Preferred Stock

Deemed dividends upon repurchase of convertible preferred stock consists of the amount by which the cash paid for the repurchase of convertible preferred stock exceeded the carrying value of such convertible preferred stock. Upon the closing of our IPO, all our convertible preferred stock was converted into our common stock.

Results of Operations

Years Ended December 31, 2022, 2021 and 2020

The following table summarizes our results of operations for the periods presented (in thousands):

	Year Ended December 31,			Change	
	2022	2021	2020	2022 vs 2021	2021 vs 2020
Revenue	$ 84,683	$ 10,650	$ 7,756	$ 74,033	$ 2,894
Operating expenses:					
Research and development	159,188	138,693	182,243	20,495	(43,550)
General and administrative	117,307	89,057	46,881	28,250	42,176
Other operating income, net	(4,754)	(2,324)	(9,431)	(2,430)	7,107
Total operating expenses	271,741	225,426	219,693	46,315	5,733
Loss from operations	(187,058)	(214,776)	(211,937)	27,718	(2,839)
Interest income, net	7,053	1,165	5,939	5,888	(4,774)
Other income (expense), net	1,887	(161)	1,526	2,048	(1,687)
Impairment of other investments	(5,000)	(36,447)	—	31,447	(36,447)
Total other income (loss), net	3,940	(35,443)	7,465	39,383	(42,908)
Net loss	(183,118)	(250,219)	(204,472)	67,101	(45,747)
Deemed dividends upon repurchase of convertible preferred stock	—	—	(3,582)	—	3,582
Net loss attributed to common stockholders	$ (183,118)	$ (250,219)	$ (208,054)	$ 67,101	$ (42,165)

Revenue

Revenue was $84.7 million and $10.7 million for the years ended December 31, 2022 and 2021, respectively, primarily related to the recognized portion of the upfront license fee pursuant to the GSK Agreement. The increase of $74.0 million was primarily related to $83.6 million in revenue adjustments driven by the mutual agreement with GSK to conclude certain research activities in June 2022 and GSK's subsequent termination of the GSK Agreement, effective December 2022, both of which resulted in changes to the measure of proportional cumulative performance. The revenue increase was offset by a decrease of $9.6 million due primarily to fewer research and development activities under the GSK Agreement for the year ended December 31, 2022. See Note 3, *License, Collaboration and Success Payment Agreements* in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8, of this Annual Report on Form 10-K for additional information about the termination of the GSK Agreement.

Research and Development Expenses

The following table summarizes the components of our research and development expenses for the periods presented (in thousands):

	Year Ended December 31,			Change	
	2022	2021	2020	2022 vs 2021	2021 vs 2020
Personnel	$ 70,483	$ 60,499	$ 54,112	$ 9,984	$ 6,387
Facilities and technology	52,153	39,092	24,560	13,061	14,532
Collaborations, research activities and outside services	41,682	35,389	98,234	6,293	(62,845)
Success payments	(5,130)	3,713	5,337	(8,843)	(1,624)
Total research and development expenses	$ 159,188	$ 138,693	$ 182,243	$ 20,495	$ (43,550)

Research and development expenses were $159.2 million and $138.7 million for the years ended December 31, 2022 and 2021, respectively. The increase of $20.5 million was primarily due to an increase of $13.1 million in facilities and technology costs, primarily related to increased infrastructure to support our expansion in research and development, manufacturing capabilities and associated headcount growth; an increase of $10.0 million in personnel-related expenses, that was primarily related to an increase in headcount to expand our research, development and manufacturing capabilities; an increase of $6.3 million in collaboration, research activities and outside services primarily driven by an increase of $5.1 million in research and laboratory costs principally due to clinical trials; and an increase of $3.3 million in professional services offset by a reduction of $2.2 million in collaboration and license fees; partially offset by a decrease of $8.8 million in success payment expenses associated with our Fred Hutch and Stanford success payment liabilities, primarily driven by the decrease in the per share fair value of our common stock.

General and Administrative Expenses

General and administrative expenses were $117.3 million and $89.1 million for the years ended December 31, 2022 and 2021, respectively. The increase of $28.3 million was primarily due to an increase of $18.3 million in stock-based compensation expense, primarily related to award modifications and new awards granted. Additionally, outside services increased by $5.1 million due primarily to higher legal expenses and corporate expenses increased $3.9 million primarily due to costs associated with operating as a public company.

Other Operating Income, Net

Other operating income, net was $4.8 million and $2.3 million for the years ended December 31, 2022 and 2021, respectively. The increase of $2.4 million was due primarily to sublease income and operating fees related to our subleases.

Interest Income, Net

Interest income, net was $7.1 million and $1.2 million for the years ended December 31, 2022 and 2021, respectively. The increase of $5.9 million was primarily driven by higher interest rates in 2022.

Other Income (Expense), Net

Other income (expense), net was $1.9 million and $(0.2) million for the years ended December 31, 2022 and 2021, respectively. The increase of $2.0 million consisted primarily of a gain of $2.9 million to record the estimated fair value of PACT Series D convertible preferred shares acquired, offset by a decrease of $1.1 million in the fair value of an equity warrant investment held.

Impairment of Other Investments

For the year ended December 31, 2022, the $5.0 million impairment of other investments consisted of the full impairment of one of our other investments. For the year ended December 31, 2021, the $36.4 million impairment of other investments consisted of the full impairment of our investment in PACT Series C-1 convertible preferred stock. See Note 5, *Other Investments*, in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8, of this Annual Report on Form 10-K for additional information.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have funded our operations primarily through the sale and issuance of convertible preferred stock, the sale of common stock in connection with our IPO and business development activities. As of December 31, 2022, we had $710.3 million in cash, cash equivalents and marketable securities. Since our inception, we have incurred significant operating losses. We have not yet commercialized any product candidates and we do not expect to generate revenue from sales of any product candidates for a number of years, if ever. We had an accumulated deficit of $767.5 million as of December 31, 2022. From June 29, 2018 (inception) through December 31, 2022, we raised an aggregate of $1,405.7 million in gross proceeds from the sales of our convertible preferred stock and the IPO.

On August 4, 2022, we entered into an Equity Distribution Agreement (the Equity Distribution Agreement) with Goldman Sachs & Co. LLC (Goldman Sachs) and BofA Securities, Inc. (BofA, and together with Goldman Sachs, the Agents) with respect to an at-the-market offering program. In accordance with the terms of the Equity Distribution Agreement, we may offer and sell from time to time through the Agents shares of our common stock having an aggregate offering amount of up to $200.0 million (the Placement Shares). Sales of the Placement Shares, if any, will be made at prevailing market prices on Nasdaq at the time of sale, or as otherwise agreed with the Agents, by any method permitted by law deemed to be an "at-the-market offering" as defined in Rule 415 of the Securities Act. We will pay commissions to the Agents of up to 3.0% of the gross proceeds of the sale of the Placement Shares sold under the Equity Distribution Agreement and reimburse the Agents for certain expenses. Neither us nor the Agents are obligated to sell any shares and to date, we have not made any sales under the Equity Distribution Agreement.

Future Funding Requirements

We expect to incur additional losses in the foreseeable future as we conduct and expand our research and development efforts, including conducting nonclinical studies and clinical trials, developing new product candidates, establishing internal manufacturing capabilities and funding our operations generally. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to meet our working capital and capital expenditure needs into 2026. However, we anticipate that we will need to raise additional capital in the future to fund our operations, including further development of our product candidates and the commercialization of any approved product candidates. In addition, we regularly consider fund-raising opportunities and may decide, from time to time, to raise additional capital, including pursuant to the Equity Distribution Agreement, based on various factors, including market conditions and our plans of operation. We are subject to the risks typically related to the development of new products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

Our future capital requirements will depend on many factors, including:

- the scope, timing, progress, costs and results of discovery, nonclinical development and clinical trials for our current and future product candidates;
- the number of clinical trials required for regulatory approval of our current and future product candidates;
- the costs, timing and outcome of regulatory review of any of our current and future product candidates;
- the cost of manufacturing clinical and commercial supplies of our current and future product candidates;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- further investment to build additional manufacturing facilities or expand the capacity of our existing ones;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- our ability to maintain existing, and establish new, collaborations, licenses, product acquisitions or other strategic transactions and the fulfillment of our financial obligations under any such agreements, including the timing and amount of any success payment, future contingent payments, milestone, royalty or other payments due under any such agreement;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- expenses to attract, hire and retain skilled personnel;

- the costs of operating as a public company;
- addressing any potential interruptions or delays resulting from factors related to the COVID-19 pandemic;
- addressing or responding to any potential disputes or litigation; and
- the extent to which we acquire or invest in businesses, products and technology platforms.

Until such time as we complete nonclinical and clinical development and receive regulatory approval of our product candidates and can generate significant revenue from product sales, if ever, we expect to finance our operations from the sale of additional equity or debt financings, or other capital which come in the form of strategic collaborations, licensing, or other arrangements. In the event that additional capital is required, we may not be able to raise it on terms acceptable to us, or at all. If we raise additional funds through the issuance of equity or convertible debt securities, including pursuant to the Equity Distribution Agreement, it may result in dilution to our existing stockholders. Debt financing or preferred equity financing, if available, may result in increased fixed payment obligations, and the existence of securities with rights that may be senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations. If we raise funds through strategic collaboration, licensing, or other arrangements, we may relinquish significant rights or grant licenses on terms that are not favorable to us. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the COVID-19 pandemic, actual or perceived changes in interest rates and economic inflation, and otherwise. If we are unable to raise additional capital when desired, our business, results of operations and financial condition would be adversely affected.

Material Cash Requirements

We continually evaluate our liquidity and capital resources to ensure that we can adequately and efficiently finance our operations. As of December 31, 2022, our material cash requirements consisted primarily of paying salaries and benefits, administering clinical trials, conducting research, improving our manufacturing capabilities, providing the technology and facilities necessary to support our operations, funding operating lease obligations and other payments related to our collaborative agreements. See Note 3, *License, Collaboration and Success Payment Agreements*, and Note 9, *Leases*, in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8, of this Annual Report on Form 10-K for additional information.

Cash Flows

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Net cash (used in) provided by:			
Operating activities	$ (169,555)	$ (126,249)	$ (160,874)
Investing activities	(11,540)	(121,573)	(273,516)
Financing activities	10,635	401,244	476,790
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (170,460)	$ 153,422	$ 42,400

Operating Activities

During the year ended December 31, 2022, net cash used in operating activities was $169.6 million, primarily reflecting our net loss of $183.1 million, a decrease of $82.0 million in net operating assets and liabilities primarily driven by a $84.7 million decrease in deferred revenue due to non-cash revenue recognized and a $2.0 million decrease in prepaid expenses, other current assets and other assets, offset by a $4.9 million increase in operating lease liabilities due primarily to tenant improvement allowances received. These decreases were partially offset by $95.6 million of non-cash expenses primarily related to stock-based compensation of $81.9 million, depreciation and amortization of $18.0 million and impairment of other investments of $5.0 million. Additionally, we recognized decreases for the $5.1 million change in the fair value of success payment liabilities and $2.9 million for the non-cash adjustment of the gain on other investments.

During the year ended December 31, 2021, net cash used in operating activities was $126.2 million, consisting primarily of our net loss of $250.2 million, partially offset by certain non-cash items such as stock-based compensation expense of $62.2 million, impairment of other investments of $36.4 million, depreciation and amortization expense of $13.6 million and the change in fair value of success payment liabilities of $3.7 million. Additionally, net operating assets

and liabilities increased $4.0 million, which included an increase in operating lease liabilities due to tenant improvement allowances received of $13.3 million offset by the recognition of $10.5 million of revenue previously recorded as deferred revenue.

Investing Activities

During the year ended December 31, 2022, cash used in investing activities was $11.5 million, consisting of purchases of property and equipment of $24.3 million offset by net maturities, sales and purchases of marketable securities of $12.7 million. During the year ended December 31, 2021, cash used in investing activities was $121.6 million, consisting of net purchases of marketable securities of $56.1 million and capital expenditures of $65.5 million.

Financing Activities

During the year ended December 31, 2022, cash provided by financing activities was $10.6 million, consisting of $9.6 million in proceeds from the exercise of stock options and $1.5 million in proceeds from the employee stock purchase plan, partially offset by $0.5 million in taxes paid related to the net share settlement of equity awards. During the year ended December 31, 2021, cash provided by financing activities was $401.2 million, consisting of $391.8 million in net proceeds from the sale of our common stock in our IPO and $9.4 million in proceeds from the exercise of stock options.

Critical Accounting Policies and Significant Judgments and Estimates

Our audited consolidated financial statements are prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the audited consolidated financial statements, as well as the reported revenue and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K, we believe that the following accounting policies are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We recognize revenue from research services generally as services are provided while revenue from non-refundable upfront fees are recognized over time by measuring progress towards satisfaction of the relevant performance obligation using the input method (i.e., cumulative actual costs incurred relative to total estimated costs).

The estimation of measure of progress is complex, involves significant judgment and is affected by our estimates of the total costs required to complete the performance obligations including the total internal personnel costs and external costs to be incurred. Changes in these estimates can have a material effect on our revenue recognition.

For a further description of our revenue recognition, see Note 2, *Basis of Presentation and Significant Accounting Policies,* in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8, of this Annual Report on Form 10-K.

Success Payments

We are required to make success payments to Fred Hutch and Stanford based on increases in the per share market value of our common stock, payable in cash or cash equivalents or, at our discretion, publicly tradeable shares of our common stock. The success payments are accounted for under Accounting Standards Codification (ASC) 718, *Compensation – Stock Compensation*, and are initially recorded at fair value with a corresponding charge to research and development expense. The liabilities are marked to market at each balance sheet date with all changes in value recognized in research and development expense in the Consolidated Statements of Operations and Comprehensive Loss. Once their service periods are complete, the success payments will be accounted for under ASC 815, *Derivatives and Hedging*, and fair value changes will be recorded in other income (expense), net. We will continue to adjust the liabilities for changes in fair value until the earlier of the achievement or expiration of the success payment obligation. To determine the estimated fair value of the success payments, we use a Monte Carlo simulation model, which models the value of the liability based on several key variables that require judgment, including the expected fair value and volatility of our common stock, estimated term and number of valuation measurement dates.

Stock-based Compensation

Stock-based compensation cost is recognized for restricted stock awards ("RSAs"), restricted stock units ("RSUs"), employee stock purchases related to the Employee Stock Purchase Plan and stock options. Stock-based compensation cost is measured at the grant date based on the fair value of the award. The fair value of stock-based awards is recognized as an expense on a straight-line basis over the requisite service period, with forfeitures recognized as they occur.

We use the Black-Scholes model to determine the fair value of our options. The Black-Scholes option pricing model requires the use of assumptions, including stock price volatility, the expected life of stock options, risk-free interest rate and the fair value of the underlying common stock on the date of grant. Our restricted stock awards and restricted stock units are valued based on the fair market value of the award on the grant date.

Prior to the closing of our IPO, the fair value of the common stock underlying our stock-based awards was estimated on each grant date by our board of directors using significant judgment to estimate the fair value of our common stock, including considering our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies; and the lack of marketability of our common stock.

Valuation of Other Investments

We have non-marketable equity investments that are accounted for using the measurement alternative. Under the measurement alternative, the carrying value is measured at cost, less any impairment, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer. Determining whether an observed transaction is similar to a security within our portfolio requires judgment based on the rights and obligations of the investments. Recording upward and downward adjustments to the carrying value of our equity investments as a result of observable price changes requires quantitative assessments of the fair value of our investments using various valuation methodologies and involves the use of estimates.

We determine at the inception of each arrangement whether an investment or other interest is considered a variable interest entity (VIE). If the investment or other interest is determined to be a VIE, we evaluate whether we are considered the primary beneficiary. The primary beneficiary of a VIE is the party that meets both of the following criteria: (i) has the power to direct the activities that most significantly impact the VIE's economic performance; and (ii) has the obligation to absorb losses or the right to receive benefits from the VIE. For any investments in VIEs in which we are considered the primary beneficiary, the assets, liabilities and results of operations of the VIE would be included in our consolidated financial statements. As of December 31, 2022 and 2021, there were no VIEs for which we were the primary beneficiary.

Non-marketable equity investments are also subject to periodic impairment reviews. Our quarterly impairment analysis considers both qualitative and quantitative factors that may have a significant effect on the investment's fair value. Qualitative factors considered include the companies' financial and liquidity position, access to capital resources and the time since the last adjustment to fair value, among others. When indicators of impairment exist, we prepare quantitative assessments of the fair value of our equity investments using both the market and income approaches that require judgment and the use of estimates, including discount rates, investee revenues and costs, and comparable market data of private and public companies reasonably available, among others. When our assessment indicates that an impairment exists, we write down the investment to its fair value.

We performed a qualitative assessment of potential indicators of impairment for 2022 and determined that indicators existed for one of our other investments with a carrying amount of $5.0 million. While there was no single event or factor, we considered the underlying company's operating cash flow requirements over the next year and liquid asset balances to fund those requirements and the uncertainty regarding the underlying company's ability to raise funds as indicators of impairment. Due to these indicators, we assessed the valuation of the investment and determined the fair value to be negligible and the impairment to be other-than-temporary in nature. As a result, we recorded a $5.0 million impairment expense for the investment for the year ended December 31, 2022, which was recorded within impairment of other investments on the Consolidated Statement of Operations and Comprehensive Loss and as a reduction of the other investments on the Consolidated Balance Sheet.

In connection with the preparation of our financial statements for 2021, we performed a qualitative assessment of potential indicators of impairment and determined that indicators existed for our $36.4 million investment in PACT Series C-1 convertible preferred stock. While there was no single event or factor, we considered PACT's operating cash flow requirements over the next year and liquid asset balances to fund those requirements and their inability to raise funds as indicators of impairment. Due to these indicators, we assessed the valuation of our investment in PACT as of

December 31, 2021 and determined the fair value to be negligible and the impairment to be other-than-temporary in nature. As a result, we recorded a $36.4 million impairment of our PACT investment in the fourth quarter of 2021. The impairment charge was recorded within impairment of other investments on the Consolidated Statement of Operations and Comprehensive Loss and as a reduction of the other investments on the Consolidated Balance Sheet.

Recently Adopted and Recent Accounting Pronouncements

See Note 2, *Basis of Presentation and Significant Accounting Policies,* in the accompanying notes to our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K for information about recent accounting pronouncements, the timing of their adoption and our assessment, to the extent we have made one yet, of their potential impact on our financial condition or results of operations.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risks in the ordinary course of our business. Our primary risks include interest rate sensitivities.

Interest Rate Risk

We had cash equivalents of $107.8 million as of December 31, 2022, which consisted of money market funds and highly liquid investments purchased with original maturities of three months or less from the purchase date. We also had marketable securities of $586.7 million as of December 31, 2022. The primary objective of our investment activities is to preserve capital to fund our operations, and we currently do not hedge our interest rate risk exposure. Because our marketable securities are primarily short-term in duration, we believe that our exposure to interest rate risk is not significant, and a hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material effect on our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K. We had no debt outstanding as of December 31, 2022.

Foreign Currency Exchange Risk

All of our employees and operations are currently located in the United States and our expenses are generally denominated in U.S. dollars. We therefore are not currently exposed to significant market risk related to changes in foreign currency exchange rates. However, we have contracted with and may continue to contract with non-U.S. vendors who we may pay in their local currency. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not had a formal hedging program with respect to foreign currency. We believe a hypothetical 1% change in exchange rates during any of the periods presented would not have a material effect on our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and our clinical trial costs. We believe that inflation has not had a material effect on our audited consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K.

Item 8. Financial Statements and Supplementary Data

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To the Stockholders and the Board of Directors of Lyell Immunopharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Lyell Immunopharma, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

VIE Accounting Considerations for the PACT Transaction

Description of the Matter	As described in notes 2, 3, 5 and 6 to the consolidated financial statements, in October 2022, the Company entered into a settlement agreement with PACT Pharma, Inc. (PACT) to resolve their outstanding legal dispute. In connection with the settlement agreement, the parties entered into a stock purchase agreement, pursuant to which PACT issued shares of PACT's Series D convertible preferred stock, representing approximately 80% of PACT's fully diluted shares, to the Company in exchange for the Company's tender of its PACT Series C-1 convertible preferred stock and resolution of the arbitration. The Company consolidates a variable interest entity (VIE) if it has a variable interest, and it is the primary beneficiary. The primary beneficiary of a VIE has both: (i) the power to direct activities of the VIE that most significantly impact the VIE's economic performance and (ii) the obligation to absorb losses of the VIE that could potentially be significant to the VIE or the right to receive benefits from the VIE that could potentially be significant to the VIE. If the Company is not the primary beneficiary of a VIE, it accounts for its interest under other applicable GAAP, according to the nature of the investment. We identified the initial accounting for the PACT Series D convertible preferred shares as a critical audit matter as there was significant complexity and judgment by management in assessing whether the Company was the primary beneficiary. This in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and in evaluating the audit evidence obtained related to this assessment.
How We Addressed the Matter in Our Audit	To test the Company's accounting for its interest in PACT, we engaged in discussions with management regarding the governance of PACT and inspected transaction documents, including the settlement agreement, preferred stock purchase agreement, amended and restated voting rights agreement and PACT's amended and restated certificate of incorporation, assessed management's judgments and conclusions regarding the primary beneficiary determination, and evaluated the effectiveness of controls related to management's assessment.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.

San Mateo, California
February 28, 2023

Lyell Immunopharma, Inc.
Consolidated Balance Sheets
(in thousands, except per share amounts)

	As of December 31,	
	2022	2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 123,554	$ 293,828
Marketable securities	516,598	320,966
Prepaid expenses and other current assets	11,143	11,492
Total current assets	651,295	626,286
Restricted cash	280	466
Marketable securities, non-current	70,117	283,531
Other investments	44,924	47,001
Property and equipment, net	123,023	120,098
Operating lease right-of-use assets	43,242	46,541
Other non-current assets	4,680	3,483
Total assets	$ 937,561	$ 1,127,406
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,917	$ 3,207
Accrued liabilities and other current liabilities	28,755	29,057
Success payment liabilities	4,356	9,486
Deferred revenue[1]	—	4,988
Total current liabilities	37,028	46,738
Operating lease liabilities, non-current	63,168	66,650
Deferred revenue, non-current[2]	—	79,665
Other non-current liabilities	4,113	4,566
Total liabilities	104,309	197,619
Commitments and contingencies (Note 16)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000 shares authorized at December 31, 2022 and 2021, respectively; zero shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 500,000 shares authorized at December 31, 2022 and 2021, respectively; 249,567 and 242,738 shares issued and outstanding at December 31, 2022 and 2021, respectively	25	24
Additional paid-in capital	1,608,306	1,515,748
Accumulated other comprehensive loss	(7,599)	(1,623)
Accumulated deficit	(767,480)	(584,362)
Total stockholders' equity	833,252	929,787
Total liabilities and stockholders' equity	$ 937,561	$ 1,127,406

(1) Includes amounts from a related-party of zero and $4,988 as of December 31, 2022 and December 31, 2021, respectively.
(2) Includes amounts from a related-party of zero and $79,665 as of December 31, 2022 and December 31, 2021, respectively.

The accompanying notes are an integral part of these consolidated financial statements.

Lyell Immunopharma, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except per share amounts)

	Year Ended December 31,		
	2022	2021	2020
Revenue[(1)]	$ 84,683	$ 10,650	$ 7,756
Operating expenses:			
Research and development	159,188	138,693	182,243
General and administrative	117,307	89,057	46,881
Other operating income, net	(4,754)	(2,324)	(9,431)
Total operating expenses	271,741	225,426	219,693
Loss from operations	(187,058)	(214,776)	(211,937)
Interest income, net	7,053	1,165	5,939
Other income (expense), net	1,887	(161)	1,526
Impairment of other investments	(5,000)	(36,447)	—
Total other income (loss), net	3,940	(35,443)	7,465
Net loss	(183,118)	(250,219)	(204,472)
Other comprehensive loss:			
Net unrealized loss on marketable securities	(5,976)	(1,879)	(198)
Comprehensive loss	$ (189,094)	$ (252,098)	$ (204,670)
Net loss attributed to common stockholders:			
Net loss	$ (183,118)	$ (250,219)	$ (204,472)
Deemed dividends upon repurchase of convertible preferred stock	—	—	(3,582)
Net loss attributed to common stockholders	$ (183,118)	$ (250,219)	$ (208,054)
Net loss per common share, basic and diluted	$ (0.74)	$ (1.84)	$ (15.69)
Weighted-average shares used to compute net loss per common share, basic and diluted	247,080	135,918	13,258

(1) Includes related-party revenue of $84,653, $10,509 and $7,756 for the years ended December 31, 2022, 2021 and 2020, respectively.

The accompanying notes are an integral part of these consolidated financial statements.

Lyell Immunopharma, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2019	152,116	$ 519,163	11,181	$ 1	$ 18,108	$ 454	$ (129,671)	$ (111,108)
Issuance of Series C convertible preferred stock, net of $533 in issuance costs	42,905	492,467	—	—	—	—	—	—
Issuance of common stock to strategic partners	—	—	275	—	1,004	—	—	1,004
Issuance of common stock for asset acquisition	—	—	688	—	4,000	—	—	4,000
Issuance of common stock upon exercise of stock options	—	—	113	—	373	—	—	373
Stock-based compensation	—	—	5,345	1	33,260	—	—	33,261
Repurchase of convertible preferred stock	(547)	(662)	—	—	(3,582)	—	—	(3,582)
Repurchase of common stock	—	—	(2,032)	—	(11,806)	—	—	(11,806)
Other comprehensive loss	—	—	—	—	—	(198)	—	(198)
Net loss	—	—	—	—	—	—	(204,472)	(204,472)
Balance as of December 31, 2020	194,474	$ 1,010,968	15,570	$ 2	$ 41,357	$ 256	$ (334,143)	$ (292,528)
Proceeds from initial public offering, net of $33,198 in issuance costs	—	—	25,000	2	391,800	—	—	391,802
Conversion of convertible preferred stock to common stock	(194,474)	(1,010,968)	194,474	20	1,010,948	—	—	1,010,968
Issuance of common stock upon exercise of stock options	—	—	2,750	—	9,442	—	—	9,442
Stock-based compensation	—	—	4,944	—	62,201	—	—	62,201
Other comprehensive loss	—	—	—	—	—	(1,879)	—	(1,879)
Net loss	—	—	—	—	—	—	(250,219)	(250,219)
Balance as of December 31, 2021	—	$ —	242,738	$ 24	$ 1,515,748	$ (1,623)	$ (584,362)	$ 929,787
Issuance of common stock upon exercise of stock options	—	—	3,601	1	9,576	—	—	9,577
Issuance of common stock under employee stock purchase plan	—	—	475	—	1,519	—	—	1,519
Issuance of common stock in connection with restricted stock units, net of tax	—	—	153	—	(461)	—	—	(461)
Stock-based compensation	—	—	2,600	—	81,924	—	—	81,924
Other comprehensive loss	—	—	—	—	—	(5,976)	—	(5,976)
Net loss	—	—	—	—	—	—	(183,118)	(183,118)
Balance as of December 31, 2022	—	$ —	249,567	$ 25	$ 1,608,306	$ (7,599)	$ (767,480)	$ 833,252

The accompanying notes are an integral part of these consolidated financial statements.

Lyell Immunopharma, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (183,118)	$ (250,219)	$ (204,472)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	81,924	62,201	33,261
Depreciation and amortization expense	18,020	13,624	4,294
Impairment of other investments	5,000	36,447	—
Change in fair value of success payment liabilities	(5,130)	3,713	5,337
Gain on other investments	(2,923)	—	—
Lease expense, net of gain on lease remeasurement	(1,553)	911	3,181
Change in fair value of equity warrant	1,067	256	(1,323)
Net amortization and accretion on marketable securities	(930)	1,901	539
Loss (gain) on property and equipment disposals, net	103	1,210	(4,884)
Expense in connection with asset acquisition	—	—	3,529
Gain on net operating lease liability disposal	—	(308)	—
Changes in operating assets and liabilities:			
Prepaid expenses, other current assets and other assets	(1,968)	(6,987)	(1,388)
Accounts payable	667	91	(278)
Accrued liabilities and other current liabilities	(463)	4,542	6,120
Deferred revenue	(84,653)	(10,508)	(7,756)
Operating lease liabilities, non-current	4,855	13,202	2,966
Other non-current liabilities	(453)	3,675	—
Net cash used in operating activities	(169,555)	(126,249)	(160,874)
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchases of property and equipment	(24,276)	(65,504)	(51,481)
Purchases of marketable securities	(406,316)	(673,465)	(864,909)
Sales and maturities of marketable securities	419,052	617,396	686,322
Purchases of other investments	—	—	(43,448)
Net cash used in investing activities	(11,540)	(121,573)	(273,516)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from exercise of stock options	9,577	9,442	373
Proceeds from employee stock purchase plan	1,519	—	—
Taxes paid related to net share settlement of equity awards	(461)	—	—
Proceeds from initial public offering, net of issuance costs	—	391,802	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	—	492,467
Payments for the repurchase of common stock	—	—	(11,806)
Payments for the repurchase of convertible preferred stock	—	—	(4,244)
Net cash provided by financing activities	10,635	401,244	476,790
Net (decrease) increase in cash, cash equivalents and restricted cash	(170,460)	153,422	42,400
Cash, cash equivalents and restricted cash at beginning of period	294,294	140,872	98,472
Cash, cash equivalents and restricted cash at end of period	$ 123,834	$ 294,294	$ 140,872
Represented by:			
Cash and cash equivalents	$ 123,554	$ 293,828	$ 140,406
Restricted cash	280	466	466
Total	$ 123,834	$ 294,294	$ 140,872
SUPPLEMENTAL CASH FLOW INFORMATION			
Cash received for amounts related to tenant improvement allowances	$ 4,761	$ 13,295	$ 2,966
Cash paid for amounts included in the measurement of lease liabilities	$ 10,870	$ 8,546	$ 5,147
Non-cash investing and financing activities:			
Purchases of property and equipment included in accounts payable and accrued liabilities	$ 1,325	$ 4,605	$ 12,740
Remeasurement of operating lease right-of-use asset for lease modification	$ 31	$ 3,873	$ (8,958)
Acquisition of PACT Series D convertible preferred shares	$ 2,923	$ —	$ —
Conversion of convertible preferred stock to common stock upon closing of initial public offering	$ —	$ 1,010,968	$ —
Operating lease right-of-use assets obtained in exchange for lease obligations	$ —	$ —	$ 30,475
Other investments received for sale of assets	$ —	$ —	$ 6,000

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization

Lyell Immunopharma, Inc. (the "Company") was incorporated in Delaware in June 2018. The Company is a clinical-stage cell therapy company advancing a pipeline of therapies for patients with solid tumors utilizing our proprietary *ex vivo* genetic and epigenetic T-cell reprogramming technologies. The Company's primary activities since incorporation have been to develop T-cell therapies, perform research and development, enter into strategic collaboration and license arrangements, build manufacturing capabilities, enable manufacturing activities in support of its product candidate development efforts, acquire technology, organize and staff the Company, conduct business planning, establish its intellectual property portfolio, raise capital and provide general and administrative support for these activities.

Initial Public Offering

In June 2021, the Company successfully completed its initial public offering ("IPO") of its common stock. In connection with its IPO, the Company issued and sold 25,000,000 shares of common stock at an IPO price of $17.00 per share. The Company received $391.8 million in net proceeds, after deducting underwriting discounts and commissions of $29.8 million and offering expenses of $3.4 million. Upon the closing of the IPO, 194,474,431 shares of convertible preferred stock then outstanding converted into an equal number of shares of common stock. The related carrying value of the converted preferred stock of $1.0 billion was reclassified to common stock and additional paid in-capital.

2. Basis of Presentation and Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. All significant intercompany transactions and balances are eliminated in consolidation. Certain prior period amounts in the consolidated financial statements and accompanying notes have been reclassified to conform to the current period's presentation.

Liquidity and Management's Plan

The Company is currently working on long-term product candidates that involve experimental technologies. The product candidates may require several years and substantial expenditures to complete and ultimately may be unsuccessful. The Company plans to finance operations with available cash resources or from the issuance of equity or debt securities. The Company believes that its available cash, cash equivalents and marketable securities as of December 31, 2022 will be adequate to fund its operations at least through the next 12 months from the date these consolidated financial statements are issued.

Summary of Significant Accounting Policies

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with GAAP requires management to make judgments, estimates and assumptions that affect reported amounts and related disclosures. Specific accounts that require management estimates include, but are not limited to, stock-based compensation, valuation of success payments, valuation of other investments, revenue recognition and accrued expenses. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results could differ materially from those estimates.

In June 2022, the Company recorded adjustments to revenue related to changes in estimates in connection with the Collaboration and License Agreement, entered into in 2019 and amended in June 2020 and December 2021 ("GSK Agreement") with GlaxoSmithKline Intellectual Property (No. 5) Limited and Glaxo Group Limited (together, "GSK"). These changes in estimates were driven by the mutual agreement to conclude certain research activities in June 2022 and GSK's termination of the GSK Agreement, effective December 24, 2022, both of which resulted in changes to the measure of proportional cumulative performance. These adjustments increased revenue by $83.6 million, decreased net loss by $83.6 million and resulted in a $0.34 reduction in the Company's basic and diluted net loss per common share for the year ended December 31, 2022.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity that are excluded from net loss. For the years ended December 31, 2022, 2021 and 2020 this was comprised of net unrealized gains and losses on the Company's marketable securities.

Cash, Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments purchased with original maturities of three months or less from the purchase date to be cash equivalents. Cash equivalents consist primarily of amounts invested in commercial paper and money market accounts.

Restricted cash is cash held in bank accounts and is used as collateral for letters of credits issued in conjunction with the Company's lease agreements and collateral associated with the Company's corporate credit card program.

Marketable Securities

The Company generally invests its excess cash in investment grade short- to intermediate-term fixed income securities. Such investments are classified as available-for-sale and are carried at fair value, with the unrealized gains and losses reported as a component of comprehensive loss. Realized gains and losses on available-for-sale securities are included in other income (expense), net. The cost of investments sold is based on the specific-identification method. The Company classifies those investments that are not required for use in current operations and that mature in more than 12 months as non-current marketable securities in the accompanying consolidated balance sheets.

Each reporting period, the Company evaluates whether declines in fair value below carrying value are due to expected credit losses, as well as the Company's ability and intent to hold the investment until a forecasted recovery occurs. Expected credit losses are recorded as an allowance through other income (expense), net.

Valuation of Other Investments

The Company determines at the inception of each arrangement whether an investment or other interest is considered a variable interest entity ("VIE"). If the investment or other interest is determined to be a VIE, the Company evaluates whether it is considered the primary beneficiary. The primary beneficiary of a VIE is the party that meets both of the following criteria: (i) has the power to direct the activities that most significantly impact the VIE's economic performance; and (ii) has the obligation to absorb losses or the right to receive benefits from the VIE. For any investments in VIEs in which the Company is considered the primary beneficiary, the assets, liabilities and results of operations of the VIE would be included in its consolidated financial statements. As of December 31, 2022 and 2021, there were no VIEs for which the Company was the primary beneficiary.

The Company accounts for its strategic equity interests in common stock and in-substance common stock in non-publicly traded companies for which it does not have the ability to exercise significant influence in accordance with Accounting Standards Codification ("ASC") 321, *Investments – Equity Securities* ("ASC 321"). Upon acquisition, these investments are measured at cost, which represents the then fair value. Under ASC 321, the Company can elect to subsequently measure the investments at initial cost, minus impairment and any changes, plus or minus, resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer ("measurement alternative"). This election must be made for each investment separately. The Company has made this election for all investments in this category and will continue to measure these investments using this method until they no longer qualify to be measured in accordance with this method. Changes in the carrying value of other investments are recognized through net loss. Each reporting period, the Company performs a qualitative assessment to evaluate whether the investment is impaired. The Company's assessment includes a review of recent operating results and trends, recent sales/acquisitions of the investee securities and other factors that raise concerns about the investee's ability to continue as a going concern. If the investment is impaired, an impairment charge is recognized in the amount by which the carrying amount of the investment exceeds the estimated fair value of the investment, with the impairment charge recognized through net loss. See Note 5, *Other Investments*, for details related to investment impairments recognized during the years ended December 31, 2022 and 2021.

Additionally, the Company holds an equity warrant investment giving it the right to acquire stock of a non-publicly traded company. Equity warrant investments are recorded within other assets at the estimated fair value, with gains and losses recognized in other income (expense), net. For the year ended December 31, 2022, in conjunction with the impairment of one of the Company's other investments, the associated equity warrant investment's fair value was

determined to be negligible. The Company reduced the equity warrant investment's fair value to zero for the year ended December 31, 2022. See Note 6, *Fair Value Measurements*, for additional details regarding the equity warrant investment.

Property and Equipment, Net

Property and equipment primarily consist of laboratory equipment, computer equipment and software, furniture and fixtures and leasehold improvements. Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method based on the estimated useful lives of the related assets, which are generally three to five years. For leasehold improvements, amortization is calculated using the straight-line method based on the shorter of the useful life or the lease term. When assets are retired or otherwise disposed of, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is recorded in other income (expense), net in the period realized. Maintenance and repairs are expensed as incurred. The Company reviews its property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

Valuation of Long-lived Assets

Long-lived assets are reviewed each reporting period for impairment or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable, which may warrant adjustments to carrying values or estimated useful lives. Recoverability is measured by comparison of the carrying amount of an asset group to the future net undiscounted cash flows that the assets are expected to generate. If the carrying amount of an asset group exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset group exceeds the fair value of the asset group. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. There has been no impairment of long-lived assets for any of the periods presented.

Acquisitions

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen to determine if substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If the screen is met, the transaction is accounted for as an asset acquisition. If the screen is not met, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs which would meet the requirements of a business in which case the transaction is accounted for using the acquisition method of accounting, which requires, among other things, that assets acquired and liabilities assumed be recognized at their estimated fair values as of the acquisition date, and that the fair value of acquired intangibles be recorded on the balance sheet. Transaction costs are expensed as incurred. Any excess of the purchase price over the assigned fair values of the net assets acquired is recorded as goodwill. If the Company determines an acquisition does not meet the definition of a business combination under the acquisition method of accounting, the transaction is accounted for as an asset acquisition.

In an asset acquisition, upfront payments allocated to in-process research and development ("IPR&D") are recorded in research and development expense if it is determined that there is no alternative future use, and subsequent milestone payments are recorded in research and development expense when achieved for technology that has not yet met product feasibility.

Leases

The Company leases certain office, laboratory and manufacturing spaces. In addition to minimum rent, the leases require payment of real estate taxes, insurance, common area maintenance charges and other executory costs. At inception of a contract, the Company determines whether an arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. For all leases, the Company determines the classification of the lease as either operating or financing. As of December 31, 2022 and 2021, all of the Company's leases were classified as operating leases.

The Company recognizes right-of-use ("ROU") assets and lease liabilities at the lease commencement date based on the present value of future lease payments over the lease term. As the Company's leases do not provide an implicit rate, an incremental borrowing rate at each lease commencement date is used to determine the present value of future lease payments. The incremental borrowing rate is the rate of interest that the Company would pay to borrow equivalent funds

on a collateralized basis at the lease commencement date. To estimate the incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating. The ROU asset includes any lease payments made prior to the lease commencement date and is reduced by any lease incentives received or deemed payable to the Company. The lease term may include options to extend or terminate the lease when it is reasonably certain that a lease option will be exercised. Lease expense is recognized on a straight-line basis over the lease term within operating expenses on the Consolidated Statements of Operations and Comprehensive Loss.

The Company has elected the practical expedient to not separate lease and non-lease components for real estate leases. Additionally, the Company has elected the short-term lease recognition exemption for all short-term leases and as a result, lease liabilities and ROU assets are not included on the consolidated balance sheets for leases with an initial term of 12 months or less.

Fair Value Measurements

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. The fair value hierarchy prioritizes valuation inputs based on the observable nature of those inputs. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The hierarchy defines three levels of valuation inputs:

Level 1 – Quoted prices in active markets for identical assets or liabilities.

Level 2 – Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

Level 3 – Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

The Company's financial instruments, in addition to those presented in Note 6, *Fair Value Measurements*, include cash, restricted cash, other investments, accounts payable and accrued liabilities and other current liabilities. The carrying amount of cash, restricted cash, accounts payable and accrued liabilities and other current liabilities approximate fair value because of the short-term nature of these instruments. As described in Note 5, *Other Investments*, other investments are carried at cost, minus impairment and any changes, plus or minus, resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

Deemed Dividends Upon Repurchase of Convertible Preferred Stock

In March 2020, 546,806 shares of the Company's Series A convertible preferred stock were repurchased by the Company at the then estimated fair value of $7.76 per share, which was higher than the carrying value of those shares. See Note 10, *Convertible Preferred Stock*. As a result, the Company recorded deemed dividends of $3.6 million for the year ended December 31, 2020. The transaction decreased convertible preferred stock by $0.7 million and reduced additional paid-in capital by $3.6 million. The deemed dividends increased the net loss attributed to common stockholders by $3.6 million.

Revenue Recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements within the scope of ASC 606, *Revenue from Contracts with Customers*, ("ASC 606") the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the performance obligation is satisfied.

In applying the ASC 606 framework, the Company must apply judgment to determine the nature of the promises within a revenue contract and whether those promises represent distinct performance obligations. In determining the transaction price, the Company does not include amounts subject to uncertainties unless it is probable that there will be no significant reversal of cumulative revenue when the uncertainty is resolved. Milestone and other forms of variable consideration that the Company may earn are subject to significant uncertainties of research and development related achievements, which generally are deemed not probable until such milestones are actually achieved. For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the

predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). Additionally, the Company develops assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. The Company then allocates the total transaction price to each performance obligation based on the estimated standalone selling prices of each performance obligation, for which it recognizes revenue as or when the performance obligations are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the variable consideration and any related constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis.

Under the Company's license agreements, the Company grants the license to a customer as it exists at the point of transfer and the nature of the license is a right to use the Company's intellectual property as transferred. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time.

Research and Development Expense

The Company records expense for research and development costs as incurred. Research and development expenses consist of costs incurred by the Company for the discovery and development of its technology platforms and product candidates and includes costs incurred in connection with strategic collaborations, costs to license technology, personnel-related costs, including stock-based compensation expense, facility and technology related costs, research and laboratory expenses, as well as other expenses, which include consulting fees and other costs. Upfront payments and milestones paid to third parties in connection with technology platforms that have not reached technological feasibility and do not have an alternative future use are expensed as incurred.

General and Administrative Expense

General and administrative costs are expensed as incurred and include personnel-related expenses, including stock-based compensation expense for personnel in executive, legal, finance and other administrative functions, legal costs, transaction costs related to collaboration and licensing agreements, as well as fees paid for accounting and tax services, consulting fees and facilities costs not otherwise included in research and development expenses. Legal costs include those related to corporate, dispute and patent matters.

Success Payments

The Company granted rights to success payments to Fred Hutchinson Cancer Center ("Fred Hutch") and The Board of Trustees of the Leland Stanford Junior University ("Stanford") pursuant to the terms of its research and collaboration agreements with each of those entities. Pursuant to the terms of these agreements, on each contractually prescribed measurement date, the Company may be required to make success payments based on increases in the estimated per share fair value of the Company's common stock. See Note 3, *License, Collaboration and Success Payment Agreements*. The success payments are accounted for under ASC 718, *Compensation – Stock Compensation*, with the expense being recorded in research and development expenses. Once the service period is complete, the instrument is accounted for under ASC 815, *Derivatives and Hedging*, and continues to be remeasured each reporting period with all changes in value recognized immediately in other income (expense), net.

The success payment liability is estimated at fair value at inception and at each subsequent reporting period, and the expense is accreted over the service period of the research and collaboration agreement. To determine the estimated fair value of the success payments, the Company uses a Monte Carlo simulation methodology which models the future movement of stock prices based on several key variables combined with empirical knowledge of the process governing the behavior of the stock price. The following variables were incorporated in the estimated fair value of the success payment liability: estimated fair value of the Company's common stock, expected volatility, risk-free interest rate and the estimated number and timing of valuation measurement dates on the basis of which payments may be triggered. The computation of expected volatility was estimated based on available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption.

Concentrations of Credit Risk and Off-balance Sheet Risk

The Company maintains its cash, cash equivalents and restricted cash with high quality, accredited financial institutions. These amounts, at times, may exceed federally insured limits. The Company also makes short-term investments in money market funds, U.S. Treasury securities, U.S. government agency securities and corporate debt securities, which can be subject to certain credit risk. However, the Company mitigates the risks by investing in high-grade instruments, limiting exposure to any one issuer or type of investment and monitoring the ongoing creditworthiness of the financial institutions and issuers. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to significant risk on these funds. The Company has no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Claims and Contingencies

From time to time, the Company may become involved in litigation and proceedings relating to claims arising from the ordinary course of business. The Company accrues a liability if the likelihood of an adverse outcome is probable and the amount is estimable. If the likelihood of an adverse outcome is only reasonably possible (as opposed to probable), or if an estimate is not determinable, the Company provides disclosure of a material claim or contingency.

Stock-based Compensation

Under ASC 718, the Company measures and recognizes expense for restricted stock awards ("RSAs"), restricted stock units ("RSUs"), employee stock purchases related to the Employee Stock Purchase Plan and stock options granted to employees, directors and consultants based on the fair value of the awards on the date of grant. The fair value of stock options is estimated using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires inputs based on certain subjective assumptions including: stock price volatility, the expected term of stock options, the risk-free interest rate, expected dividends, and the fair value of the underlying common stock on the date of grant.

The expected volatility is based on the historical volatility of the stock of similar entities within the Company's industry over periods commensurate with the Company's expected term assumption. The expected term of stock option grants represents the period the options are expected to remain outstanding and is based on the "simplified" method where the expected term is the midpoint between the vesting date and the end of the contractual term for each option. The Company used the simplified method as provided for under the applicable guidance for entities with a limited history of relevant stock option exercise activity. The Company bases the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term. In reference to the expected dividend yield assumption, the Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend.

Prior to the closing of the IPO, the Company utilized significant estimates and assumptions in determining the fair value of its common stock for financial reporting purposes. The Company recorded expense for RSAs and stock options at prices not less than the estimated fair market value of its common stock as determined by the board of directors, taking into consideration input from management and an independent third-party valuation analysis, and in accordance with the American Institute of Certified Public Accountants ("AICPA") Accounting and Valuation Guide, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*. Following the closing of the IPO, the fair value of the Company's common stock is based on its closing price as reported on the NASDAQ Global Select Market on the date of grant.

Stock-based compensation expense for RSAs, RSUs and stock options is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. The Company accounts for forfeitures as they occur.

The Company also granted stock options that vest in conjunction with certain performance conditions to certain key employees. At each reporting date, the Company is required to evaluate whether achievement of the performance conditions is probable. Compensation expense is recorded over the appropriate service period based upon the Company's assessment of accomplishing each performance provision.

Income Taxes

The Company determines its deferred tax assets and liabilities based on the differences between the financial reporting and tax basis of assets and liabilities. The deferred tax assets and liabilities are measured using the enacted tax rates that will be in effect when the differences are expected to reverse. A valuation allowance is recorded when it is more

likely than not that the deferred tax asset will not be recovered. The Company applies judgment in the determination of the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The Company recognizes any material interest and penalties related to unrecognized tax benefits in income tax expense.

Segments

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment and one reportable segment.

Recent Accounting Pronouncements

None.

3. License, Collaboration and Success Payment Agreements

Fred Hutch

License Agreement - In 2018, the Company entered into a license agreement with Fred Hutch that grants the Company a worldwide, sublicensable license under certain patent rights (exclusive) and certain technology (non-exclusive), to research, develop and commercialize products and processes for all therapeutic uses for the treatment of human cancer.

The Company is also required to pay Fred Hutch annual license maintenance payments of $50,000 on the second anniversary of the effective date, and each anniversary of the effective date thereafter until the first commercial sale of a licensed product.

Collaboration - In 2018, the Company entered into a research and collaboration agreement with Fred Hutch ("Fred Hutch Collaboration Agreement"), focused on research and development of cancer immunotherapy products. The Company funded aggregate research performed by Fred Hutch of $12.0 million under the Fred Hutch Collaboration Agreement and the research is conducted in accordance with a research plan and budget approved by the parties. The Fred Hutch Collaboration Agreement has a six-year term. During 2021, one of the research plans on which the success payment service term is based, was extended from January 31, 2022 to December 31, 2022. The Company incurred $1.7 million, $4.2 million and $4.1 million in expense in connection with the Fred Hutch Collaboration Agreement for the years ended December 31, 2022, 2021 and 2020, respectively.

Success Payments - In 2018, the Company granted Fred Hutch rights to certain success payments, pursuant to the terms of the Fred Hutch Collaboration Agreement. The potential payments for the Fred Hutch success payments are based on multiples of increased value ranging from 10x to 50x based on a comparison of the per share fair market value of the Company's common stock (as all shares of Series A convertible preferred stock were converted into an equivalent number of shares of common stock upon the closing of the IPO) relative to its original $1.83 per share issuance price. The aggregate success payments to Fred Hutch are not to exceed $200.0 million, which would only occur upon a 50 times increase in value. Each threshold is associated with a success payment, ascending from $10.0 million at $18.29 per share to $200.0 million at $91.44 per share, payable if such threshold is reached during the measurement period. Any previous success payments made are credited against the success payment owed as of any valuation date, such that Fred Hutch does not receive multiple success payments in connection with the same threshold. The term of the success payment agreement ends on the earlier to occur of (i) the nine-year anniversary of the date of the agreement and (ii) a change in control transaction.

The following table summarizes the aggregate potential success payments, which are payable to Fred Hutch in cash or cash equivalents, or at the Company's discretion, publicly-tradeable shares of the Company's common stock:

Multiple of initial equity value at issuance	10x	20x	30x	40x	50x
Per share common stock price required for payment	$ 18.29	$ 36.58	$ 54.86	$ 73.15	$ 91.44
Aggregate success payment(s) (in millions)	$ 10	$ 40	$ 90	$ 140	$ 200

The success payments will be owed if the per share fair value of the Company's common stock on the contractually specified valuation measurement dates during the term of the success payment agreement equals or exceeds

the above outlined multiples. The valuation measurement dates are triggered by the following events: the one-year anniversary of the Company's IPO and each two-year anniversary of the Company's IPO thereafter, the closing of a change in control transaction and the last day of the term of the success payment agreement, unless the term has ended due to the closing of a change of control transaction. As of December 31, 2022, no success payments have been incurred as the per share fair value of the Company's common stock was below the price required for payment.

The estimated fair values of the success payments to Fred Hutch as of December 31, 2022 and 2021 were $2.5 million and $8.5 million, respectively. The success payment liability is estimated at the fair value at inception and at each subsequent reporting period and the expense is accreted over the service period of the Fred Hutch Collaboration Agreement. The success payment liability was $2.5 million and $6.4 million as of December 31, 2022 and 2021, respectively. With respect to the Fred Hutch Collaboration Agreement success payment obligations, the Company recognized a gain of $3.9 million for the year ended December 31, 2022, and success payment expense of $1.2 million and $4.8 million for the years ended December 31, 2021 and 2020, respectively.

Stanford

License Agreement - In 2019, the Company entered into a license agreement with Stanford to license specified patent rights. The Company is also required to pay Stanford annual license maintenance payments of $50,000 on the second anniversary of the effective date, and each anniversary of the effective date thereafter until the date of the first commercial sale of a licensed product.

Milestone payments to Stanford of up to a maximum of $3.7 million per target are payable upon achievement of certain specified clinical and regulatory milestones. The Company is also obligated to pay Stanford $2.5 million collectively for all licensed products upon the achievement of a certain commercial milestone. Additionally, low single-digit tiered royalties based on annual net sales of the licensed products are payable to Stanford.

Collaboration Agreement - In October 2020, the Company entered into a research and collaboration agreement with Stanford ("Stanford Collaboration Agreement"), focused on research and development of cellular immunotherapy products. The Stanford Collaboration Agreement has a four-year term. The Company is committed to fund aggregate research performed by Stanford of $12.0 million under the Stanford Collaboration Agreement, and the research will be conducted in accordance with a research plan and budget approved by the parties. The Company incurred $3.0 million, $3.0 million and $0.8 million in expense in connection with the Stanford Collaboration Agreement for the years ended December 31, 2022, 2021, and 2020, respectively.

Success Payments - In October 2020, the Company granted Stanford rights to certain success payments, pursuant to the terms of the Stanford Collaboration Agreement. The potential payments for the Stanford Collaboration Agreement success payments are based on multiples of increased value ranging from 10x to 50x based on a comparison of the per share fair market value of the Company's common stock (as all shares of Series A convertible preferred stock were converted into an equivalent number of shares of common stock upon the closing of the IPO) relative to its original $1.83 per share issuance price. The aggregate success payments to Stanford are not to exceed $200.0 million, which would only occur upon a 50 times increase in value. Each threshold is associated with a success payment, ascending from $10.0 million at $18.29 per share to $200.0 million at $91.44 per share, payable if such threshold is reached during the measurement period. Any previous success payments made are credited against the success payment owed as of any valuation date, so that Stanford does not receive multiple success payments in connection with the same threshold. The term of each success payment agreement ends on the earlier to occur of (i) the nine year anniversary of the date of the agreement and (ii) a change in control transaction.

The following table summarizes the aggregate potential success payments, which are payable to Stanford in cash or cash equivalents, or at the Company's discretion, publicly-tradeable shares of the Company's common stock:

Multiple of initial equity value at issuance	10x	20x	30x	40x	50x
Per share common stock price required for payment	$ 18.29	$ 36.58	$ 54.86	$ 73.15	$ 91.44
Aggregate success payment(s) (in millions)	$ 10	$ 40	$ 90	$ 140	$ 200

The success payments will be owed if the per share fair value of the Company's common stock on the contractually specified valuation measurement dates during the term of the success payment agreement equals or exceeds the above outlined multiples. The valuation measurement dates are triggered by the following events: the one-year anniversary of the Company's IPO and each two-year anniversary of the Company's IPO thereafter, the closing of a change in control transaction and the last day of the term of the success payment agreement, unless the term has ended due to the

closing of a change of control transaction. As of December 31, 2022, no success payments have been incurred as the per share fair value of the Company's common stock was below the price required for payment.

The estimated fair values of the success payments to Stanford as of December 31, 2022 and 2021 were $3.3 million and $9.9 million, respectively. The success payment liability is estimated at the fair value at inception and at each subsequent reporting period and the expense is accreted over the service period of the Stanford Collaboration Agreement. The success payment liability was $1.9 million and $3.1 million as of December 31, 2022 and 2021, respectively. With respect to the Stanford Collaboration Agreement success payment obligations, the Company recognized a gain of $1.2 million for the year ended December 31, 2022, and success payment expense of $2.5 million and $0.6 million for the years ended December 31, 2021 and 2020, respectively.

GSK

In 2019, the Company entered into the GSK Agreement with GSK for potential T-cell therapies that apply the Company's platform technologies and cell therapy innovations with T-cell receptors ("TCRs") or chimeric antigen receptors ("CARs") under distinct collaboration programs. The GSK Agreement defined two initial collaboration targets, LYL331 and LYL132, and allowed GSK to nominate seven additional targets through July 2024, noting no additional targets were nominated over the life of the GSK Agreement. The Company was expected to perform research and development services for each selected target up until a defined point (the "GSK Option Point"), at which time GSK would decide whether or not to exercise an option to obtain a license from the Company ("License Option") and take over the future development and commercialization. In April 2021, GSK exercised the License Option on LYL331 (NY-ESO-1 TCR with c-Jun) and assumed sole responsibility for future development and commercialization of the program at its own cost and expense. The IND application for LYL132 was cleared in January 2022, though no patients were treated, and the IND for LYL331 was not submitted to the U.S. Food and Drug Administration. GSK terminated the GSK Agreement effective December 24, 2022 and Lyell has discontinued any further work on these programs. There are no future performance obligations associated with the GSK Agreement.

The Company received a non-refundable upfront payment of $45.0 million under the GSK Agreement. In connection with the GSK Agreement, in May 2019, the Company also entered into a stock purchase agreement with GSK ("GSK Stock Purchase Agreement"), pursuant to which the Company agreed to sell 30,253,189 shares of Series AA convertible preferred stock at a price of $6.78 per share, which was above the issuance date estimated fair value of $4.84 per share. The difference between the per share values resulted in $58.6 million additional deemed consideration, bringing the total upfront consideration of the GSK Agreement to $103.6 million.

The GSK Agreement was deemed to be within the scope of ASC 606 because GSK engaged the Company to initially provide research and development services, which were outputs of its ongoing activities, in exchange for consideration. During the year ended December 31, 2022, the Company recorded adjustments to revenue related to changes in estimates to complete its performance obligations under the GSK Agreement. These changes in estimates were driven by the mutual agreement to conclude certain research activities in June 2022 and the termination of the GSK Agreement, effective December 24, 2022, both of which resulted in changes to the measure of proportional cumulative performance. These adjustments increased revenue by $83.6 million, decreased net loss by $83.6 million and resulted in a $0.34 reduction in the Company's basic and diluted net loss per common share for the year ended December 31, 2022.

The Company recognized revenue related to the research and development services related to the two initial targets of $84.7 million, $10.5 million and $7.8 million for the years ended December 31, 2022, 2021 and 2020 respectively. No license revenue was recognized for the year ended December 31, 2022. As of December 31, 2022 and 2021, the Company had deferred revenue of zero and $84.7 million, respectively, related to the GSK Agreement. As of December 31, 2022, there were no contract assets or contract liabilities related to the license contract.

PACT

In June 2020, the Company entered into a commitment agreement ("PACT Commitment Agreement") with PACT to jointly develop and test a next generation personalized anti-cancer T-cell therapy against solid tumors. The Company paid PACT an upfront non-refundable payment of $50.0 million upon execution of the PACT Commitment Agreement. In November 2020, the parties agreed to suspend research and development activity under the PACT Commitment Agreement, and neither party would be required to conduct any further work under the development plan (including manufacturing development) nor incur any financial obligations (including milestone payments) that might otherwise arise, for as long as the parties continued to negotiate in good faith to resolve the issues that have arisen between them relating to the PACT Commitment Agreement.

In June 2020 in connection with the entry into the PACT Commitment Agreement, the Company also entered into a stock purchase agreement with PACT ("PACT SPA"), pursuant to which the Company purchased 17,806,901 shares of PACT Series C-1 convertible preferred stock at a purchase price of $2.81 per share. As of the purchase date, the estimated fair value of the Series C-1 convertible preferred stock was $2.05 per share, and the difference between the estimated fair value of the preferred stock as of the purchase date and the purchase price of $13.6 million was deemed to be additional consideration for the PACT Commitment Agreement and recognized as research and development expense. As a result, the total upfront consideration paid in connection with the PACT Commitment Agreement was $63.6 million and was included in research and development expenses. The remaining $36.4 million associated with the PACT Series C-1 convertible preferred stock was recorded in other investments. In the fourth quarter of 2021, the Company fully impaired the remaining balance of $36.4 million. See Note 5, *Other Investments*, for additional details regarding the PACT investment impairment.

In February 2021, the Company filed a demand for arbitration seeking, among other things, rescission of the PACT Commitment Agreement and the PACT SPA and recovery of the consideration paid thereunder. Arbitration hearings occurred in March and April 2022.

On October 1, 2022, the Company entered into a settlement agreement with PACT, pursuant to which the parties agreed to resolve their outstanding legal dispute. In connection with the settlement agreement, the parties also entered into a stock purchase agreement, pursuant to which PACT issued shares of PACT's Series D convertible preferred stock to the Company in exchange for the Company's tender of its PACT Series C-1 convertible preferred stock and resolution of the arbitration. The issuance of PACT's Series D convertible preferred stock, which are non-voting, have limited conversion rights and carry no right to appoint directors, resulted in the Company's ownership increasing to approximately 80% of PACT's fully diluted shares outstanding. The settlement agreement also included the termination of the PACT Commitment Agreement to jointly develop a next generation anti-cancer T-cell therapy against solid tumors. The Company recorded a gain of $2.9 million on October 1, 2022 for the estimated fair value of the PACT Series D convertible preferred stock received as part of the settlement agreement. The PACT Series D convertible preferred stock was recorded at its estimated fair value as of the settlement date and is included in other investments in the Company's Consolidated Balance Sheets.

4. Cash Equivalents and Marketable Securities

The fair value and amortized cost of cash equivalents and marketable securities by major security type are as follows (in thousands):

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 67,970	$ —	$ —	$ 67,970
U.S. Treasury securities	277,056	—	(5,257)	271,799
U.S. government agency securities	135,460	1	(1,416)	134,045
Corporate debt securities	221,608	3	(930)	220,681
Total cash equivalents and marketable securities	$ 702,094	$ 4	$ (7,603)	$ 694,495

Classified as:	Fair Value
Cash equivalents	$ 107,780
Marketable securities	516,598
Marketable securities, non-current	70,117
Total cash equivalents and marketable securities	$ 694,495

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 206,245	$ —	$ —	$ 206,245
U.S. Treasury securities	290,909	2	(1,205)	289,706
U.S. government agency securities	93,864	2	(240)	93,626
Corporate debt securities	285,338	—	(182)	285,156
Total cash equivalents and marketable securities	$ 876,356	$ 4	$ (1,627)	$ 874,733

Classified as:	Fair Value
Cash equivalents	$ 270,236
Marketable securities	320,966
Marketable securities, non-current	283,531
Total cash equivalents and marketable securities	$ 874,733

The fair value of securities held by the Company in an unrealized loss position for less than 12 months were $287.8 million and $602.9 million, as of December 31, 2022 and 2021, respectively. The fair value of securities held by the Company in an unrealized continuous loss position for greater than 12 months were $278.7 million and zero as of December 31, 2022 and 2021, respectively. As of December 31, 2022 and 2021, all of the Company's marketable securities had a maturity date of two years or less, were available for use and were classified as available-for-sale. The Company does not intend to sell these securities nor does the Company believe that it will be required to sell these securities before recovery of their amortized cost basis. The Company determined that there was no material change in the credit risk of the above investments during the years ended December 31, 2022 and 2021. As such, an allowance for credit losses has not been recognized. Gross realized gains and losses were *de minimis* for the years ended December 31, 2022 and 2021 and as a result, amounts reclassified out of accumulated other comprehensive loss for the years ended December 31, 2022 and 2021 were also *de minimis*. See Note 6, *Fair Value Measurements*, for additional information regarding cash equivalents and marketable securities.

5. Other Investments

From time to time, the Company makes minority ownership strategic investments. As of December 31, 2022 and 2021, the aggregate carrying amounts of the Company's strategic investments in non-publicly traded companies were $44.9 million and $47.0 million, respectively. These investments are measured at initial cost, minus impairment, if any, and plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

In connection with the preparation of the financial statements for 2022, the Company performed a qualitative assessment of potential indicators of impairment and determined that indicators existed for one of the Company's other investments with a carrying amount of $5.0 million. While there was no single event or factor, the Company considered the underlying company's operating cash flow requirements over the next year and liquid asset balances to fund those requirements and the underlying company's inability to raise funds as indicators of impairment. Due to these indicators, the Company assessed the valuation of the investment and determined the fair value to be negligible and the impairment to be other-than-temporary in nature. As a result, the Company recorded a $5.0 million impairment expense for the investment for the year ended December 31, 2022, which was recorded within impairment of other investments on the Consolidated Statement of Operations and Comprehensive Loss and as a reduction to the investment balance within other investments on the Consolidated Balance Sheet. No other investments were impaired for the year ended December 31, 2022.

In October 2022, the Company received non-voting preferred stock pursuant to the settlement agreement with PACT (See Note 3, *License, Collaboration and Success Payment Agreements*). The Company determined that PACT is a VIE as PACT does not have sufficient equity at risk. The Company evaluated whether it was the primary beneficiary of PACT, including the Company's ongoing rights and responsibilities, to assess whether the Company has the power to direct the activities of PACT. The Company's only involvement in PACT is its PACT Series D convertible preferred stock investment, which are non-voting, have limited conversion rights and carry no right to appoint directors. Based on the above noted factors, the Company determined that it is not the primary beneficiary and does not consolidate PACT since it does not have the power to direct the activities that most significantly impact PACT's economic performance. The

Company does not have the ability to exercise significant influence over PACT and accounts for its investment in PACT preferred stock under the measurement alternative. The Company recognized its investment in PACT preferred stock at its estimated fair value of $2.9 million on October 1, 2022, which is included in the Company's Consolidated Balance Sheets within other investments. The Company's maximum exposure to loss from PACT is limited to the carrying value of its investment in PACT preferred stock.

In connection with the preparation of the financial statements for 2021, the Company performed a qualitative assessment of potential indicators of impairment and determined that indicators existed for its $36.4 million investment in PACT Series C-1 convertible preferred stock. While there was no single event or factor, the Company considered PACT's operating cash flow requirements over the next year and liquid asset balances to fund those requirements and PACT's inability to raise funds as indicators of impairment. Due to these indicators, the Company assessed the valuation of the investment in PACT as of December 31, 2021 and determined the fair value to be negligible and the impairment to be other-than-temporary in nature. As a result, the Company recorded a $36.4 million impairment expense for the PACT investment in the fourth quarter of 2021, which was recorded within impairment of other investments on the Consolidated Statement of Operations and Comprehensive Loss and as a reduction to the investment balance within other investments on the Consolidated Balance Sheet. Aside from the investment in PACT, no other investments were impaired for the year ended December 31, 2021.

In November 2020, the Company made a strategic equity investment of $13.0 million in Outpace Bio, Inc. ("Outpace"), a privately-held company, which represented a minority ownership interest at the time of the strategic investment. Outpace is engaged in the research and development of protein and cell technology platforms and has financed its activities via issuances of preferred stock. The Company determined that Outpace is a VIE and the at-risk equity holders, as a group, lack the characteristics of a controlling financial interest. The Company does not have majority voting rights, representation on Outpace's board of directors or the power to direct the activities of this entity, and therefore it is not the primary beneficiary. As of both December 31, 2022 and 2021, the carrying value of the Company's investment in Outpace was $13.0 million, which is recorded in other investments.

6. Fair Value Measurements

The following table sets forth the fair value of the Company's financial assets and liabilities measured at fair value on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market funds	$ 67,970	$ —	$ —	$ 67,970
U.S. Treasury securities	—	271,799	—	271,799
U.S. government agency securities	—	134,045	—	134,045
Corporate debt securities	—	220,681	—	220,681
Total financial assets	$ 67,970	$ 626,525	$ —	$ 694,495
Financial liabilities:				
Success payment liabilities	$ —	$ —	$ 4,356	$ 4,356
Total financial liabilities	$ —	$ —	$ 4,356	$ 4,356

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
Financial assets:				
Money market funds	$ 206,245	$ —	$ —	$ 206,245
U.S. Treasury securities	—	289,706	—	289,706
U.S. government agency securities	—	93,626	—	93,626
Corporate debt securities	—	285,156	—	285,156
Equity warrant investment	—	—	1,067	1,067
Total financial assets	$ 206,245	$ 668,488	$ 1,067	$ 875,800
Financial liabilities:				
Success payment liabilities	$ —	$ —	$ 9,486	$ 9,486
Total financial liabilities	$ —	$ —	$ 9,486	$ 9,486

The Company measures the fair value of money market funds based on quoted prices in active markets for identical assets or liabilities. The Level 2 marketable securities include U.S. Treasury securities, U.S. government agency securities and corporate debt securities. The Company's Level 2 securities are valued using third-party pricing sources. The pricing services applied industry standard valuation models. Inputs utilized include market pricing based on real-time trade data for the same or similar securities and other significant inputs derived from or corroborated by observable market data.

The Level 3 financial instruments include an equity warrant investment and the success payment liabilities. For the year ended December 31, 2022, in conjunction with the impairment of one of the Company's other investments, the associated equity warrant investment's fair value was determined to be negligible as of December 31, 2022. The Company reduced the equity warrant investment's fair value from $1.1 million as of December 31, 2021 to zero as of December 31, 2022. See Note 5, *Other Investments*, for additional details regarding the impairment of the other investment. The Company's Level 3 financial instruments are valued using valuation models which include the Black-Scholes model for valuing the equity warrant investment and a Monte Carlo simulation for the success payment liabilities. To determine the estimated fair value of the success payment liabilities, the Company uses a Monte Carlo simulation methodology that models the future movement of stock prices based on several key variables combined with empirical knowledge of the process governing the behavior of the stock price. The following variables were incorporated in the estimated fair value of the success payment liabilities: fair value of the Company's common stock, expected volatility, the risk-free interest rate and the estimated number and timing of valuation measurement dates on the basis of which payments may be triggered. The computation of expected volatility was estimated based on available information about the historical volatility of stocks of similar publicly traded companies for a period matching the expected term assumption.

The following assumptions were incorporated into the calculation of the estimated fair value of the Fred Hutch success payment liability:

	December 31,	
	2022	2021
Fair value of common stock	$ 3.47	$ 7.74
Risk-free interest rate	3.58% - 4.65%	0.19% - 1.88%
Expected volatility	80.0 %	75.0 %
Expected term (in years)	0.46 - 4.97	0.46 - 5.97

The following assumptions were incorporated into the calculation of the estimated fair value of the Stanford success payment liability:

	December 31,	
	2022	2021
Fair value of common stock	$ 3.47	$ 7.74
Risk-free interest rate	3.58% - 4.65%	0.19% - 1.88%
Expected volatility	80.0 %	75.0 %
Expected term (in years)	0.46 - 6.75	0.46 - 7.75

The Company utilizes estimates and assumptions in determining the estimated success payment liabilities and associated expense. A small change in the valuation of the Company's common stock may have a relatively large change in the estimated fair value of the success payment liability and associated expense.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial assets and liabilities (in thousands):

	Equity Warrant Investment	Success Payment Liabilities
Balance at December 31, 2020	$ 1,323	$ 5,773
Change in fair value [1]	(256)	3,713
Balance at December 31, 2021	1,067	9,486
Change in fair value [1]	(1,067)	(5,130)
Balance at December 31, 2022	$ —	$ 4,356

(1) The changes in fair value associated with the equity warrant investment held are recorded in other income (expense), net and the changes in fair value associated with success payment liabilities are recorded in research and development expense.

In October 2022, the Company received non-voting series D preferred stock pursuant to the settlement agreement with PACT (See Note 3, *License, Collaboration and Success Payment Agreements*). The Company determined the fair value of PACT was a fraction of the aggregate liquidation preference of the Company's PACT Series D preferred stock. The Company determined that the fair value of its investment in PACT preferred stock is approximated by the fair value of the PACT business since the Company is the only party invested in PACT preferred stock series D as of October 1, 2022, the most senior class of stock issued by PACT. The fair value of PACT was estimated at $2.9 million as of October 1, 2022 using the cost approach. Under this approach, the fair value of an asset is measured by the cost to reconstruct or replace such asset with another one of like utility. The fair value of PACT was estimated by using significant unobservable inputs, including an estimate of insignificant fair value associated with PACT intangible assets. Accordingly, the Company classified the fair value measurement of PACT preferred stock on October 1, 2022 as Level 3 under the fair value hierarchy.

7. Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	December 31,	
	2022	2021
Leasehold improvements	$ 116,930	$ 95,001
Laboratory equipment	31,982	27,039
Computer equipment and software	1,630	1,610
Furniture and fixtures	717	384
Construction in progress	4,148	10,577
Property and equipment, at cost	155,407	134,611
Less: Accumulated depreciation and amortization	(32,384)	(14,513)
Total property and equipment, net	$ 123,023	$ 120,098

Depreciation and amortization expense was $18.0 million, $13.5 million and $4.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

8. Accrued Liabilities and Other Current Liabilities

Accrued liabilities and other current liabilities consisted of the following (in thousands):

	December 31,	
	2022	2021
Accrued compensation and related benefits	$ 15,447	$ 17,296
Accrued property and equipment	732	4,055
Accrued legal	930	2,619
Accrued research and development expenses	4,760	2,449
Current lease liabilities	4,534	1,169
Other	2,352	1,469
Total accrued liabilities and other current liabilities	$ 28,755	$ 29,057

9. Leases

The Company's lease portfolio is comprised of operating leases for laboratory, office and manufacturing facilities located in South San Francisco, California, and Seattle and Bothell, Washington with contractual periods expiring between December 2028 and March 2031. In addition to minimum rent, the leases require payment of real estate taxes, insurance, common area maintenance charges and other executory costs. These additional charges are considered variable lease costs and are recognized in the period in which the costs are incurred.

In 2018, the Company entered into an operating lease for approximately 34,000 square feet of office and laboratory space in Seattle, Washington, with an initial lease term expiring in December 2028. The Company has two five-year options to extend the lease, which are not reasonably assured.

In 2019, the Company entered into an operating lease for approximately 34,000 square feet of office and laboratory space in South San Francisco, California. In December 2020, the Company exercised its early termination right and remeasured the remaining consideration in the contract, resulting in a gain of $2.9 million, which was recognized in other operating income, net. The lease termination was effective October 2021, resulting in a gain of $0.3 million, which was recognized in other operating income, net for the year ended December 31, 2021. Additionally, the Company recognized a loss of $0.6 million at lease termination on leasehold improvements unable to be moved to its new corporate headquarters in South San Francisco, California, which was recognized in other operating income, net for the year ended December 31, 2021.

In 2019, the Company entered into two operating lease agreements for a combined approximately 73,000 square feet of space to develop a cell therapy manufacturing facility located in Bothell, Washington, with initial terms expiring in May 2030. The Company has two 90-month options to extend the leases, which are not reasonably assured.

In 2019, the Company entered into an operating lease agreement for approximately 108,000 square feet of office and laboratory space located in South San Francisco, California. The initial lease term expires in January 2031 with the option to extend the term for another 10 years, which is not reasonably assured. In January 2021, the Company amended the lease term to extend the lease expiration to March 2031, which resulted in an increase to the right-of-use asset and lease liability of $4.2 million.

The following table summarizes the Company's future minimum operating lease commitments, including expected lease incentives to be received, as of December 31, 2022 (in thousands):

Year Ending December 31:		
2023	$	10,101
2024		11,347
2025		11,859
2026		12,209
2027		12,569
Thereafter		35,525
Total undiscounted lease payments		93,610
Less: imputed interest		(25,908)
Total operating lease liabilities	$	67,702

Reported as of December 31, 2022:		
Short-term portion of lease liabilities (included in accrued liabilities and other current liabilities)	$	4,534
Operating lease liabilities, non-current		63,168
Total	$	67,702

The operating lease costs for all operating leases were $9.3 million, $9.4 million and $11.2 million for the years ended December 31, 2022, 2021 and 2020, respectively. The operating lease costs and total commitments for short-term leases were *de minimis* for the years ended December 31, 2022, 2021 and 2020. Variable lease costs for operating leases were $5.1 million, $4.1 million and $2.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. The weighted-average remaining lease terms for operating leases were 7.8 and 8.8 years as of December 31, 2022 and 2021, respectively. The weighted-average discount rates for operating leases were 8.5% and 8.4% as of December 31, 2022 and 2021, respectively.

In May 2021, the Company entered into a sublease, whereby the Company agreed to sublease approximately 11,000 square feet of its space in South San Francisco, California currently leased by the Company. The sublease is classified as an operating lease and will expire in March 2031. The Company recognized sublease income for this sublease of $0.8 million and $0.4 million for the years ended December 31, 2022 and 2021, respectively.

In September 2021, the Company entered into a sublease with Sonoma Biotherapeutics, Inc. ("Sonoma"), a related party, whereby the Company agreed to sublease approximately 18,000 square feet of space in South San Francisco, California currently leased by the Company. See Note 17, *Related-Party Transactions*. As a part of the sublease, in September 2021, the Company received a $4.6 million tenant improvement contribution payment, which will be recognized over the term of the sublease. The sublease is classified as an operating lease and will expire in March 2031. The Company recognized Sonoma sublease income of $1.9 million and $0.6 million for the years ended December 31, 2022 and 2021, respectively.

The Company's sublease income is recognized within other operating income, net in the Consolidated Statements of Operations and Comprehensive Loss.

10. Convertible Preferred Stock

In March 2020, the Company sold 42,905,042 shares of its Series C convertible preferred stock at a price of $11.49 per share for proceeds of $492.5 million, net of issuance costs of $0.5 million.

In March 2020, the Company repurchased 546,806 shares of its Series A convertible preferred stock from a related party for a purchase price of $4.2 million.

Upon the closing of the IPO, 194,474,431 shares of convertible preferred stock then outstanding converted into an equal number of shares of common stock. As of December 31, 2022, no shares of convertible preferred stock were outstanding.

11. Stockholders' Equity

Preferred Stock

The Company is authorized to issue 10.0 million shares of preferred stock with a par value $0.0001 per share. As of December 31, 2022 and 2021, no shares of preferred stock were outstanding.

Common Stock

The Company is authorized to issue 500.0 million shares of common stock with a par value of $0.0001 per share. As of December 31, 2022 and 2021, there were 249,567,343 shares and 242,738,350 shares of the Company's common stock outstanding, respectively, excluding zero and 2,600,002 shares, respectively, of RSAs outstanding that are subject to vesting requirements. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of the Company's common stock are entitled to receive dividends out of funds legally available if the Company's board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that the Company's board of directors may determine.

In March 2020, the Company repurchased 2,032,166 shares of its common stock from a related party for a purchase price of $11.8 million.

On August 4, 2022, the Company entered into an Equity Distribution Agreement with Goldman Sachs & Co. LLC ("Goldman Sachs") and BofA Securities, Inc. ("BofA", and together with Goldman Sachs, "the Agents") with respect to an at-the-market offering program (the "Equity Distribution Agreement"). In accordance with the terms of the Equity Distribution Agreement, the Company may offer and sell from time to time through the Agents shares of the Company's common stock having an aggregate offering amount of up to $200.0 million ("the Placement Shares"). Sales of the Placement Shares, if any, will be made at prevailing market prices on Nasdaq at the time of sale, or as otherwise agreed with the Agents, by any method permitted by law deemed to be an "at-the-market offering" as defined in Rule 415 of the Securities Act of 1933, as amended. The Company will pay commissions to the Agents of up to 3.0% of the gross proceeds of the sale of the Placement Shares sold under the Equity Distribution Agreement and reimburse the Agents for certain expenses. Neither the Company nor the Agents are obligated to sell any shares and, to date, the Company has not made any sales under the Equity Distribution Agreement.

12. Stock-based Compensation

2021 Equity Incentive Plan

In June 2021, the Company adopted the 2021 Equity Incentive Plan ("2021 Plan"), which on the date of the underwriting agreement related to the Company's IPO became effective with an initial reserve of 26,662,087 shares, plus any shares subject to outstanding awards granted under the 2018 Equity Incentive Plan ("2018 Plan") that, on or after the effectiveness of the 2021 Plan, terminate or expire before exercise or settlement, are not issued because the award is settled in cash, are forfeited because of the failure to vest or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. In addition, the number of shares reserved for issuance under the 2021 Plan automatically increases on January 1 of each year for a period of ten years, beginning on January 1, 2022 and continuing through January 1, 2031, in an amount equal to (1) 5% of the total number of shares of the Company's common stock outstanding on December 31 of the immediately preceding year, or (2) a lesser number of shares determined by the Company's board of directors no later than December 31 of the immediately preceding year. On January 1, 2022, the Company reserved an additional 12,266,917 shares of common stock for issuance under the 2021 Plan representing 5% of the total common shares outstanding as of December 31, 2021. Under the 2021 Plan, the Company may grant incentive stock options, non-statutory stock options, RSAs, RSUs, stock appreciation rights, performance awards and other stock-based awards. Terms of stock awards, including vesting requirements, are determined by the Company's board of directors or by a committee authorized by the Company's board of directors, subject to provisions of the 2021 Plan. The term of any stock option granted under the 2021 Plan cannot exceed ten years. Generally, awards granted by the Company vest over four years, but may be granted with different vesting terms. In conjunction with adopting the 2021 Plan, the Company discontinued the 2018 Plan with respect to new equity awards.

As of December 31, 2022, 20,264,523 shares were available for future issuance pursuant to the 2021 Plan.

2021 Employee Stock Purchase Plan

In June 2021, the Company adopted the 2021 Employee Stock Purchase Plan ("2021 ESPP"), which became effective immediately prior to the execution of the underwriting agreement related to the Company's IPO with an initial reserve of 2,470,000 shares. The 2021 ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their earnings, subject to plan limitations. Unless otherwise determined by the Company's board of directors, employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock on the first date of an offering or on the purchase date. The number of shares of the Company's common stock reserved for issuance under the 2021 ESPP automatically increases on January 1 of each year for a period of ten years, beginning on January 1, 2022 and continuing through January 1, 2031, by the lesser of (1) 1% of the total number of shares of the Company's common stock outstanding on December 31 of the immediately preceding year, and (2) 4,940,000 shares; provided, however, that the Company's board of directors may act to provide a lesser increase in number of shares. On January 1, 2022, the Company reserved an additional 2,453,383 common shares for issuance under the 2021 ESPP representing 1% of the total common shares outstanding as of December 31, 2021. The Company may specify offerings with durations not more than 27 months and may specify shorter purchase periods within each offering. Under the 2021 ESPP, 475,363 and zero shares have been issued for the years ended December 31, 2022 and 2021, respectively.

As of December 31, 2022, 4,448,020 shares were available for future issuance pursuant to the 2021 ESPP.

2018 Equity Incentive Plan

In 2018, the Company established the 2018 Plan that provided for the grant of incentive stock options, non-statutory stock options, RSAs, RSUs, stock appreciation rights and other stock-based awards. Terms of stock awards, including vesting requirements, were determined by the board of directors or by a committee authorized by the Company's board of directors, subject to provisions of the 2018 Plan. The term of any stock option granted under the 2018 Plan cannot exceed ten years. Generally, awards granted by the Company vest over four years, but could have been granted with different vesting terms. Pursuant to the terms of the 2021 Plan, any shares subject to outstanding options originally granted under the 2018 Plan that terminate, expire or lapse for any reason without the delivery of shares to the holder thereof become available for issuance pursuant to awards granted under the 2021 Plan. While no shares are available for future issuance under the 2018 Plan, it continues to govern outstanding equity awards granted thereunder.

Stock-based Compensation Expense

Stock-based compensation expense by classification included within the Consolidated Statements of Operations and Comprehensive Loss was as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Research and development	$ 16,721	$ 15,328	$ 14,977
General and administrative	65,203	46,873	18,284
Total stock-based compensation expense	$ 81,924	$ 62,201	$ 33,261

Stock-based compensation expense for the year ended December 31, 2021 included the impact of an award accelerated in connection with the Company's IPO of $2.6 million.

Stock Options and RSA Modifications

In December 2022, the Company's former chief executive officer ("CEO") resigned. Under the terms of the separation agreement, the former CEO will be available to provide consulting services to the Company through June 15, 2024, with vested options continuing to be exercisable and unvested options continuing to vest through that date. The Company concluded that the obligation to provide consulting services is nonsubstantive, and therefore resulted in a modification of their options due to the reduction of their service level. As their remaining service period was determined to be nonsubstantive, the entire incremental expense of $3.7 million associated with the modification was recognized in the fourth quarter of 2022.

In 2021, the Company had modifications due to the reduction in the service level for a previous CEO, who resigned as Executive Chairman in the fourth quarter of 2021, as well as an increase to certain awards' post-termination exercise periods. In 2020, the Company had modifications due to the reduction in the service level for a previous CEO,

changes in vesting schedules for certain individuals and increases to certain awards' post-termination exercise periods. The 2021 and 2020 modifications impacted both vested and unvested awards. Expense associated with vested awards is recognized in the period of the modification and expense associated with unvested awards is recognized over the remaining service life of the options or RSAs.

The following table shows the total incremental stock-based compensation expense associated with modifications by the year in which the modification occurred in the years December 31, 2022, 2021 and 2020 (in thousands):

	December 31,		
	2022	2021	2020
Previous CEO - Options[1]	$ 3,741	$ —	$ —
Previous CEO - Options[2]	—	21,948	15,052
Other - Options[3]	—	1,019	4,717
Previous CEO - RSA[4]	—	10,908	20,799
Other - RSA[5]	—	—	9,029
Total	$ 3,741	$ 33,875	$ 49,597

(1) The modification for Previous CEO - Options for 2022 is for Ms. Elizabeth Homans, who resigned in December 2022.
(2) The modifications for Previous CEO - Options for 2021 and 2020 is for Dr. Richard Klausner, who resigned as Executive Chairman in October 2021 and is now the Chair of Lyell's Board.
(3) The modifications for Other - Options are represented by one individual in 2021 and four individuals in 2020.
(4) The modifications for Previous CEO - RSAs for 2021 and 2020 are for Dr. Richard Klausner, who resigned as Executive Chairman in October 2021 and is now the Chair of Lyell's Board.
(5) The modifications for Other - RSAs are represented by three individuals in 2020.

At December 31, 2022, total stock-based compensation cost related to unvested awards not yet recognized was $98.5 million, which is expected to be recognized over a remaining weighted-average period of 2.86 years.

Restricted Stock Awards

A summary of the Company's RSA activity was as follows:

	Number of Shares	Weighted-Average Value at Grant Date Per Share
Unvested shares as of December 31, 2021	2,600,002	$ 0.0001
Vested	(2,600,002)	$ 0.0001
Unvested shares as of December 31, 2022	—	$ —

The fair value of RSAs vested during the years ended December 31, 2022, 2021 and 2020 was $15.2 million, $57.1 million and $29.4 million, respectively.

Restricted Stock Units

A summary of the Company's RSU activity was as follows:

	Number of Shares	Weighted-Average Value at Grant Date Per Share
Unvested RSUs as of December 31, 2021	0	$ —
RSUs granted	1,330,962	$ 5.98
RSUs vested	(223,200)	$ 5.98
RSUs forfeited or canceled	(235,685)	$ 5.98
Unvested RSUs as of December 31, 2022	872,077	$ 5.98

The fair value of RSUs vested during the year ended December 31, 2022 was $1.5 million. No RSUs vested during the years ended December 31, 2021 and 2020.

Stock Options

A summary of the Company's stock option activity was as follows:

	Number of Stock Options	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Options outstanding as of December 31, 2021	41,775,179	$ 5.05	7.84	$ 142,076
Granted	18,399,530	$ 4.89		
Exercised	(3,600,478)	$ 2.66		
Canceled or forfeited	(2,725,186)	$ 6.28		
Options outstanding as of December 31, 2022	53,849,045	$ 5.09	7.84	$ 24,887
Options exercisable as of December 31, 2022	28,115,416	$ 4.43	6.78	$ 23,462

The fair value of stock options granted to employees, directors and consultants was estimated on the date of grant using the Black-Scholes option pricing model using the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	2.93 %	0.80 %	0.79 %
Expected volatility	87.3 %	78.7 %	75.0 %
Expected term (in years)	6.03	6.10	6.11
Expected dividend yield	0 %	0 %	0 %

The weighted-average grant date fair value of options granted for the years ended December 31, 2022, 2021 and 2020 was $3.60 per share, $6.59 per share and $3.36 per share, respectively. The intrinsic value of options exercised during the years ended December 31, 2022, 2021 and 2020 was $13.9 million, $16.1 million and $0.3 million, respectively.

13. Income Taxes

The Company has reported pre-tax operating losses for all periods presented. The Company's net losses are derived solely from within the U.S. The Company has not reflected any benefit for corresponding tax net operating loss carryforwards in the accompanying consolidated financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

As of December 31, 2022 and 2021, the Company had U.S. federal net operating loss ("NOL") carryforwards of approximately $383.3 million and $271.0 million, respectively, which were available to reduce future taxable income and do not expire. The Company also had U.S. state NOL carryforwards of $372.5 million that begin to expire in 2038. The Company had gross U.S. federal and state tax credits of $15.8 million and $9.8 million as of December 31, 2022 and 2021,

respectively, which may be used to offset future tax liabilities. The federal NOL carryforward period is indefinite, while the tax credits will begin to expire in 2039. The attributed carryforwards may become subject to annual limitations in the event of certain cumulative changes in the ownership interest of significant stockholders. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities.

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows:

	Year Ended December 31,		
	2022	2021	2020
Federal statutory tax	21.00 %	21.00 %	21.00 %
State tax, net of federal benefit	5.10	6.39	4.71
Valuation allowance	(28.89)	(22.43)	(24.60)
Collaboration revenue	6.72	—	—
Stock-based compensation	(6.11)	(5.92)	(1.77)
Tax credits	2.33	0.99	0.95
Other	(0.15)	(0.03)	(0.29)
Effective income tax rate	0.00 %	0.00 %	0.00 %

The principal components of the Company's net deferred tax assets were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 106,530	$ 70,855
Tax credit carryforwards	14,317	8,338
Accrued liabilities and allowances	3,692	3,879
Deferred revenue	904	8,224
Amortization	4,585	15,961
Capitalized research and development	26,199	—
Investment basis difference	14,235	13,587
Lease liability	17,656	18,429
Stock-based compensation	7,471	2,872
Other	1,171	2,613
Gross deferred tax assets	196,760	144,758
Valuation allowance	(180,132)	(127,226)
Deferred tax assets, net of valuation allowance	16,628	17,532
Deferred tax liabilities:		
Operating lease right-of-use assets	(11,277)	(12,647)
Property and equipment	(5,351)	(4,885)
Deferred tax liabilities	(16,628)	(17,532)
Net deferred tax assets	$ —	$ —

The Tax Cuts and Jobs Act contained a provision that requires the capitalization of Section 174 costs incurred in years beginning on or after January 1, 2022. Section 174 costs are expenditures that represent research and development costs that are incident to the development or improvement of a product, process, formula, invention, computer software or technique. This provision changes the treatment of Section 174 costs such that the expenditures are no longer allowed as an immediate deduction but rather must be capitalized and amortized over five years for domestic research and development and fifteen years for foreign research and development. The Company has included the impact of this provision, which results in a deferred tax asset of approximately $26.2 million as of December 31, 2022.

The Company maintains a full valuation allowance on its net U.S. deferred tax assets. The assessment regarding whether a valuation allowance is required considers the evaluation of both positive and negative evidence when concluding

whether it is more likely than not that deferred tax assets are realizable. In making this assessment, significant weight is given to evidence that can be objectively verified. In its evaluation, the Company considered its cumulative loss in recent years and its forecasted losses in the near-term as significant negative evidence. Based upon a review of the four sources of income identified within ASC 740, *Accounting for Income Taxes* ("ASC 740"), the Company determined that the negative evidence outweighed the positive evidence and a full valuation allowance on its U.S. net deferred tax assets will be maintained. The valuation allowance relates primarily to net U.S. deferred tax assets from net operating loss carryforwards, research and development tax credit carryforwards, research and development expenses capitalized and amortized for tax but deducted for GAAP and stock-based compensation.

The Company will continue to assess the realizability of its deferred tax assets and adjust the valuation allowance as required by ASC 740. The increase in the valuation allowance was $52.9 million and $56.1 million for the years ended December 31, 2022 and 2021, respectively.

The Company evaluates its uncertain tax positions based on a determination of whether it is more likely than not such position will be sustained based upon its technical merits and upon examination by the relevant income tax authorities with all facts known. The Company applies judgment in its measurement of an uncertain tax position recorded in its consolidated financial statements and tax return. As of December 31, 2022 and 2021, there are no penalties or accrued interest recorded in the consolidated financial statements.

The Company is generally subject to examination by the U.S. federal and local income tax authorities for all tax years in which a loss carryforward is available. The Company is currently not under examination by the Internal Revenue Service or other jurisdictions for any tax years.

The following table summarized changes to the Company's unrecognized tax benefits (in thousands):

	Year Ended December 31,	
	2022	2021
Beginning balance	$ 796	$ —
Additions based on tax position related to the current year	—	396
Adjustments based on prior year tax positions	(396)	400
Ending balance	$ 400	$ 796

14. Net Loss Per Share

Basic and diluted net loss per share attributed to common stockholders is calculated by dividing net loss attributed to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. The Company's potentially dilutive shares, which include preferred stock, unvested RSAs, unvested RSUs and options to purchase common stock, are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive. Shares subject to options to purchase common stock, preferred stock, unvested RSAs and unvested RSUs were all excluded from consideration in the calculation of diluted net loss per share in all periods presented due to their anti-dilutive effects.

15. Employee Benefit Plan

In January 2019, the Company adopted a 401(k) retirement and savings plan (the "401(k) Plan") covering all of its employees. The 401(k) Plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the IRS. Beginning in 2022, the Company sponsors a defined-contribution savings plan with matching 401(k) contributions based upon the amount of the employees' contributions subject to certain limitations. The Company made matching contributions to the 401(k) Plan on behalf of participants of $1.0 million for the year ended December 31, 2022 and none for the years ended December 31, 2021 and 2020.

16. Commitments and Contingencies

Collaboration and License Agreements

The Company has entered into certain collaboration and license agreements, including those identified in Note 3, *License, Collaboration and Success Payment Agreements* above, with third parties that include the funding of certain development, manufacturing and commercialization efforts with the potential for future milestone and royalty payments

upon the achievement of pre-established developmental, regulatory and/or commercial milestones. The Company's obligation to fund these efforts is contingent upon continued involvement in the programs and/or the lack of any adverse events that could cause the discontinuance of the programs, including termination of such agreements. Due to the nature of these agreements, the future potential payments are inherently uncertain, and accordingly no amounts had been recorded for the potential future achievement of these targets as of December 31, 2022 and 2021.

17. Related-Party Transactions

In September 2021, the Company entered into a sublease with Sonoma, with whom the Company has common stockholders with board seats, whereby the Company agreed to sublease approximately 18,000 square feet of space in South San Francisco, California currently leased by the Company. Dr. Klausner, the Chair of the Company's board of directors, also serves as a member of the board of directors of Sonoma. As a part of the sublease, a $4.6 million tenant improvement contribution payment was made by Sonoma, which is recognized over the term of the sublease. As of December 31, 2022 and 2021, there were accrued liabilities and other current liabilities of $0.5 million and $0.5 million, respectively, and other non-current liabilities of $3.5 million and $4.0 million, respectively, in connection with the sublease with Sonoma. Income of $2.6 million and $1.8 million was recognized in other operating income, net for the years ended December 31, 2022 and 2021, respectively, of which $1.9 million and $0.6 million was attributed to sublease income for the years ended December 31, 2022 and 2021, respectively. See Note 9, *Leases*, for more detail on the Sonoma sublease.

The Company was party to the GSK Agreement, who is a holder of more than 10% of the Company's outstanding common stock. See Note 3, *License, Collaboration, and Success Payment Agreements*. Deferred revenue of zero and $5.0 million as of December 31, 2022 and 2021, respectively, and deferred revenue, non-current of zero and $79.7 million as of December 31, 2022 and 2021, respectively, were in connection with the GSK Agreement. Revenue recognized in connection with the GSK agreement was $84.7 million, $10.5 million and $7.8 million for the years ended December 31, 2022, 2021 and 2020, respectively. GSK terminated the GSK Agreement effective December 24, 2022. See Note 3, *License, Collaboration, and Success Payment Agreements,* for additional details regarding the termination of the GSK Agreement.

In March 2020, the Company repurchased 546,806 shares of its Series A convertible preferred stock and 2,032,166 shares of its common stock from a related party. See Note 10, *Convertible Preferred Stock* and Note 11, *Stockholders' Equity*.

18. Asset Acquisition

In May 2020, the Company completed the acquisition of 100% of the outstanding equity of Immulus, Inc. ("Immulus"), a company focused on developing technology platforms that enable the development and production of cell therapeutics. As consideration for the acquisition, the Company paid $3.5 million in cash and issued an aggregate of 688,463 shares of its common stock, with an estimated fair value of $4.0 million. The Company also incurred $0.5 million of direct expenses, for total consideration of $8.0 million.

The Company concluded the acquisition did not meet the accounting definition of a business as inputs were acquired, but no processes or outputs were acquired. Consequently, the Company accounted for the transaction as an asset acquisition with the value concentrated in IPR&D. The following table summarizes the fair value of assets acquired (in thousands):

Other assets	$	487
In-process research and development (IPR&D)		7,528
Total assets acquired	$	8,015

The amount allocated to the IPR&D asset was charged to research and development expenses for the year ended December 31, 2020 as this asset had no alternative future use at the time of the acquisition transaction.

In addition, the Company is also required to make milestone payments of up to $37.0 million to the former stockholders of Immulus upon successful completion of specified development milestones. Triggering of these milestones payments was not considered probable as of the date of the acquisition, and no expense has been recorded for these milestones for the years ended December 31, 2022, 2021 and 2020.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

As of December 31, 2022, management, with the participation and supervision of our Chief Executive Officer and Chief Financial Officer, have evaluated our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2022, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Inherent Limitations on Controls and Procedures

Our management, including the principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures and our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well designed and operated, can only provide reasonable assurances that the objectives of the control system are met. The design of a control system reflects resource constraints; the benefits of controls must be considered relative to their costs. Because there are inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, for our company have been or will be detected. As these inherent limitations are known features of the disclosure and financial reporting processes, it is possible to design into the processes safeguards to reduce, though not eliminate, these risks. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns occur because of simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls is based in part upon certain assumptions about the likelihood of future events. While our disclosure controls and procedures and our internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives, there can be no assurance that any design will succeed in achieving its stated goals under all future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining an adequate internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) for our company. Our management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework set forth in "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on an evaluation under that framework, our management concluded that our internal control over financial reporting was effective at the reasonable assurance level as of December 31, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report in Part II, Item 8 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Lyell Immunopharma, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Lyell Immunopharma, Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Lyell Immunopharma, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholder's equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes and our report dated February 28, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Mateo, California

February 28, 2023

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022.

Our Code of Business Conduct and Ethics applies to all of our employees, officers and directors. This includes our principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The full text of our Code of Business Conduct and Ethics may be viewed at the investors relations portion of our website at https://ir.lyell.com, in the section entitled "Governance Highlights" under "Corporate Governance." We intend to satisfy the disclosure requirements under Item 5.05 of the SEC Form 8-K regarding an amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics by posting such information on our website at the website address and location specified above.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2022.

PART IV

Item 15. Exhibit and Financial Statement Schedules

(a) The following documents are being filed as part of this report:

(1) The following financial statements and the Report of Independent Registered Public Accounting Firm are included in Part II, Item 8:

(2) All financial statement schedules are omitted because the information is inapplicable or presented in the Notes to Consolidated Financial Statements.

(3) The following Exhibits are filed as part of this report.

		Incorporation by Reference				
Exhibit Number	Exhibit Description	Form	File Number	Exhibit/ Appendix Reference	Filing Date	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation.	S-8	333-257249	4.1	6/21/2021	
3.2	Amended and Restated Bylaws.	S-8	333-257249	4.2	6/21/2021	
4.1	Form of Common Stock Certificate.	S-1/A	333-256470	4.1	6/9/2021	
4.2	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated March 5, 2020.	S-1	333-256470	4.2	5/25/2021	
4.3	Description of Securities					X
10.1	Lyell Immunopharma, Inc. 2018 Equity Incentive Plan, as amended.	S-1	333-256470	10.1	5/25/2021	
10.2	Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise and Restricted Stock Award Agreement under the Lyell Immunopharma, Inc. 2018 Equity Incentive Plan.	S-1	333-256470	10.2	5/25/2021	
10.3	Lyell Immunopharma, Inc. 2021 Equity Incentive Plan.	S-1/A	333-256470	10.3	6/9/2021	
10.4	Forms of Stock Option Grant Notice, Stock Option Agreement and Notice of Exercise under the Lyell Immunopharma, Inc. 2021 Equity Incentive Plan.	S-1/A	333-256470	10.4	6/9/2021	
10.5	Forms of Restricted Stock Unit Grant Notice and Award Agreement under the Lyell Immunopharma, Inc. 2021 Equity Incentive	S-1/A	333-256470	10.5	6/9/2021	
10.6	Lyell Immunopharma, Inc. 2021 Employee Stock Purchase Plan.	S-1/A	333-256470	10.6	6/9/2021	
10.7	Lyell Immunopharma, Inc. 2021 Non-Employee Director Compensation Policy.	S-1/A	333-256470	10.7	6/9/2021	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.8	Lyell Immunopharma, Inc. Officer Severance Plan.	10-K	001-40502	10.8	3/29/2022	
10.9	Form of Indemnification Agreement by and between the Registrant and its directors and executive officers.	S-1	333-256470	10.9	5/25/2021	
10.10	Amended Offer Letter by and between the Registrant and Richard Klausner, dated July 23, 2020.	S-1	333-256470	10.10	5/25/2021	
10.11	Offer Letter, by and between the Registrant and Lynn Seely, dated December 14, 2022	8-K	001-40502	10.2	12/16/2022	
10.12	Offer Letter by and between the Registrant and Charles Newton, dated February 3, 2021.	S-1	333-256470	10.12	5/25/2021	
10.13	Offer Letter by and between the Registrant and Rahsaan W. Thompson, dated September 12, 2022.	10-Q	001-40502	10.2	11/8/2022	
10.14	Offer Letter by and between the Registrant and Stephen Hill, dated May 9, 2019.	S-1	333-256470	10.14	5/25/2021	
10.15	Severance Waiver by and between the Registrant and Stephen Hill, dated April 19, 2022.	10-Q	001-40502	10.1	5/10/2022	
10.16	Separation, Transition and General Release Agreement, by and between Elizabeth Homans and Lyell Immunopharma, Inc., dated December 15, 2022	8-K	001-40502	10.1	12/16/2022	
10.17	License Agreement by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated January 29, 2019.	S-1	333-256470	10.16	5/25/2021	
10.18	Success Payment Agreement, by and between the Registrant and The Board of Trustees of the Leland Stanford Junior University, dated October 1, 2020.	S-1	333-256470	10.17	5/25/2021	
10.19	Success Payment Agreement, by and between the Registrant and Fred Hutchinson Cancer Research Center, dated December 19, 2018.	S-1	333-256470	10.18	5/25/2021	
10.20	Standard Office Lease for Building C by and between the Registrant and Bre Wa Office Owner LLC, dated August 28, 2019.	S-1	333-256470	10.19	5/25/2021	
10.21	Standard Office Lease for Building E by and between the Registrant and Bre Wa Office Owner LLC, dated August 28, 2019.	S-1	333-256470	10.20	5/25/2021	
10.22	Lease by and between the Registrant and BMR-500 Fairview Avenue LLC, dated November 27, 2018, as amended.	S-1	333-256470	10.21	5/25/2021	
10.23	Lease Agreement by and between the Registrant and ARE-San Francisco No. 65, LLC, dated August 15, 2019, as amended.	S-1	333-256470	10.22	5/25/2021	
23.1	Consent of independent registered public accounting firm.					X

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
24.1	Power of Attorney (included on signature page).					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a).					X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a).					X
32.1	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350.					X
101.INS	XBRL Instance Document.	The XBRL instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document.					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.					X
104	Cover Page Interactive Data File.	Formatted as Inline XBRL and contained in Exhibit 101.				

*Portions of this exhibit (indicated by [*]) have been omitted because the registrant has determined that the information is both not material and is the type that the registrant treats as private or confidential.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Act of 1934, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California on February 28, 2023.

LYELL IMMUNOPHARMA, INC.

By: /s/ LYNN SEELY
Name: **Lynn Seely, M.D.**
Title: President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Lynn Seely, Charles Newton and Rahsaan Thompson, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1934, this Annual Report on Form 10-K has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ LYNN SEELY **Lynn Seely, M.D.**	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 28, 2023
/s/ CHARLES NEWTON **Charles Newton**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 28, 2023
/s/ RICHARD D. KLAUSNER **Richard D. Klausner, M.D.**	Chair of the Board of Directors	February 28, 2023
/s/ HANS BISHOP **Hans Bishop**	Director	February 28, 2023
/s/ OTIS BRAWLEY **Otis Brawley, M.D.**	Director	February 28, 2023
/s/ CATHERINE FRIEDMAN **Catherine Friedman**	Director	February 28, 2023
/s/ ELIZABETH NABEL **Elizabeth Nabel, M.D.**	Director	February 28, 2023
/s/ ROBERT NELSEN **Robert Nelsen**	Director	February 28, 2023
/s/ WILLIAM RIEFLIN **William Rieflin**	Director	February 28, 2023

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